Literature Seminar 16/6/2009 K. Majima

Nucleophilic Organocatalyst ~ Phosphine Catalyst ~

Basicity and nucleophilicity of Phosphines

○ The order of basicity (J. Am. Chem. Soc. 1960, 82, 5791)

$(\bigcirc)_3P$ > Et_3P > Me_3P > $EtPMe_2$ ≈ Et_2PMe > Bu_3P > $i\text{-}Bu_3P$ ≫ PPh_3

pKa 9.70 8.69 8.65 8.62 8.62 8.33 7.97 2.73 (in nitromethane)

The basicity of tertiary phosphine is largely determined by the inductive effect.

○ The order of nucleophilicity (J. Am. Chem. Soc, 1960, 82, 5794) against EtI

$EtPMe_2$ > Et_2PMe > Me_3P > $(\bigcirc)_3P$ > Bu_3P > Et_3P ≫ iBu_3P ≈ PPh_3

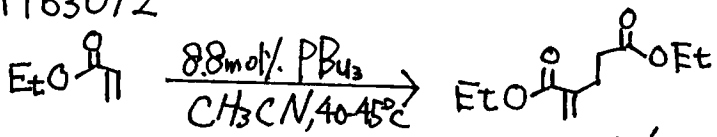
Phosphine containing methyl group increase the nucleophilicity of phosphine. Size effect and hybridization effect.

Other tertiary phosphines give same tendency with the basicity.

$(i\text{-}C_4H_9)_3P$ is highly sterically crowded, so that one of methyl group is compelled at all time effectively cover the electron pair.

early examples

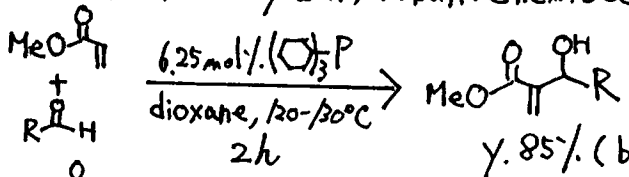
1) Rauhult, M.M.; Currier, H. U.S. Patent, American Cyanamide Co., 1963, 3074999 19630/2



y. 46% (31% recovery of SM)

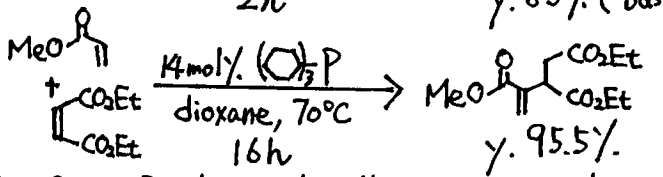
Dimerization of acrylates. Phosphine catalyzed Michael reaction.

2) Morita, K.; Suzuki, Z.; Hirose, H. Bull. Chem. Soc. Jpn. 1968, 41, 2815.
Morita, K.; Kobayashi, T. Bull. Chem. Soc. Jpn. 1969, 42, 2732.



y. 85% (based on recovery of SM)

First example of Morita-Baylis-Hillman reaction.



y. 95.5%

In 1972, Baylis and Hillman reported same reaction using tertiary amine (eg. DABCO, quinuclidine) as a nucleoplic catalyst. (Baylis, A.B.; Hillman, M.E.D. German Patent 2155113, 1972.)

Contents

1. Reactions of yne-carbonyl compounds. (Isomerization, α, β, γ-addition, [3+2], [4+2])
2. Intrmolecular reactions of enone. (Intramolecular MBH reaction, Intramolecular Rauhult-Currier reaction)
3. Catalytic reactions of ylide.

1. Reaction of yne-carbonyl compounds

J. Am. Chem. Soc. **1992**, *114*, 7933-7935

Internal Redox Catalyzed by Triphenylphosphine

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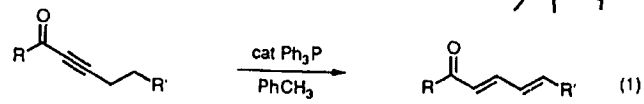
Stanford, California 94305-5080

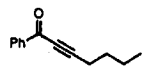
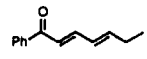
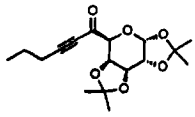
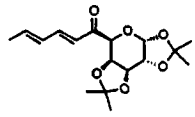
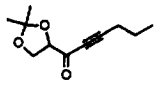
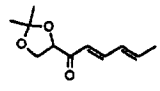
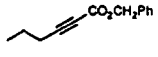
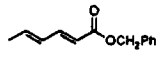
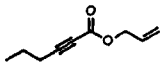
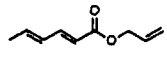
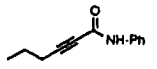
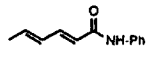
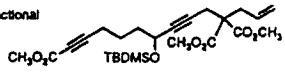
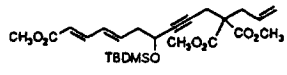
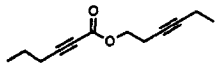
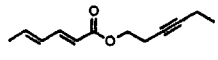
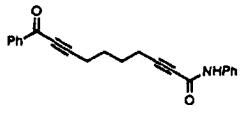
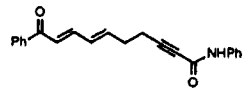
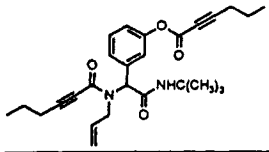
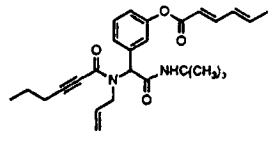
Received April 20, 1992

First report of yne-carbony isomerization cat. by phophine



(1)

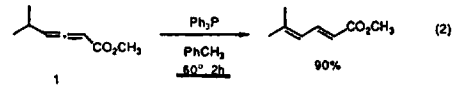
Table I. Isomerization of Yne–Carbonyl to Diene–Carbonyl[a]

Entry	Substrate	Temp/Time(h)	Product[a]	Isolated Yield
A. Ketones				
1		80°/4		83%
2		110°/16		83%
3		110°/2		88%
B. Ester				
4[b]		110°/6		75%
5[b]		110°/14		83%
C. Amide				
6[b,c]		140°/14		84%
D. Polyfunctional				
7[b]		110°/14		69%
8[b,c]		60°/5		79%
9		110°/14		82%
10[d]		100°		71%

[a] All reactions were performed at 0.5–1 M in toluene with 10–40 mol % Ph_3P. [b] 50 mol % of acetic acid added. [c] Reaction performed in xylene. [d] Reaction performed in C_6D_6 at 100 °C. [e] All new compounds have been satisfactorily characterized. [f] See ref 5.

reactivity order
ketone > ester > amide

For ester, amide, addition of AcOH was needed.



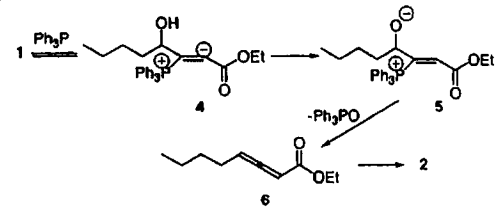
(2)

Allene would be intermediate.
cat. phosphite - No reaction
cat. HMPA or Bu_3P - oligomer formation.
cat. amine - No reaction.
Nucleophilic phosphine catalyst.

- J. Chem. Soc., Chem. Commun. 1993, 394. Stoichiometric amount.
- J. Chem. Soc., Perkin Trans 1 1993, 1921 Cat. amount of phosphine.

Proposed reaction mechanism

Scheme 5



reaction mixture -- absorption at 1965 cm^{-1}
↓
existence of allene.

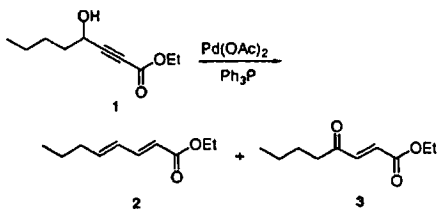
reaction proceeded at room temp.

A Novel Deoxygenation–Isomerization Reaction of 4-Hydroxy-2-ynoic Esters and γ-Hydroxy-α,β-ynones

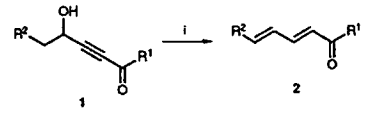
Cheng Guo and Xiyan Lu*

Shanghai Institute of Organic Chemistry, Academia Sinica, 345 Lingling Lu, Shanghai 200032, China

Scheme 4



$Pd(OAc)_2$ (mol%)	Ph_3P (mol%)	2 (%)	3 (%)
2.5	35	33	10
2.5	55	52	11
2.5	100	88	0
0	100	88	0



Yield 2 (%)

a; R^1 = OEt, R^2 = Et 85
b; R^1 = OEt, R^2 = Pr^n 86
c; R^1 = Bu^n, R^2 = Pr^n 83
d; R^1 = n-C_5H_{11}, R^2 = Et 86

Scheme 2 *Reagents and conditions*: i, Ph_3P (1 equiv.), benzene, room temp., 8 h

without $Pd(OAc)_2$, reaction proceeded.

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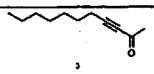
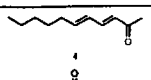
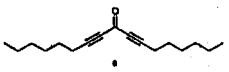
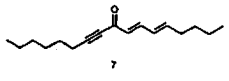
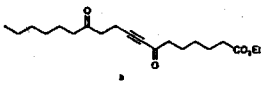
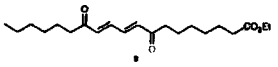
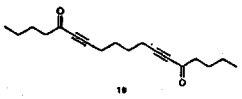
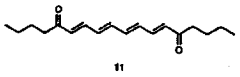
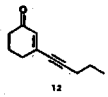
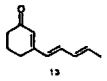
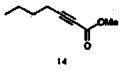
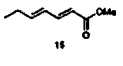
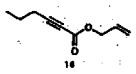
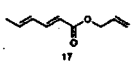
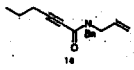
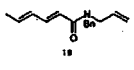
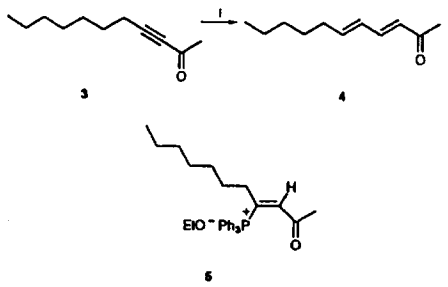
Reinvestigation on the Catalytic Isomerisation of Carbon–Carbon Triple Bonds

Cheng Guo and Xiyan Lu*
Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Lu, Shanghai 200032, China

Table 1 Isomerisation of yne-carbonyl Compounds[a]

Entry	Substrate	R_3P (mol %)	Temp (T/°C)/Time (t/h)	Product	Isolated yield (%)
1		Ph_3P (10)	25/34		84
2		Ph_3P (10)	25/47		89
3		Ph_3P (10)	25/47		86
4		Ph_3P (20)	25/46		83
5		Ph_3P (100)	110/35		0[b]
6	12	Bu_3P (20)	110/30	13	89
7		Ph_3P (100)	25/35		0[b]
8	14	Bu_3P (20)	110/24	15	82
9		Bu_3P (20)	25/48		80
10		Bu_3P (20)	110/24		60

[a] All reactions were performed as described in the Experimental section. [b] Starting material was recovered.

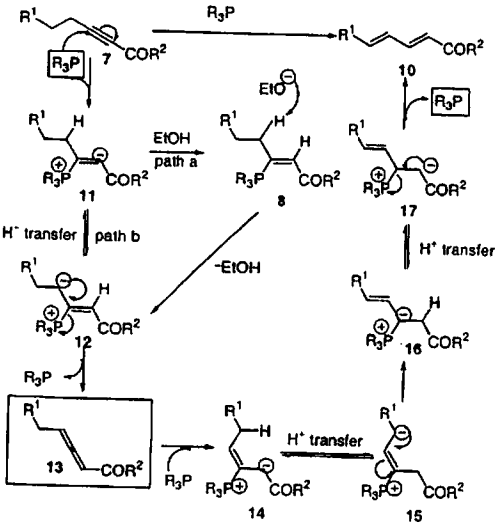


Scheme 2 *Reagents, conditions and yields:* i, Ph_3P (100 mol%), EtOH (100 mol%), benzene, reflux, 35 h, 72%

reactivity order
ketone > ester > amide

For less reactive substrate more nucleophilic Bu_3P gave good result.

