Literature Seminar   040929   H. Kakei (D1)

Radical Reactions Using Persistant Radical Effect

⟨Content⟩

1. Introduction

2. Application to organic synthesis using the Persistant radical effect of alkoxyamine

3. Radical coupling reaction with organotellurium compounds

1. Introduction

The Persistant Radical Effect (PRE) is a general principle that explains the highly specific formation of the cross-coupling product R^1-R^2 between two radicals R^1 and R^2 when one species is persistent $(R^1\cdot)$ and the other is transcient $(R^2\cdot)$ and the two radicals are formed at equal rates

$$R_1-R_2 \xrightarrow{k_h} R_1\cdot + R_2\cdot \text{ (homolysis)}$$

$$R_1\cdot + R_2\cdot \xrightarrow{k_c} R_1-R_2 \text{ (cross coupling)}$$

$$R_2\cdot + R_2\cdot \xrightarrow{k_d} R_2-R_2 \text{ (dimerization)}$$

$$(R_1\cdot + R_1\cdot \not\rightarrow R_1-R_1)$$

$[R^1-R^2]$ = 0.1M
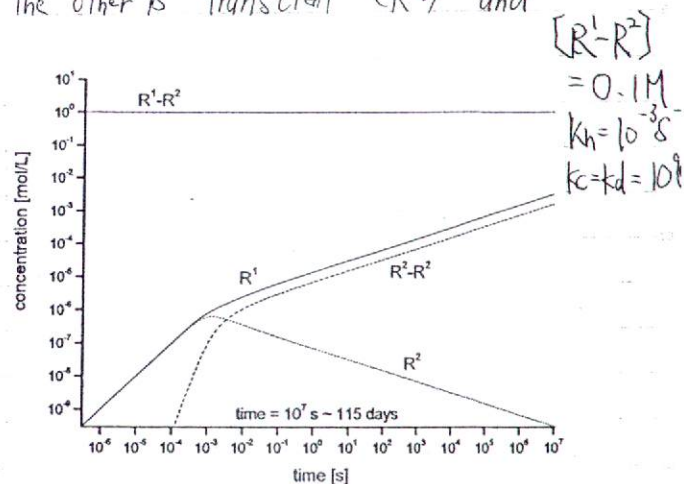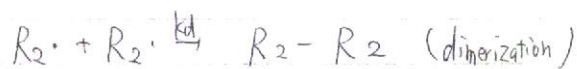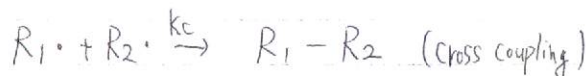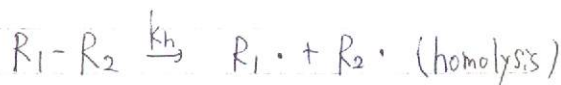$k_h = 10^{-3} s$
$k_c = k_d = 10^9$

Fig. 1 Simulation of the first 115 days of a reaction obeying the principle of the PRE.

The first report of PRE was published in 1936 by Bachman and Wiselogle.

J. Org. Chem. 1936. 1. 354

THE RELATIVE STABILITY OF PENTAARYLETHANES. III.[1]
THE REVERSIBLE DISSOCIATION OF PENTA-ARYLETHANES*

W. E. BACHMANN AND F. Y. WISELOGLE

$$R_4C-CHR_4 \rightarrow R_4C- + R_4CH- \qquad (5)$$

$$R_4C- \rightarrow \text{decomposition products*} \qquad (6)$$

$$2R_4CH- \rightarrow R_4CH-CHR_4 \qquad (7) \qquad R=Ar$$

yellow color

$$2R_4C-CHR_4 \underset{n}{\overset{n}{\rightleftharpoons}} 2R_4C- \quad 2R_4CH- \qquad (9)$$
$$R_4C-CR_4 + R_4CH-CHR_2$$
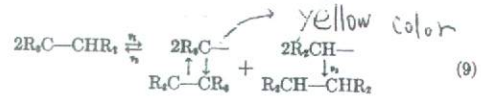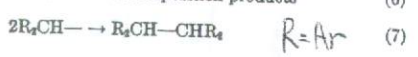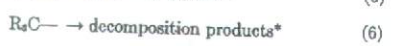
s-tetra-p-biphenylethane after being heated for two hours in o-dichlorobenzene at 100°, the original compound being recovered in 87 per cent. yield. This relative stability of pentaarylethanes, in marked contrast to their reactivity at these temperatures, made it seem very probable that *the dissociation of pentaarylethanes is a reversible reaction for which the position of equilibrium is practically entirely in favor of the pentaarylethane.* Moreover the immediate appearance of color on heating a solution of pentaarylethane above 100° precludes an explanation of the stability in terms of a slow irreversible dissociation process.

TABLE III
TIMES REQUIRED FOR 0.00125 MOLAR SOLUTIONS OF PENTAARYLETHANES IN o-DICHLOROBENZENE TO ABSORB 0.5 MOLE OF OXYGEN AT 100°*

COMPD.	MIN.	COMPD.	MIN.	COMPD.	MIN.	COMPD.	MIN.
0-	4.5	1-	3.5	1,1-	2.5	1,1,1-	2.0
2-	3.5	1,2-	2.5	1,1,2-	1.5	1,1,1,2-	1.0
2,2-	2.5	1,2,2-	1.5	1,1,2,2-	1.0	1,1,1,2,2-	0.8

* The effect of replacing phenyl groups on the "1" carbon by biphenyl groups is apparent from reading horizontally; the effect of introducing biphenyl groups on the "2" carbon is shown in the vertical columns.
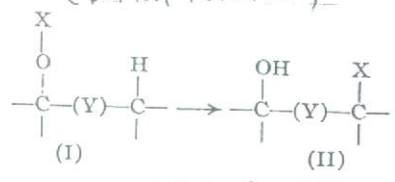
The chief product of the oxidation of a pentaarylethane at 100° was found to be the unsymmetrical triarylmethyl-(diarylmethyl)-peroxide, $R_4C-O-O-CHR_2$;*