Scheme 8

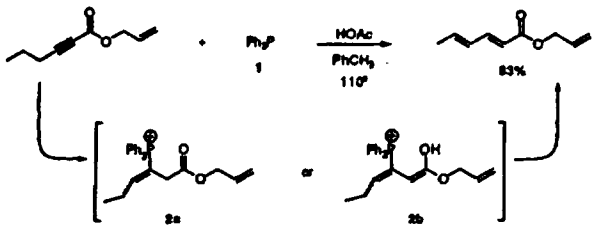


δ-addition of yne-carbonyl
i) carbon nucleophile

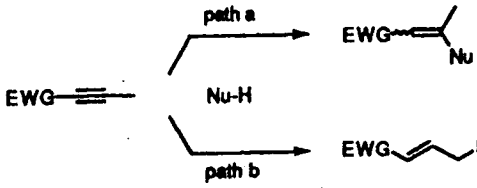
J. Am. Chem. Soc. **1994**, *116*, 3167–3168

Novel "Umpolung" in C–C Bond Formation Catalyzed by Triphenylphosphine

Barry M. Trost* and Chao-Jun Li



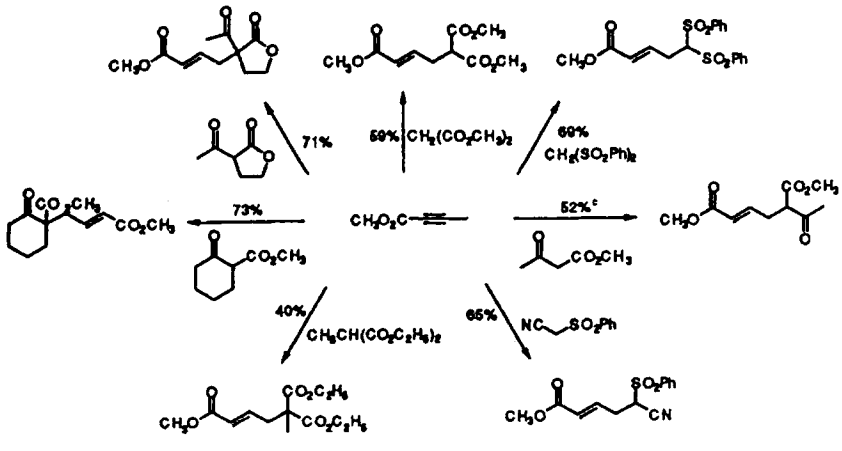
- Only E olefins were observed.
- Pronucleophiles for which pKa < 16 serve satisfactory



(1)

path a : Michael reaction, β-addition
path b : δ-addition

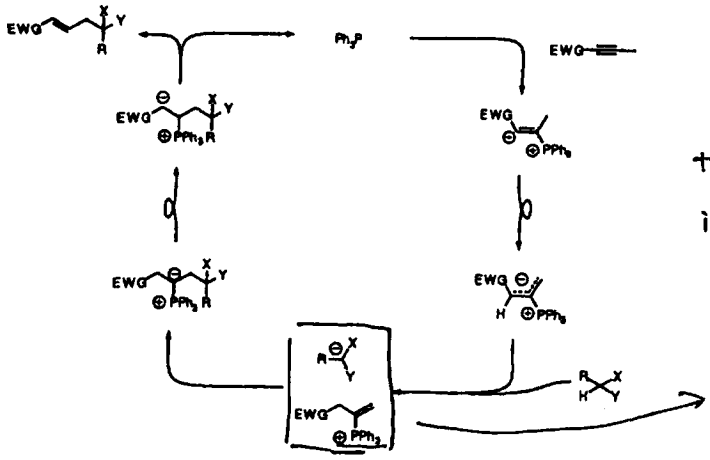
Scheme 1. γ-Addition to an Ynoate by Pronucleophiles[a,b]



[a] All reactions were run using 35 mol % of triphenylphosphine, 50 mol % of acetic acid, and 50 mol % of sodium acetate in toluene at 80 or 110 °C unless otherwise noted. [b] For all new products, see ref 5. [c] In this case, 1 equiv of sodium acetate was employed.

3/16

Scheme 2. Rationale for Nucleophilic γ-Addition to Acetylenes Bearing Electron-Withdrawing Groups



Aliphatic phosphine .. too nucleophilic and led only to uncharacterized oligomer formation.

the role of triphenylphosphine is proposed as a nucleophilic trigger

Formation of zwitterion intermediate.

June 1995

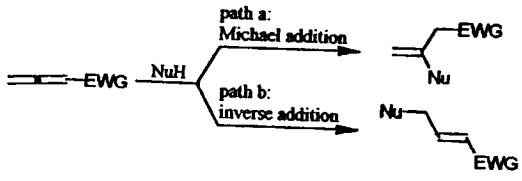
Umpolung Addition Reaction of Nucleophiles to 2,3-Butadienoates Catalyzed by a Phosphine

Chunming Zhang and Xiyan Lu*

Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China

Fax: 86-21-4166128

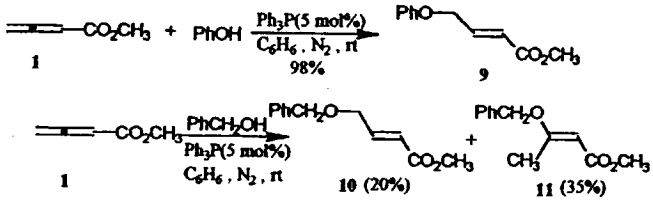
Received 17 April 1995

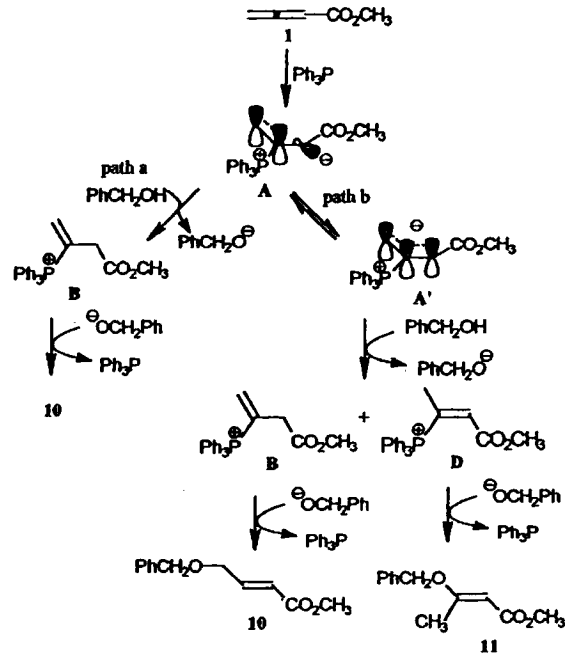


Scheme 1

Allenoate was used as a substrate.

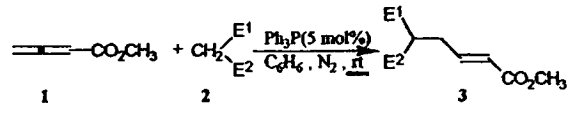
Higher reactivity was obtained than using γ-carbonyl as a substrate.





Scheme 3

Table1. The inverse addition of carbon nucleophiles to methyl 2,3-butadienoate.[a]

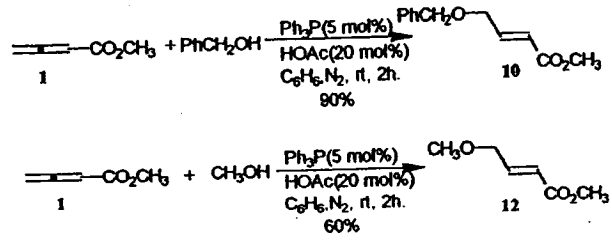


Entry	2	Time (h)	Product 3	Yield (%)[b]	E/Z[c]
1	2a: E^1=E^2=CO_2CH_3	5	3a	65	>97/3
2	2b: E^1=E^2=$COCH_3$	5	3b	65	>97/3
3	2c: E^1=CN, E^2=SO_2Ph	5	3c	87	>97/3
4	2d: E^1=$COCH_3$, E^2=CO_2CH_3	5	3d	65	44:56
5[d]	2d	1	3d	56	>97/3

a. Reactions are normally carried out with 1 (1.0 mmol), 2 (1.0 mmol) and Ph_3P (0.05 mmol) in benzene (5 mL) at rt under N_2. b. Isolated yield. c. Determined by 300 MHz ^1H NMR. d. The reaction is carried out with Ph_3P (0.05 mmol), HOAc (0.5 mmol) and NaOAc (1.0 mmol) in benzene at 80°C.

For oxygen pronucleophile, addition of acetic acid was need for regio-selectivity.

Lower acidity of benzylalcohol made the reaction sequence to both b.(A→A')



4/16

ii) oxgen nucleophile

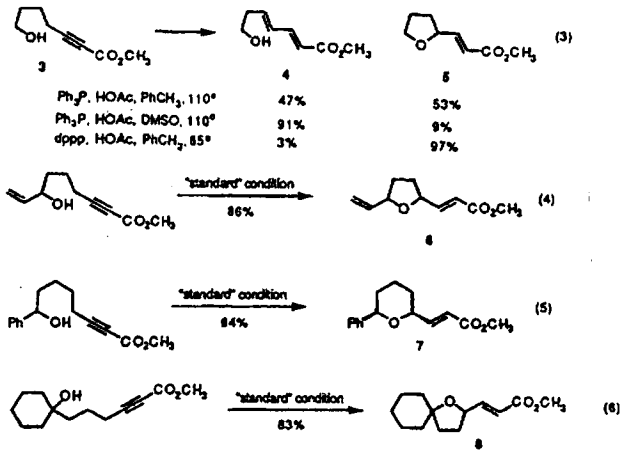
J. Am. Chem. Soc. **1994**, *116*, 10819−10820

Phosphine-Catalyzed Isomerization−Addition of Oxygen Nucleophiles to 2-Alkynoates

Barry M. Trost* and Chao-Jun Li

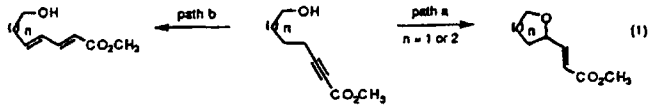
Department of Chemistry, Stanford University
Stanford, California 94305-5080

Received June 27, 1994



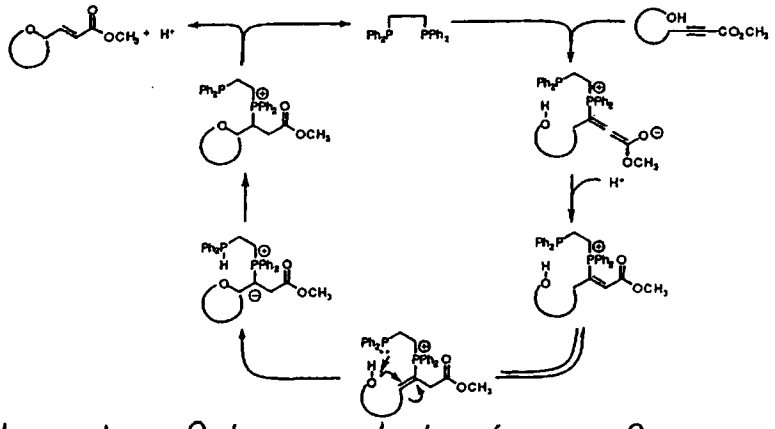
Primary, Secondry and tertiary alcohol could be used as a pronucleophile.

Intramolecular β-addition of oxgen pronucleophile.



Standard condition of C-pronucleophile -- 1:1 mixter
More polar DMSO -- path b was favored.
Using a bidentate ligand -- path a was dominant.

Scheme 1. Mechanistic Rationale for Phosphine-Catalyzed Internal Redox



the ability of the second phosphine to function as a general base catalyst made β-addition possible.

iii) nitrogen pronucleophile

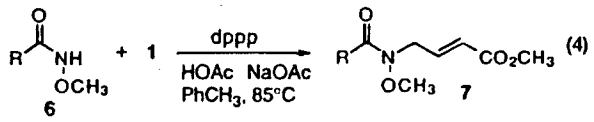
J. Org. Chem. **1997**, *62*, 5670−5671

Nitrogen Pronucleophiles in the Phosphine-Catalyzed γ-Addition Reaction

Barry M. Trost* and Gregory R. Dake

Department of Chemistry, Stanford University,
Stanford, California 94305-5080

Received May 13, 1997



R = a) $^nCH_3CH_2CH_2CH_2$, 60% b) $(CH_3)_2CH$, 33%

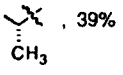
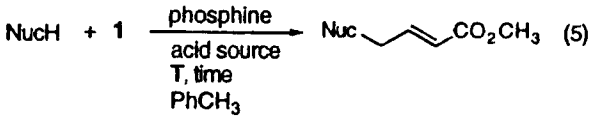
c)  , 39%

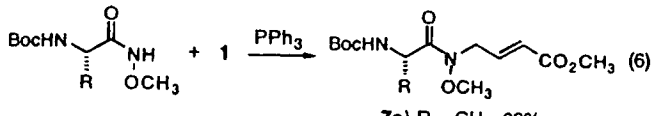
Table 1

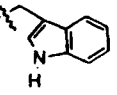


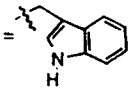
entry	NucH	phosphine[a]	acid source[b]	T (°C)	t (h)	% yield
1	6b	10% dppp	HOAc−NaOAc	90	5.5	35
2	6b	15% dppp	HOAc−NaOAc	90	2	33
3	6b	20% dppp	HOAc−NaOAc	90	2	42
4	6b	10% PPh_3	HOAc−NaOAc	85	3.5	21
5	6b	10% PPh_3	HOAc−NaOAc	110	10	61
6	6c	10% dppp	HOAc−NaOAc	85	18	39
7	6c	10% dppp	PhOH	85	18	25
8	6c	10% dppp	PhOH−NaOPh	85	18	14
9	6c	10% dppp	HOAc−TMG	85	18	–
10	6c	10% dppba	HOAc−NaOAc	85	18	–
11	6c	10% PPh_3	HOAc−NaOAc	110	18	68

[a] dppba = 2-(diphenylphosphino)benzoic acid. [b] 50 mol % each was used for each reagant. TMG = tetramethylguanidine.

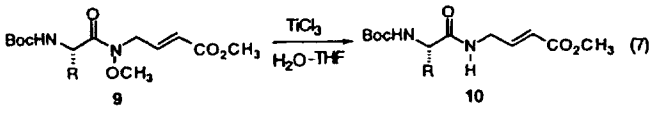
No Michael reaction was observed.



6c) R = CH_3
8a) R = $CH(CH_3)_2$
8b) R = 
8c) R = $CH_2CH_2SCH_3$

7c) R = CH_3, 68%
9a) R = $CH(CH_3)_2$, 67%
9b) R =  , 76%
9c) R = $CH_2CH_2SCH_3$, 72%

Higher temperature and triphenylphosphine gave best result.



a) R = $CH(CH_3)_2$, 80% c) R = $CH_2CH_2SCH_3$, 88%

Conversion to amino acid derivatives.

5/16

α-Addition

J. Am. Chem. Soc. **1997**, *119*, 7595–7596

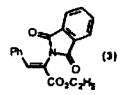
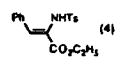
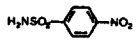
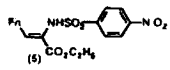
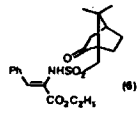
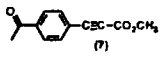
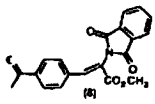
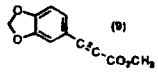
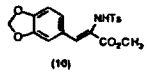
Nucleophilic α-Addition to Alkynoates. A Synthesis of Dehydroamino Acids

Barry M. Trost* and Gregory R. Dake

Department of Chemistry, Stanford University
Stanford, California 94305

Received April 18, 1997

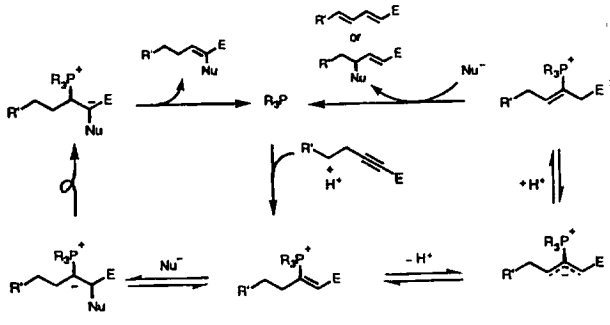
Table 1. α-Addition of Nitrogen Nucleophiles to Conjugated Alkynoates[a]

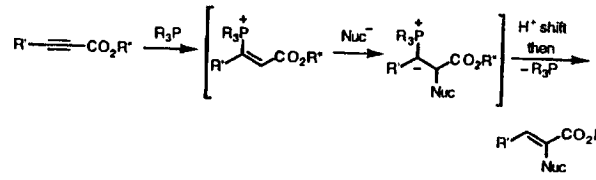
Entry	Alkynoate	Nucleophile	Time (h)	Product	Isolated Yield
1	$HC{\equiv}CCO_2C_2H_5$		18	 (1)	95%
2	$PhC{\equiv}CCO_2C_2H_5$		18	 (3)	82%
3	$PhC{\equiv}CCO_2C_2H_5$	H_2NTs	18	 (4)	82%
4	$PhC{\equiv}CCO_2C_2H_5$		5	 (5)	57%
5	$PhC{\equiv}CCO_2C_2H_5$		18	 (6)	66%
6	 (7)		18	 (8)	66%
7	 (9)	H_2NTs	18	 (10)	56%

[a] All reactions were run in $PhCH_3$ at 105 °C with 10 mol % Ph_3P, 50 mol % HOAc, and 50 mol % NaOAc.

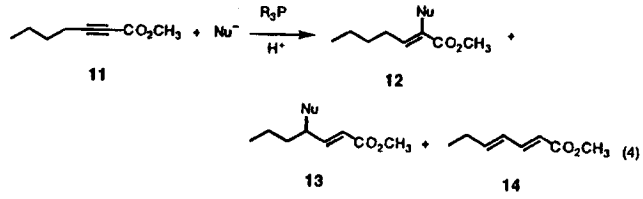
Olefin geometry is all Z-isomer
Thermodynamically stable

Scheme 1. Competitive Pathways in Phosphine-Catalyzed Nucleophilic Addition





α-addition of nitrogen pronucleophile.
Alkynoates which have aryl and H at β-position gave α-adduct.
Same conditions as β-addition of nitrogen pronucleophile.



11 : several possibility.
α-addition 12.
β-addition 13.
redox isomerization 14.

Table 2. Reactions of Methyl 2-Heptynoate[a]

Entry	Nucleophile	Phosphine	Co-Catalyst	% 12	% 13	% 14	Yield
1	$TsNH_2$	Ph_3P	HOAc/NaOAc	12%	—	88%	92%
2	$TsNH_2$	DPPBA	—	—	—	—	0%
3	$TsNH_2$	$(i\text{-}C_3H_7O)_3P$	HOAc/NaOAc	—	—	—	0%
4	$TsNH_2$	dppp	HOAc	100%	—	—	45%
5	$TsNH_2$	dppp	HOAc/NaOAc	76%	—	24%	82%
6		dppp	HOAc/NaOAc	—	—	100%	70%
7		dppp	PhOH	45%	—	55%	73%
8		dppp	PhOH	87%	13%	—	67%

[a] All reactions were performed in toluene at 105 °C.

Bidentate phosphine gave the α-adduct.
Phenol gave α-product mainly.
To maintain the homogeneous solution.

By only changing base (PBu_3 for β-addition vs dppp for α-addition) regioselectivity is changed.

6/16

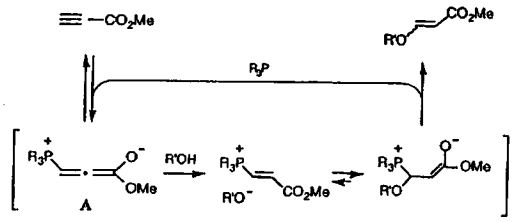
β - addition

CHEMISTRY LETTERS, pp. 241-244, 1993.

Michael addition of oxgen pronucleophile.

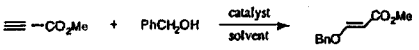
Organic Synthesis with Trialkylphosphine Catalysts. Conjugate Addition of Alcohols to α,β-Unsaturated Alkynic Acid Esters

Junji INANAGA,* Yoshiyasu BABA, and Takeshi HANAMOTO
Institute for Molecular Science, Myodaiji, Okazaki 444



Scheme 1.

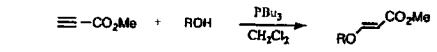
Table 1. Examination of Catalysts and Solvents [a]



Entry	Catalyst [b]	Solvent	Time	Yield [c] /%	E / Z [c]
1	PPh_3	PhH	8 h	86	3 / 1
2	PPh_3	CH_2Cl_2	8 h	85	5 / 1
3	PPh_3	THF	8 h	62	3 / 1
4	PPh_3	CH_3CN	8 h	>98	5 / 1
5	PBu_3	PhH	10 min	83	E
6	PBu_3	CH_2Cl_2	10 min	>98	E
7	PBu_3	THF	10 min	>98	E
8	PBu_3	CH_3CN	10 min	>98	99 / 1
9	$P(c\text{-Hex})_3$	CH_3CN	2 h	66	7 / 1
10	$P(OMe)_3$	CH_3CN	8 h	N.R.	

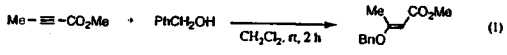
a) The reactions were performed at room temperature. b) The catalyst (0.1 equiv.) was used. c) Determined by ^1H NMR (400 MHz) analysis.

Table 2. PBu_3-Catalyzed Conjugate Addition of Alcohols to Methyl Propiolate [a]



Entry	ROH	Time / min	Yield [b] /%	E / Z [c]
1		10	>98	11 / 1
2		3	91	E
3		5	90	E
4		5	>98	E
5 [d]		10	96	E
6 [d]		10	95	E
7		30	14	E
8		10	53	E
9		10	96 [c]	E
10 [c]	Cholesterol	10	82	E
11	$n\text{-}C_{18}H_{37}SH$	3	95	E

a) The reactions were carried out at room temperature in CH_2Cl_2 (2 mL) under argon by using methyl propiolate (0.2 mmol), alcohols (0.2 mmol), and PBu_3 (0.03 mmol) unless otherwise stated. b) Isolated yield. c) Determined by ^1H NMR (400 MHz) analysis. d) PBu_3 (0.2 equiv.) was used. e) PBu_3 (0.5 equiv.) was used.



(1)

PBu_3 (0.2 equiv.) 67%

PMe_3 (0.2 equiv.) 76%

E isomer was major product
High nucleophilic
PBu_3 is best catalyst

Tandem addition

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Tandem Reactions to Construct Heterocycles via Phosphine-Catalyzed Umpolung Addition and Intramolecular Conjugate Addition

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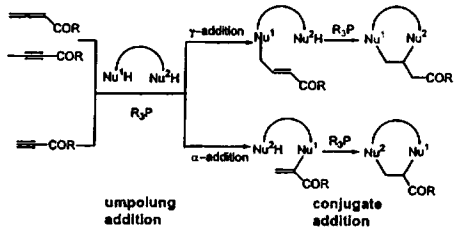
Scheme 1



2b, 2c >> 2a
Higher γ-addition of ketone than ester
entry 1-12
allenic substrate γ-addition and β-addition.

Scheme 3

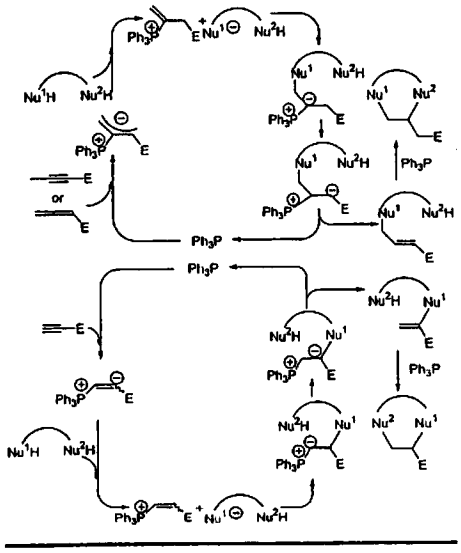


Table 1. Phosphine-Catalyzed Tandem Nucleophilic Additions [a,a]

entry	NuH	allenes or alkynes	T(°C)/ T (h)	product	yield (%) [b]
1	 1a	2a R=OEt	110/24	 5a	68
2 [c]	1a	2b R=Me	70/2	5b	84
3 [c]	1a	2c R=Ph	70/5	5c	70
4 [c]	 1b R¹=Me	2b	70/5	 5d	66 [d]
5 [c]	1c R¹=OEt	2b	70/5	5e	77 [d]
6	1a	 3d R=OBn	110/48	 5f	71
7	1a	3e R=Cy	110/48	5g	92
8 [e]	1d X=NTs	3b R=Me	80/24	 5h	93
9 [e]	1d	3c R=Ph	80/24	5i	81 [e]
10 [e]	1d	3e R=Cy	80/24	5j	96
11 [e]	1e X=O	3b	80/24	5k	66 [g]
12 [e]	1e	3e	80/24	5l	66 [e]
13 [f]	1d	4a R=OEt	80/24	 5m	86
14 [f]	1d	4f R=ⁿPr	80/24	5n	83 [e]
15 [f]	1f	4a	80/72	 5o	88

[a] Reaction conditions: a solution of bifunctional nucleophile (0.5 mmol), allene or alkyne (0.5 mmol), and Ph_3P (0.1 mmol) were heated at the indicated temperature. For details of the reaction conditions, see ref 8. [b] Isolated yield. [c] Used 0.025 mmol of Ph_3P. [d] Solution of 1 equiv of allenone in toluene was added dropwise to the solution of 5 equiv of 1,3-dicarbonyl compound in toluene, and the yields were based on the allenone. [e] CH_3CN was used as solvent. [f] Toluene–CH_3CN(v:v = 4:1) was used as a solvent. [g] Alkynone (1.1 equiv) in toluene or CH_3CN was added dropwise.

entry 13-15: No γ-addition

7/16

As a nucleophile.

J. Org. Chem. 1996, 61, 4516–4519

Synthesis of Highly Functionalized γ-Butyrolactones from Activated Carbonyl Compounds and Dimethyl Acetylenedicarboxylate†

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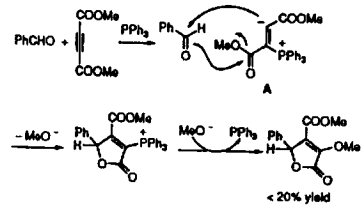
Received October 11, 1995

Scheme 1



A don't protonize, but nucleophile attack to carbonyl compound.

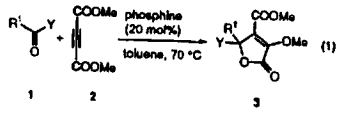


Table 1. Tertiary Phosphine-Catalyzed Lactone Formation from Electron-Deficient Carbonyl Compounds 1 and Dimethyl Acetylenedicarboxylate (2)

run	substrate 1	R^1	R^2	phosphines	time (h)	yield of 3 (%)[a,b]
1	1a	4-$NO_2C_6H_4$	COOMe	PPh_3	22	94
2	1b	Ph	COOMe	PPh_3	8	11[c]
3	1c	4-ClC_6H_4	COOMe	PPh_3	22	[c]
4	1d	Ph	CN	PPh_3	8	58
5	1e	4-MeC_6H_4	CN	PPh_3	19	58
6	1f	4-$MeOC_6H_4$	CN	PPh_3	19	67
7	1g	4-ClC_6H_4	CN	PPh_3	22	30[d]
8	1h	4-$NO_2C_6H_4$	CN	PPh_3	22	<30[d,e]
9	1i	c-C_6H_{11}	CN	PPh_3	22	38
10	1j	Ph	CH_3	PPh_3	22	[c]
11	1k	Ph	CF_3	PPh_3	17	75
12	1a	4-$NO_2C_6H_4$	COOMe	(S)-BINAP[f]	49	6[c] (8)
13	1a	4-$NO_2C_6H_4$	COOMe	(R)-MeO-MOP[g]	47	41[c] (10)
14	1a	4-$NO_2C_6H_4$	COOMe	(+)-NMDPP[h]	48	5[c] (5)

[a] Isolated yield. [b] %ee for 3 are shown in parentheses. The absolute configuration of the major isomer has not been determined. [c] The unreacted starting materials were recovered. [d] A complex mixture was obtained. [e] The product was not obtained in pure form. [f] (S)-BINAP = (S)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl. [g] (R)-MeO-MOP = (R)-2-(diphenylphosphino)-2′-methoxy-1,1′-binaphthyl. [h] (+)-NMDPP = (1S,2S,5R)-neomenthyldiphenylphosphine.

α-keto ester, α-keto nitrile, ααα-trifluoroacetophenone was good substrate.

For α-keto ester, electron-withdrawing R_1 gave good result,

For α-keto nitrile, electron-donating R_1 gave good result. → CN group itself is good leaving group. To prevent undesired reaction, electron-donating R_1 was needed.

α-diketone is also good substrate for this reaction, see, J. Chem. Soc., Perkin Trans. 1, 1997, 3129.

1,3-dipolaphile - [3+2] addition

X. Lu et al.

Imine [3+2] : TL, 1997, 38, 3461.
JOC, 1998, 63, 5031.

Imine + substituted allene or alkyne [3+2] : TL, 1999, 549,

Construction of spirocycle [3+2] : JOC, 2002, 67, 8901.
JOC, 2003, 68, 6763.

J. Org. Chem. **1995**, *60*, 2906–2908

Phosphine-Catalyzed Cycloaddition of 2,3-Butadienoates or 2-Butynoates with Electron-Deficient Olefins. A Novel [3 + 2] Annulation Approach to Cyclopentenes

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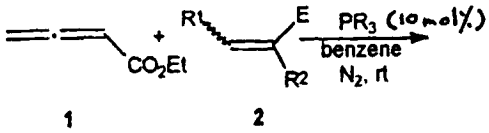
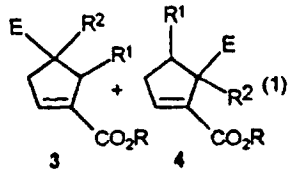
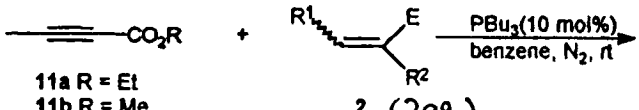
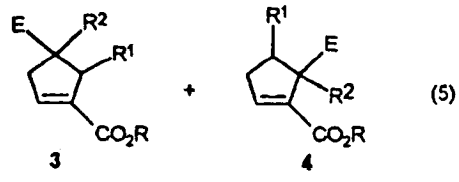
Received January 3, 1995



1 + PPh_3 (10 mol%) → Dimerization of 1







PBu_3 has higher reactivity.

Table 1. Phosphine-Catalyzed Cycloaddition of 2,3-Butadienoates with Electron-Deficient Olefins

entry	olefin 2	olefin E	PR_3	products yield (%)	products 3:4[a]
1	2a[b]	COOEt	PPh_3	76	75:25
2	2a	COOEt[c]	PBu_3	66	75:25
3	2b[b]	COOMe	PPh_3	81	80:20
4	2b	COOMe[c]	PBu_3	66	85:15
5	2c[b]	COMe	PPh_3	55	63:37
6	2d[b]	CN	PPh_3	79	83:17[d]

[a] Ratios were determined by isolation. [b] $R^1 = R^2 = H$. [c] 2 equiv of olefin was used. [d] Ratio was determined by ^1H NMR spectra.

Electron-deficient olefins gave good results.

Table 2. Cycloaddition of 2-Butynoates with Electron-Deficient Olefins under the Catalysis of Tributylphosphine

entry	11	2	products yield (%)	products 3:4[a]
1	11a	2a[b]	85	89:11 (3a:4a)
2	11a	2b[b]	78	84:16 (3b:4b)
3	11a	2d[b]	80	93:7 (3d:4d)[c]
4	11a	2e	88	*trans*-6
5	11a	2f	91	*trans*-6
6	11b	2b	62	87:13 (3b′:4b′)
7	11b	2g[d]	46	72:28 (3g:4g)

[a] Ratios were determined by isolation. [b] See Table 1. [c] Ratio was determined by ^1H NMR spectra. [d] 2g: R^1 = H, R^2 = Me, E = CO_2Me.

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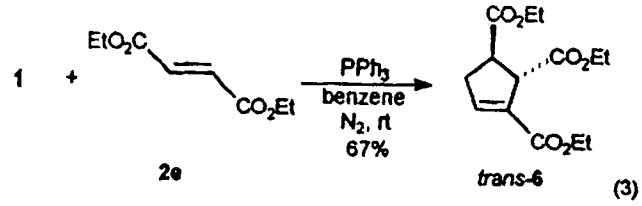

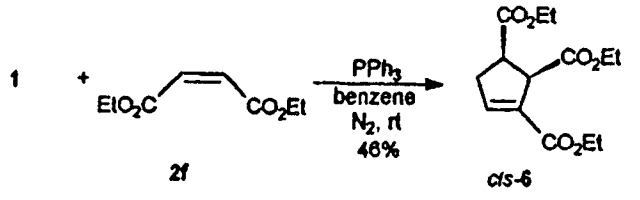

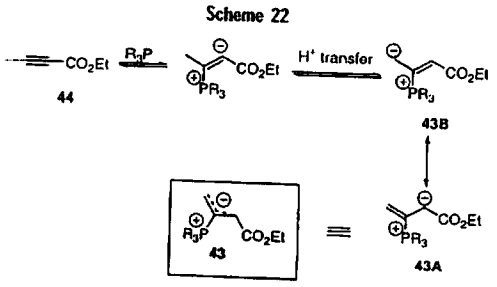

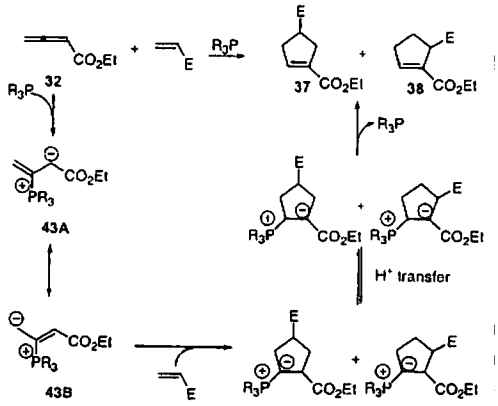

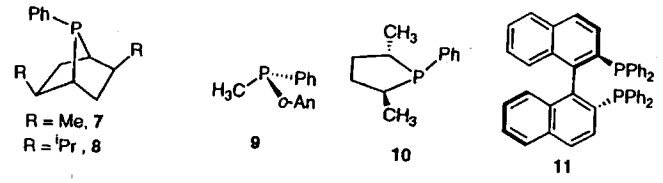

J. Am. Chem. Soc. 1997, *119*, 3836−3837

Asymmetric [3 + 2] Cycloaddition of 2,3-Butadienoates with Electron-Deficient Olefins Catalyzed by Novel Chiral 2,5-Dialkyl-7-phenyl-7-phosphabicyclo[2.2.1]heptanes

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Received December 31, 1996

Figure 3.

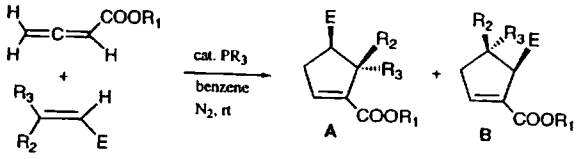

Table 1. Phosphine-Catalyzed Asymmetric [3 + 2] Cycloaddition[a]

entry	phosphine	E	R_1	R_2	R_3	solvent	T (°C)[e]	yield (%)	A:B[b]	% ee of A[b]	config[c]
1	7	COOEt	Et	H	H	benzene	rt	66	95:5	81	(−) *R*
2	8	COOEt	Et	H	H	benzene	rt	76	97:3	81	(−) *R*
3	9	COOEt	Et	H	H	benzene	rt	80	80:20	56	(+) *S*
4	10	COOEt	Et	H	H	benzene	rt	83	72:29	6	(+) *S*
5	11	COOEt	Et	H	H	benzene	rt	33	73:27	12	(−) *R*
6	7	COO^{t}Bu	Et	H	H	benzene	rt	46	100:0	86	(−) *R*
7	7	COO^{t}Bu	Et	H	H	benzene	rt	69	95:5	89	(−) *R*
8	7	COO^{t}Bu	Et	H	H	toluene	0	42	97:3	93	(−) *R*
9	8	COOMe	Et	H	H	benzene	rt	87	96:4	79	(−) *R*
10	8	COO^{t}Bu	Et	H	H	benzene	rt	92	100:0	88	(−) *R*
11	8	COO^{t}Bu	Et	H	H	toluene	0	88	100:0	93	(−) *R*
12	8	COO^{t}Bu	Et	H	H	benzene	rt	75	95:5	88	(−) *R*
13	7	COOEt	^{t}Bu	H	H	benzene	rt	13	97:3	89	(−) *R*
14	8	COOEt	^{t}Bu	H	H	benzene	rt	84	94:6	69	(−) *R*
15[d]	8	COOEt	Et	COOEt	H	toluene	0	49		79	(+)
16[d]	8	COOMe	Et	H	COOMe	benzene	rt	84		36	(−)

[a] The reaction was carried out under N_2 with a chiral phosphine (10 mol %), 2,3-butadienoate (100 mol %), and electron deficient olefins (1000 mol %). [b] A:B and % ee were measured by GC with β and γ-DEX columns. [c] The absolute configuration was determined by comparing the optical rotation with the literature value.[16] [d] Olefins (200 mol %) were used. [e] rt = room temperature.

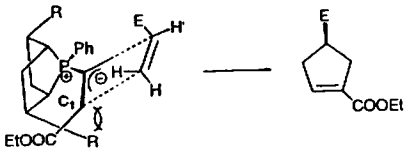

Figure 4.

1,4 - Dipolarphile - [4+2] addition

■ J. AM. CHEM. SOC. 2003, *125*, 4716−4717

J|A|C|S COMMUNICATIONS

Published on Web 03/28/2003

An Expedient Phosphine-Catalyzed [4 + 2] Annulation: Synthesis of Highly Functionalized Tetrahydropyridines

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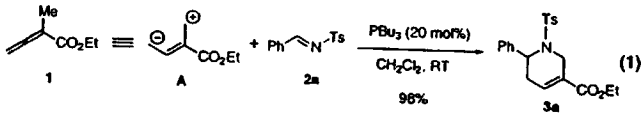
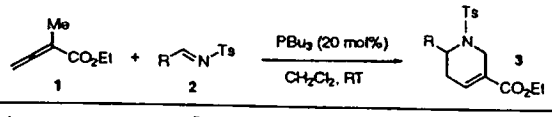


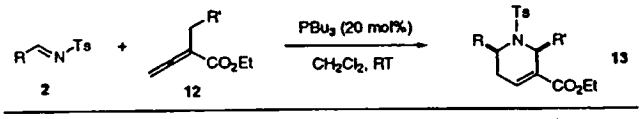
Table 1. Synthesis of Tetrahydropyridines 3 from Ethyl 2-Methyl-2,3-butadienoate and *N*-Tosylaldimines[a]



entry	R	product	yield (%)[b]
1	Ph (2a)	3a[c]	98
2	4-OMeC$_6$H$_4$ (2b)	3b	99
3	4-MeC$_6$H$_4$ (2c)	3c	95
4	3-ClC$_6$H$_4$ (2d)	3d	96
5	2-ClC$_6$H$_4$ (2e)	3e	93
6	4-FC$_6$H$_4$ (2f)	3f	95
7	4-CNC$_6$H$_4$ (2g)	3g	98
8	2-CF$_3$C$_6$H$_4$ (2h)	3h	98
9	1-naphthyl (2i)	3i	96
10	2-furyl (2j)	3j	97
11	4-pyridyl (2k)	3k	92[d]
12	4-NO$_2$C$_6$H$_4$ (2l)	3l	86
13	2-OHC$_6$H$_4$ (2m)	3m	0
14	2-OTBSC$_6$H$_4$ (2n)	3n	93
15	2-pyrrolyl (2o)	3o	0
16	*N*-Boc-2-pyrroyl (2p)	3p	99
17	*trans*-styrenyl (2q)	3q	trace[e]
18	*t*-butyl (2r)	3r	86[f]
19	*n*-propyl (2s)	3s	0[g]

[a] See Supporting Information for a detailed experimental procedure. [b] Isolated yields. [c] The structure was confirmed by X-ray crystallographic analysis. [d] 30 mol % PBu$_3$ was used. [e] The product was inseparable from the starting imine. [f] 3 equiv of Na_2CO_3 was added. [g] The imine was decomposed to aldehyde and *p*-toulenesulfonamide.

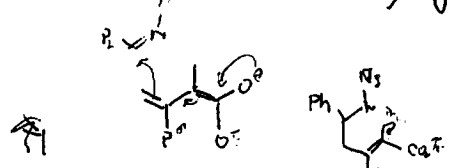
Table 2. Synthesis of Tetrahydropyridines 13 from Ethyl 2-Benzyl-2,3-butadienoates and *N*-Tosylaldimines[a]



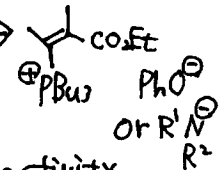
entry	R	R′	product	yield (%)[b]	dr[c]
1	Ph (2a)	4-CNC$_6$H$_4$ (12a)	13a	99	98:2
2	Ph (2a)	2-FC$_6$H$_4$ (12b)	13b	99	97:3
3	Ph (2a)	3-OMeC$_6$H$_4$ (12c)	13c	99	98:2
4	Ph (2a)	2-MeC$_6$H$_4$ (12d)	13d	82	88:12
5	Ph (2a)	Ph (12e)	13e[d]	99	98:2
6	4-OMeC$_6$H$_4$ (2b)	Ph (12e)	13f	99	97:3
7	4-NO$_2$C$_6$H$_4$ (2l)	Ph (12e)	13g	90	95:5
8	3-ClC$_6$H$_4$ (2d)	4-CNC$_6$H$_4$ (12a)	13h	99	98:2
9	2-CF$_3$C$_6$H$_4$ (2h)	4-CNC$_6$H$_4$ (12a)	13i	80	90:10
10	2-ClC$_6$H$_4$ (2e)	3-OMeC$_6$H$_4$ (12c)	13j	96	83:17
11	4-MeC$_6$H$_4$ (2c)	3-OMeC$_6$H$_4$ (12c)	13k	99	98:2

[a] See Supporting Information for a detailed experimental procedure. [b] Isolated yields. [c] Diastereomer ratio determined by ^{1}H NMR (500 MHz). [d] The structure was confirmed by X-ray crystallographic analysis.

To change the reaction of 1,3-dipolar to 1,4-dipolar, substitution of the hydrogen at the 2-position of 2,3-butadienoates with methyl group.

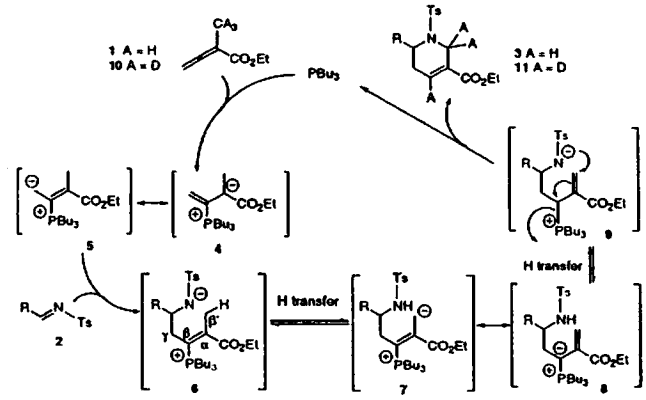


- Entry 13 vs 14 and 15 vs 16: Acidic proton retarded the reaction.

5 or 4 + PhOH or R'_2NH ⟶ 

- Entry 17 and 19: No or low reactivity of alkyl imine.

Scheme 1. Mechanistic Rationale for the Formation of 3



- 10 + 2a —PBu3→ 11 sluggish 31% y.
proton transfer process would be rate determing step.
- Proton transfer of 6 → 7 is energetically less favorable.

To accelerate this (11) process, they introduced benzyl substituent.

2 + 12 → 13. quantitative yield and high diastereoselectivity.

ortho-substituent gave poor results.
steric bulk.

10/16

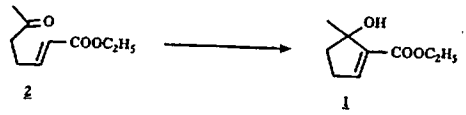
2. Intramolecular reaction of enone

Tetrahedron Letters, Vol. 33, No. 8, pp. 1045-1048, 1992
Printed in Great Britain

AN INTRAMOLECULAR BAYLIS-HILLMAN REACTION

First report of intramolecular Morita-Baylis-Hillman reaction.

Fides Roth, Peter Gygax, Georg Fráter*
GIVAUDAN-ROURE, Dübendorf, Switzerland



2 → 1

Table 1 Cyclisation experiments 2 → 1

Entry	Catalyst, Solvent[a]	Time	Mol%cat.	%2	%1	Remarks
1	DABCO	32d	15	81	-	19% cis-2
	DABCO, THF	30d	37	80	-	20% cis-2
2	$NaOC_2H_5$, C_2H_5OH, (-30° → rt)	2h	100	10	-	40% 4?
3	LiTMP[b], ether (-50° → rt)	1d	3	10	-	a.o. 5?
4	Quinidine, C_2H_5OH, THF	10d	10	100	-	
5	Li-quinidinate, HMPA	5h	25	0	0	mixture of unidentified products
6	$(n\text{-}Bu)_3P$	1d	25	25	75(GLC)	isolated 39% 1
7	$(CH_3)_2(C_6H_5)P$	1d	25	35	65(GLC)	
8	" CH_3CN	5d	30	70	30(GLC)	
9	$(i\text{-}Bu)_2CH_3C_6H_5)P$	30d	25	50	50	
10	$CH_3(C_6H_5)_2P$	40d	25	100	-	
11	(-)PAMP(6, 78%ee)[a]	20d	20	100	-	
12	(-)CAMP(7, 62%ee)[a]	10d	18	25	75(GLC)	isolated 40% 1 (14%ee)[a]

a) if not otherwise mentioned, reactions were carried out without solvent at room temperature; b) Lithium-2,2,6,6-tetramethylpiperidide; c) NMR, optishift, CH_3-triplet of the ester group separated, $[\alpha]_D^{20}$ 0° (c=1,EtOH).

Phosphines was useful in this reaction.

Amine bases (ex. DABCO, Quinidine) didn't give the cyclized product.

For asymmetric reaction, (-)-PAMP, (-)-CAMP gave the product with low ee.

Pergamon
TETRAHEDRON
Tetrahedron 57 (2001) 7771–7784

Assessing the scope of the tandem Michael/intramolecular aldol reaction mediated by secondary amines, thiols and phosphines

Elinor L. Richards,[a] Patrick J. Murphy,[a,*] Francesca Dinon,[a] Silvia Fratucello,[a] Paul M. Brown,[a] Thomas Gelbrich[b] and Michael B. Hursthouse[b]
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Received 7 March 2001; revised 20 June 2001; accepted 12 July 2001

P.J. Murphy et al.
Tandem Michael/Aldol, piperidine cat. TL, 1997, 38, 8561.
" phosphine cat. TL, 1999, 40, 3279.
Tandem Michael/Michael, phosphine cat. TL, 2002, 43, 8707.

5-ring formation

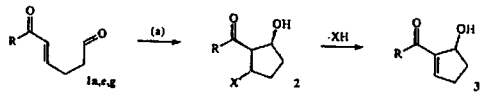

Table 4.

Entry	Substrate	R	Method	X	2[a]	3
1	1a	Ph	1.3 equiv. piperidine, $CDCl_3$, 10 min	Piperidyl	4, 90%[b]	-
2	1a	Ph	0.3 equiv. piperidine, $CDCl_3$, 144 h	Piperidyl	-	3a, 50%
3	1a	Ph	1.3 equiv. TolSH, $CHCl_3$, 16 h	TolS	2aT, 77%	-
4	1a	Ph	0.2 equiv. $n\text{-}Bu_3P$, $CDCl_3$, 17 h	-	-	3a, 20%
5	1f	OEt	1.3 equiv. piperidine, $CDCl_3$, 2 days	Piperidyl	Dec[c]	-
6	1f	OEt	0.3 equiv. piperidine, $CDCl_3$, 2 days	Piperidyl	Dec[c]	-
7	1f	OEt	2 equiv. TolSH, 0.2 TolSNa, Δ, 16 h	TolS	2fT, 72%	-
8	1f	OEt	0.4 equiv. $n\text{-}Bu_3P$, $CDCl_3$, 28 days	-	-	3f, 40%

[a] P refers to adducts derived from piperidine, T from p-TolSH.
[b] As observed by NMR of the progress of the reaction.

6-ring formation

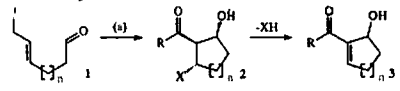

Table 5.

Entry	Substrate	R	n	Method[a]	X	2[b]	3
1	1b	Ph	2	1.3 equiv. piperidine, 10 min	Piperidyl	2bP, 90%[c]	-
2	1b	Ph	2	0.3 equiv. piperidine, 14–28 days	Piperidyl	-	3b, 24–30%
3	1b	Ph	2	1.3 equiv. TolSH, 16 h rt	TolS	2bT, 93%	-
4	1b	Ph	2	0.2 equiv. nBu_3P, 2 h	-	-	3b, 75%
5	E-1g	OEt	2	1.3 equiv. piperidine	Piperidyl	Dec[d]	-
6	E-1g	OEt	2	0.3 equiv. piperidine	Piperidyl	Dec[d]	-
7	E-1g	OEt	2	2 equiv. TolSH, 0.2 TolSNa, Δ, 16 h	TolS	2gT,[c] 75%	-
8	E-1g	OEt	2	0.2 equiv. $n\text{-}Bu_3P$, 24 h	-	-	3g, 50%
9	Z-1g	OEt	2	0.2 equiv. $n\text{-}Bu_3P$, 24 h	-	-	3g, 70%

[a] All reactions performed in $CHCl_3$ or $CDCl_3$ at rt unless specified.
[b] P refers to adducts from piperidine, T from p-TolSH.
[c] As observed by NMR of the progress of the reaction.
[d] Largely composed of products derived from aldol condensation.

•Piperidine gave 2 quickly, but formation of 3 was slow for both case
•n-BP gave 3 with low reactivity for 5-membered ring and high reactivity for 6membered ring.

Tandem Michael/Michael

2402 VOL. 124, NO. 11, 2002 ■ J. AM. CHEM. SOC.

J|A|C|S
COMMUNICATIONS

Published on Web 02/26/2002

Organocatalytic Michael Cycloisomerization of Bis(enones): The Intramolecular Rauhut–Currier Reaction

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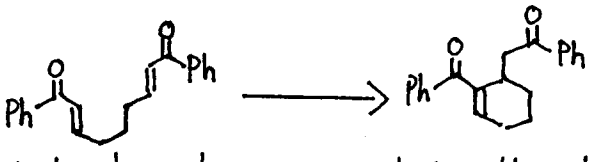
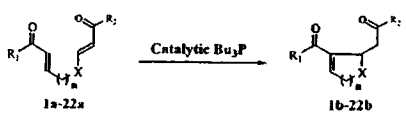
University of Texas at Austin, Department of Chemistry and Biochemistry, Austin, Texas 78712

Received September 13, 2001



high polar solvent gave product quickly with some digoners.
For highly electrophilic bis(enone), EtOAc is solvent,
For less electrophilic bis(enone), Acetone is best.
For less reactive substrate, ^tBuOH with reflux is solvent of choice.

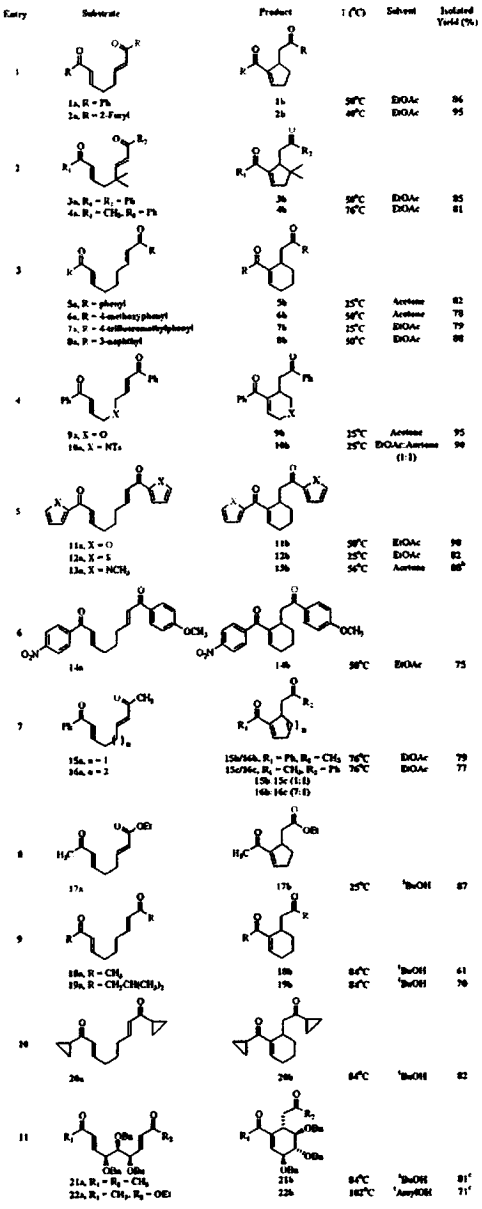


1a-22a → 1b-22b

Intramolecular tandem Michael/Michael reaction of bis(enones)
(2 examples of enone/enoate)
5,6-membered ring formation

11/16

Table 1. Phosphine-Catalyzed Cycloisomerization of Bis(enones)[a]



[a] Procedure: Tributylphosphine was added to a 0.1 M solution of substrate in the indicated solvent and the reaction was allowed to stir at the indicated temperature until complete. [b] Yield based on recovered starting material. [c] 20 mol % PBu_3 used.

Entry 15 and 16 : aromatic and aliphatic bis (enone)

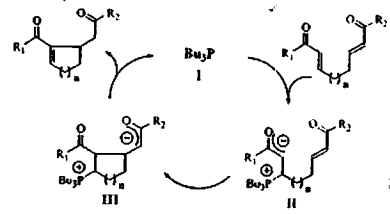
. 15 , 5-membered ring , kinetic phosphine adduct

16 , 6-membered ring , preequilibrium phosphine adduct

Entry 17 : mono-enone, enoate , single isomer

Entry 14 : electronic effect. phosphine addition of more electron deficient olefin.

Entry 3 and 4 : steric effect . single isomer.



III : zwitterionic intermediate

2404 VOL. 124, NO. 11, 2002 ■ J. AM. CHEM. SOC.

J|A|C|S COMMUNICATIONS

Published on Web 02/26/2002

The Vinylogous Intramolecular Morita–Baylis–Hillman Reaction: Synthesis of Functionalized Cyclopentenes and Cyclohexenes with Trialkylphosphines as Nucleophilic Catalysts

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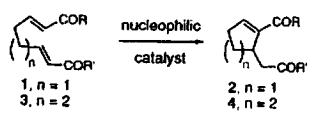
Department of Chemistry, University of Michigan, Ann Arbor, Michigan 48109-1055

Received September 20, 2001; Revised Manuscript Received January 10, 2002



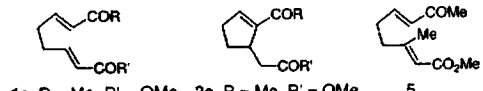
1, n = 1
3, n = 2

nucleophilic catalyst

2, n = 1
4, n = 2

Intramolecular tandem Michael/Michael of bis (enones), bis(enoates) enone/enal, enoate/enal, bis (enal)

5, 6-membered ring formation



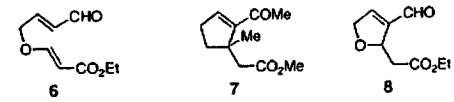
1a, R = Me, R' = OMe
1b, R = Me, R' = OEt
1c, R = R' = Me
1d, R = H, R' = Me
1e, R = H, R' = OMe

2a, R = Me, R' = OMe
2b, R = Me, R' = OEt
2c, R = R' = Me
2d, R = H, R' = Me
2e, R = H, R' = OMe

5

PBu_3 in CH_3CN or PMe_3 in t-amyl-OH

5-membered ring.



6 7 8

Table 1. Synthesis of Substituted Cyclopentenes via the Intramolecular Vinylogous Morita–Baylis–Hillman Reaction[a]

entry	substrate	catalyst (%)	solvent	concn (M)	time (h)	product	yield[b]	regioselectivity[c]	% aldol[d]
1	**1a**	PBu_3 (10)	CH_3CN	0.05	24	**2a**	80	95:5	
2	**1a**	PBu_3 (10)	CH_3CN	0.1	8	**2a**	61	95:5	
3	**1a**	PBu_3 (10)	*tert*-amyl-OH	0.1	11	**2a**	88	96:4	
4	**1a**	PMe_3 (10)	CH_3CN	0.1	4	**2a**	71	94:6	
5	**1a**	PMe_3 (10)	*tert*-amyl-OH	0.05	3	**2a**	91	97:3	
6	**1a**	PMe_3 (10)	*tert*-amyl-OH	0.1	1	**2a**	95	97:3	
7	**1a**	PMe_3 (10)	*tert*-amyl-OH	1.0	0.75	**2a**	81	96:4	
8	**1c**	PMe_3 (10)	*tert*-amyl-OH	0.05	4	**2c**	54		13
9	**1c**	PMe_3 (10)	CH_2Cl_2	0.05	2	**2c**	96		0
10	**1d**	PMe_3 (20)	*tert*-amyl-OH	0.01	0.75	**2d**	79	89:11	trace
11[e]	**1d**	PMe_3 (20)	*tert*-amyl-OH	0.1	2	**2d**	48	93:7	trace
12	**1e**	PMe_3 (20)	*tert*-amyl-OH	0.1	0.25	**2e**	43	only	-
13	**1e**	PMe_3 (20)	*tert*-amyl-OH	0.01	4	**2e**	90	only	-
14	**5**	PMe_3 (100)	*tert*-amyl-OH	0.05	17	**7**	32	only	-
15	**5**	PMe_3 (100)	*tert*-amyl-OH	0.01	44	**7**	51	only	-
16	**5**	PMe_3 (200)	*tert*-amyl-OH	0.01	44	**7**	60	only	-
17	**6**	PMe_3 (50)	CH_3CN	0.01	2	**8**	38	only	-

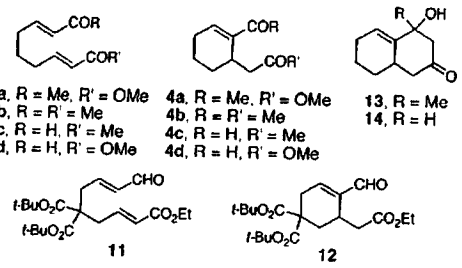
[a] All reactions were performed by addition of the phosphine reagent to a solution of substrate in the indicated solvent at 23 °C, unless noted otherwise. [b] Isolated yield of product. Compounds **2a** and **2d** were isolated as mixtures with the regioisomeric cyclopentene product. [c] Regioselectivity refers to the ratio of the two regioisomeric cyclopentenes. [d] Products **2c** and **2d** underwent aldol cyclization under the reaction conditions (see text). [e] Substrate **1d** was added via syringe pump to the phosphine catalyst over 1 h.

entry 8 and 9 : CH_2Cl_2 supress aldol cyclization of 2c.

entry 10 ~ 12 : low concentration was best to prevent self condensation of 1d.

selectivity ; Phosphine reacted with the more electrophic Michael acceptor.

12/16



3a, R = Me, R' = OMe
3b, R = R' = Me
3c, R = H, R' = Me
3d, R = H, R' = OMe

4a, R = Me, R' = OMe
4b, R = R' = Me
4c, R = H, R' = Me
4d, R = H, R' = OMe

13, R = Me
14, R = H

6-membered ring

For 3d, 1eq of PMe_3 was necessary.

11 12

Table 2. Synthesis of Substituted Cyclohexenes via the Intramolecular Vinylogous Morita–Baylis–Hillman Reaction[a]

entry	substrate	catalyst (%)	solvent	concn (M)	time (h)	product	yield[b]	regioselectivity	% aldol
1	3a	PMe_3 (25)	*tert*-amyl-OH	0.1	8	4a	83	92:8	
2	3b	PMe_3 (25)	*tert*-amyl-OH	0.05	1.5	4b	46		23
3	3b	PMe_3 (25)	CH_2Cl_2	0.05	20	4b	64		20
4	3c	PBu_3 (50)	CH_3CN	0.06	0.5	4c	55	90:10	-
5	3c	PMe_3 (50)	*tert*-amyl-OH	0.01	0.75	4c	45	95:5	11
6	3d	PMe_3 (100)	*tert*-amyl-OH	0.01	6	4d	47	95:5	
7	3d	PMe_3 (100)	CH_3CN	0.01	8	4d	67	97:3	
8	11	PMe_3 (50)	CH_3CN	0.01	22	12	74	97:3	

[a] All reactions were performed as described in Table 1. [b] All products were isolated as mixtures with the regioisomeric cyclohexenes except for **4b**.

Other type of substrate : enoate/thioenoate and enone/thioenoate
Krische et. al. Org. Lett. 2003, 5, 1737.
MBH reaction of thioester/aldehyde
Keck et al. Org. Lett, 2002, 4, 3687.

8696 ■ J. AM. CHEM. SOC. 2003, *125*, 8696–8697

J|A|C|S COMMUNICATIONS

Published on Web 06/18/2003

β-addition of hydroxide and alkoxide.

Phosphine-Catalyzed Hydration and Hydroalkoxylation of Activated Olefins: Use of a Strong Nucleophile to Generate a Strong Base

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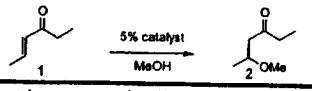
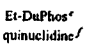
Received March 19, 2003; E-mail: bergman@cchem.berkeley.edu; fdtoste@uclink.berkeley.edu

Table 1. Catalyst Survey[a]



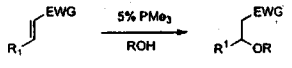
1 2

entry	catalyst	time (h)	T (°C)	% conv.[b]
1	PMe_3	6	45	95
2	PBu_3	6	45	95
3	Me-BPE[c]	4	45	93
4		20	105	45
5	*rac*-BINAP[d]	18	75	0
6	Et-DuPhos[e]	22	75	0
7	quinuclidine[f]	48	45	54
8	DABCO[f,g]	16	45	0
9	Et_3N[f]	25	45	0
10	$O{=}PMe_3$[f]	20	45	0

[a] Reaction conditions: 1 mmol 4-hexen-3-one, 0.05 mmol catalyst in 0.3 mL CD_3OD. [b] Determined by ^1H NMR spectroscopy. [c] Me-BPE = 1,2-bis(2,5-dimethylphospholano)ethane. [d] BINAP = 2,2′-Bis(diphenylphosphino)-1,1′-binaphthyl. [e] Et-DuPhos = 1,2-Bis(2,5-diethylphospholano)benzene. [f] 10 mol % catalyst. [g] DABCO = bicyclo[2.2.2]-1,4-diazaoctane.

Entry 1~3 vs 4~6 : Trialkyl phosphines were more reactive than aryl phosphines.
Entry 7-9 : N-nucleophiles were less effective.
Entry 10 : Phosphine-oxide was not effective catalyst.

Table 2. Phosphine-Catalyzed Hydration and Hydroalkoxylation[a]

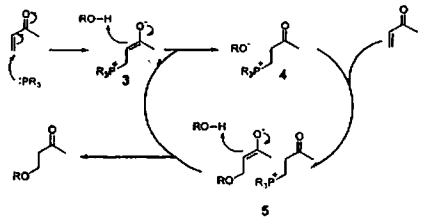


entry	EWG	R^1	ROH	time (h)	% yield[b]
1	COEt	Me	H_2O	20	77
2			MeOH	24	85
3[c]				16	63
4	COMe	H	MeOH	1	56
5[c]			Me_2CHOH	1	83
6[c]			PhOH	16	59
7		Ph	MeOH	72	0
8	CO_2Me	Me	MeOH	36	71
9	CN	H	MeOH	4	79

[a] Reaction conditions: see ref 9. [b] Isolated yield after purification. [c] Run in CH_3CN.

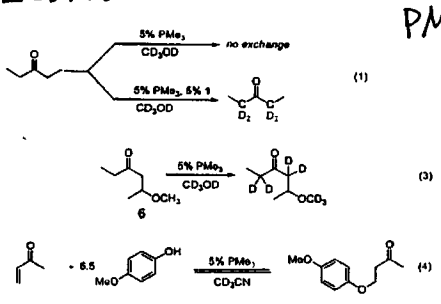
Scope and limitations
Entry 7: highyl conjugated substrate was unreactive
H_2O, primary, secondary and aryl alcohol gave product.
No retro-aldol or ketalization product was observed.

Scheme 1. Proposed Catalytic Cycle



3 acts as strong base to deprotonate alcohol

Phosphine don't function as a base, because of no reation using Et_3N.



PMe_3 + 1 generates base.
(3) : Check of reversibility.
(4) : Variable temperature NMR. product increased by raising temperature.

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J|A|C|S COMMUNICATIONS

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Phosphine Catalyzed α-Arylation of Enones and Enals Using Hypervalent Bismuth Reagents: Regiospecific Enolate Arylation via Nucleophilic Catalysis

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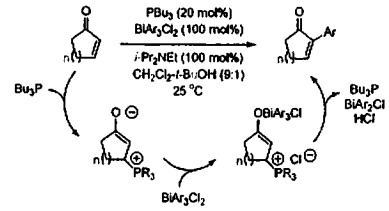
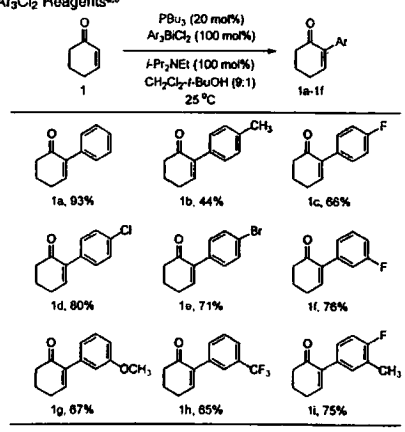
Scheme 1. Proposed Mechanism for Catalytic Enone α-Arylation under the Conditions of Nucleophilic Catalysis



Lewis acid - Lewis base compatible.
Bi(V)-mediated oxidation is slow compared with arylation.

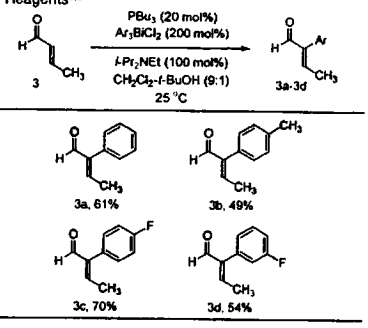
Table 1. Phosphine Catalyzed Arylation of Cyclohexenone Using $BiAr_3Cl_2$ Reagents[a,b]



[a] See Supporting Information for a detailed experimental procedure. [b] Isolated yields after purification by silica gel chromatography.

meta-substituents gave good results.

Table 3. Phosphine Catalyzed Arylation of Crotonaldehyde Using $BiAr_3Cl_2$ Reagents[a,b]



[a] See Supporting Information for a detailed experimental procedure. [b] Isolated yields after purification by silica gel chromatography.

limitation of this reaction

- Pronucleophile must be substituted at the β-position to prevent competitive anion polymerization.
- Pronucleophile must readily adopt an *S*-trans-conformation.

acyclic enone system gave product with low yield.

Strong π-donating substituents in the para-position diminish the aryl transfer efficiency.

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Novel Phosphine-Catalyzed Zipper Cyclization of Aliphatic Diyne–Dione and Yne–Dione Systems

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Scheme 1

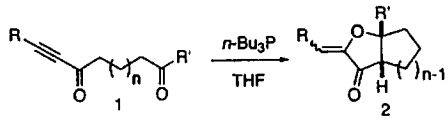
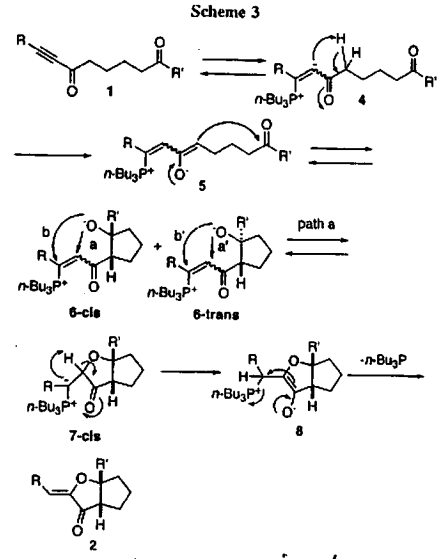


Table 1. Tri-*n*-butylphosphne-Catalyzed Cyclization of 1[a]

run	R	R′	*n*	1 and 2	1 − 2 yield (%)[b]
1	*n*-Bu	*n*-BuC≡C	2	a	59
2	Ph	PhC≡C	2	b	63
3	Ph	PhC≡C	3	c	73
4	Ph	PhC≡C	4	d	0
5	Ph	H	2	e	50
6	*n*-Bu	CH_3	3	f	41

[a] The reaction was carried out at room temperature in THF (0.5 M) in the presence of *n*-Bu_3P (20 mol %) as a catalyst. [b] Isolated yield by SiO_2 column.

Scheme 3



High regioselective and diastereoselective reaction.
run 4 : oligomerization occured.

4 → 5 : Nucleophic attack of elolate
6cis is more stable than 6-

Direction of bis(enone) is same

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Phosphine-Mediated [4 + 2] Annulation of Bis(enones): A Lewis Base Catalyzed "Mock Diels–Alder" Reaction

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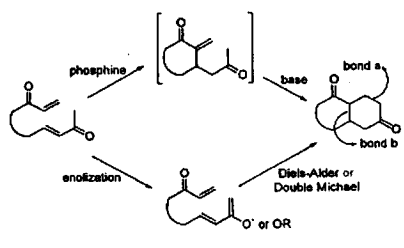
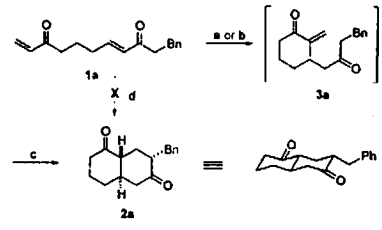
Scheme 1



Scheme 2[a]



[a] Key: (a) Cy_3P, benzene, rt, 77%; (b) (*R,R*)-Et-BPE, benzene, rt, 79%, er 60:40; (c) CsF, MeCN, reflux, 50%, er 60:40; (d) CsF, MeCN, reflux, 0%.

Phosphine work as a nucleophilic catalyst and as a base to promote Michael reaction.

3a → 2a : Phosphine doesn't have sufficient Lewis basicity to promote the Michael reaction.

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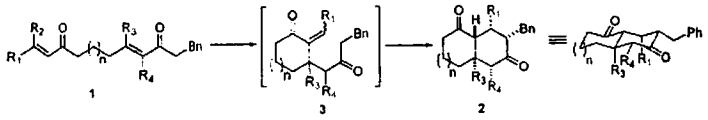
Table 1. Organocatalytic [4 + 2] Cycloisomerization of Bis(enones)[a]



entry	substrate	R_1	R_2	R_3	R_4	n	catalyst	solvent	time (h)	major product[b]	yield[c] (%)	isomeric ratio[a]
1	1a	H	H	H	H	1	Cy_3P	benzene	1	3a	77	
2	1a	H	H	H	H	1	(*R*,*R*)-Me-BPE	benzene	2	3a	79	er 60:40[f]
3	3a[d]	H	H	H	H	1	CsF	MeCN	1.5	2a	50	er 60:40[f]
4	1a	H	H	H	H	1	Cy_3P/CsF	MeCN	10	2a	64	12:1:1
5	1a	H	H	H	H	1	Cy_3P/H_2O	MeCN	24	2a	50	12:1:1
6	1a	H	H	H	H	1	*n*-Bu_3P	*i*-PrOH	2	2a	46[e]	12:1:1
7	1b	H	H	H	H	0	Cy_3P	MeCN			0	
8	1c	H	H	H	H	2	Cy_3P/CsF	MeCN	30	2c	58	9:1:1
9	1d	Me	H	H	H	1	Me_3P/CsF	MeCN	11	2d	71	8:3:2:1
10	1e	H	Me	H	H	1	Me_3P/CsF	MeCN	8	2d	74	8:3:2:1
11	1f	H	H	H	Me	1	Cy_3P/CsF	MeCN	15	2f	76	12:2:2:1
12	1g	H	H	Me	H	1	Cy_3P/Cs_2CO_3	MeCN	2.5	2g	33	6:3:1
13	1h	Me	H	Me	Me	1	Me_3P/Cs_2CO_3	MeCN	16	2h	75	4:3:2:1

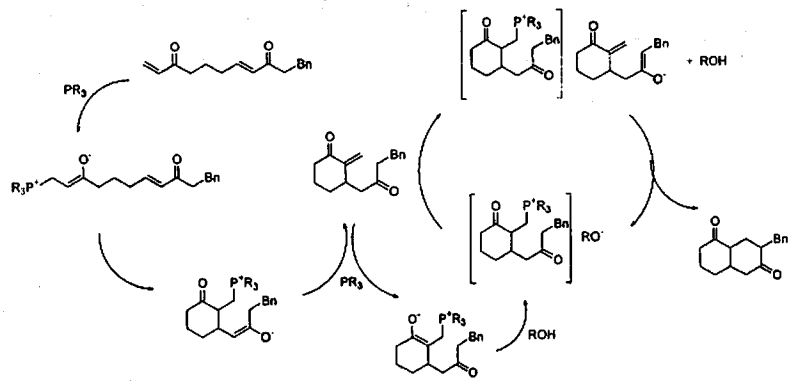
[a] Determined by ^1H NMR. [b] Relative stereochemistry determined by single-crystal X-ray analysis. [c] Isolated yield after purification. [d] Reaction conditions: see ref 11. [e] Reaction performed using 20 mol % of catalyst at 20 °C. [f] Determined by chiral HPLC analysis. [g] er 60:40.

- To check the retro-Michael and Diels-Alder reaction occurence, 3a was subjected the reaction condition. Er was not changed. No such a reaction pathway.
- Entry 3: Only CsF, no reaction and no Diels-Alder reaction
- Entry 8,9: Terminal substituent. PMe_3 was needed for low reactivity of substrate.

- With a drop of H_2O also promoted the reaction in the absence of base.
- Enolate work as a base to deprotonate the alcohol.
- In situ generation of base.

3. Catalytic reaction of ylide.

Scheme 3. Proposed Catalytic Cycle in Protic Solvents

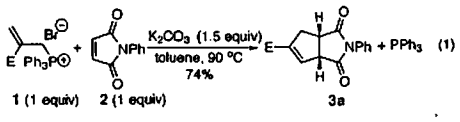


Catalytic C–P Ylide Reaction

A Catalytic Carbon–Phosphorus Ylide Reaction: Phosphane-Catalyzed Annulation of Allylic Compounds with Electron-Deficient Alkenes**

Yishu Du, Xiyan Lu, and Chunming Zhang*

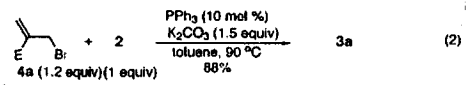
Angew. Chem. Int. Ed. 2003, 42, 1035.



1 (1 equiv) 2 (1 equiv) 3a

1 was prepared from 4a + PPh_3

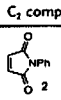
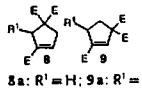
catalytic reaction would be possible



4a (1.2 equiv)(1 equiv) 3a

E = CO_2Et

Table 1: Phosphane-catalyzed annulation reaction of ylides.[a]

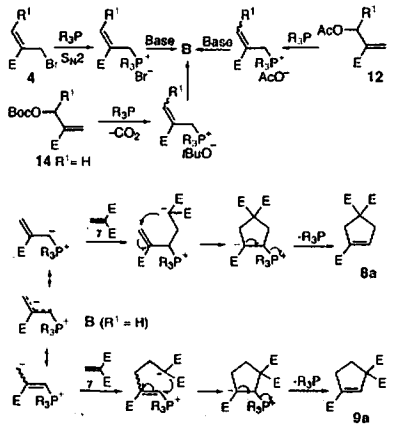
Entry	C_3 component	C_2 component	T [°C]	t [h]	Product	Yield [%][a]
	 4	 2			 3	
1[b]	4a: R^1 = H	2	90	12	3a: R^1 = H	88
2[b]	4b: R^1 = Ph	2	110	4	3b: R^1 = Ph	50[b]
3	4b	2	110	4	3b	68[b]
4	4c: R^1 = *p*-MeC_6H_4	2	110	4	3c: R^1 = *p*-MeC_6H_4	66[b]
5	4d: R^1 = *p*-$O_2NC_6H_4$	2	110	4	3d: R^1 = *p*-$O_2NC_6H_4$	71[b]
6	4e: R^1 = *p*-$MeOC_6H_4$	2	110	4	4e: R^1 = *p*-$MeOC_6H_4$	74[b]
7	4f: R^1 = *n*Pr	2	110	4	4f: R^1 = *n*Pr	60[b]
8	4a	 5	110	20	 6	70[b]
		 7			 8 9	
9	4a	7	110	20	8a: R^1 = H; 9a: R^1 = H	61[f]
10	4d	7	110	6	8d: R^1 = *p*-$O_2NC_6H_4$	66
		 10			 11	
11	4a	10a: X = H	110	20	11a: X = H	72[d]
12	4a	10b: X = MeO	110	20	11b: X = MeO	65
	 12					
13	12a: R^1 = H	2	70	4	3a	76
14	12b: R^1 = Ph	2	110	4	3b	62[b]
15	 12c	2	30	2	 13	64
16[h]	 14	2	110	2	3a	74

[a] For the typical reaction conditions, see the Experimental Section. E = CO_2Et, E' = COPh. [b] Yield of isolated product. [c] The reaction conditions were similar to those in [a], except without slow addition. [d] *trans*:*cis* > 97:3 (relative stereochemistry of the R^1 group and the other substituents). [e] A minor by-product was also isolated which was not fully characterized. [f] 8a:9a = 90:10. [g] The regioselectivity of the reaction was higher than 97:3. [h] The reaction conditions were similar to those in [a], except without the addition of K_2CO_3. Boc = *tert*-butyloxycarbonyl.

Entry 1~7: Aromatic aliphatic substituent gave good results.

Entry 13~15: Allyl acetate also good substrate.

Entry 16: Boc group. in situ generation of base.



Scheme 2. Proposed mechanism of the phosphane-catalyzed annulation reaction of ylides.

Mechanistic proposal.

From 4: S_N2 reaction gave B.

From 12, 14: S_N2' reaction gave B.

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Phosphine-Catalyzed Regiospecific Allylic Amination and Dynamic Kinetic Resolution of Morita–Baylis–Hillman Acetates

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Scheme 1. Intermolecular Phosphine-Catalyzed Regioretentive Allylic Amination

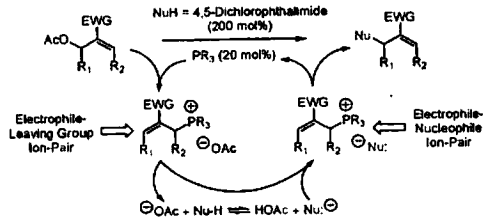
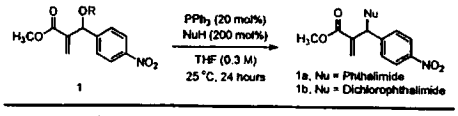


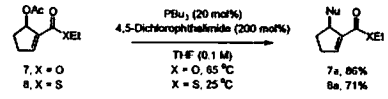
Table 1. Optimization of Phosphine-Catalyzed Allylic Alkylation of Morita–Baylis–Hillman Adducts[a]



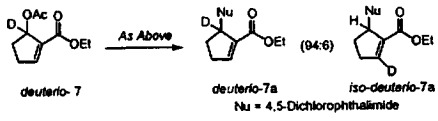
entry	substrate	nucleophile (NuH)	yield (%)
1	R = $PO(OEt)_2$	4,5-dichlorophthalimide	3
2	R = BOC	phthalimide	12
3	R = BOC	4,5-dichlorophthalimide	77
4	R = Bz	4,5-dichlorophthalimide	79
5	R = p-NO_2Bz	4,5-dichlorophthalimide	32
6	R = Ac	phthalimide	8
7	R = Ac	4,5-dichlorophthalimide	90

[a] Procedure: To a reaction vessel charged with 1 (0.5 mmol, 100 mol %), imide (1.0 mmol, 200 mol %), and PPh_3 (0.1 mmol, 20 mol %) was added THF (1.6 mL, 0.3 M). The reaction was allowed to stir at ambient temperature for 24 h, at which point the reaction mixture was evaporated onto silica gel and the product was isolated by silica gel chromatography.

Scheme 2. Phosphine-Catalyzed Regioretentive Allylic Amination of Cyclic MBH Acetates 7 and 8



Scheme 3. Deuterium Labeling Study Corroborates Proposed Tandem S_N2'–S_N2' Mechanism



Scheme 4. Establishing the Feasibility of Deracemization via Chiral Phosphine Catalysts

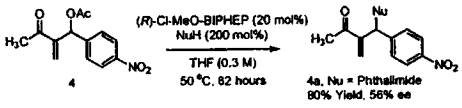
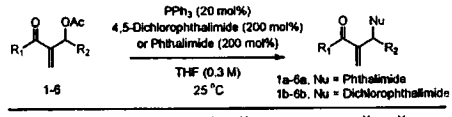
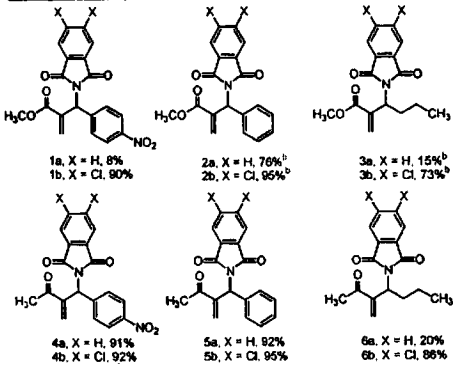


Table 2. Intermolecular Phosphine-Catalyzed Allylic Alkylation of Morita–Baylis–Hillman Acetates 1–6[a,b]





[a] Procedure: as described in Table 1. [b] Reaction performed at 50 °C.

Nitrogen Pronucleophile

△Pka between the conjugated acid of the leaving group and the pronucleophile is crucial to reaction.

Combination of acetate and 4,5-dichlorophthalimide gave the product with high yield.

Scope and limitation

For ester substrate 4,5-dichloro phthalimide gave higher yield.

but for ketone substrate, both nucleophile gave high yield.

Check the direct substitution

Favor of retention of regiochemistry.

tandem S_N2'-S_N2' mechanism.

Dynamic kinetic resolution

was possible using chiral phosphine.

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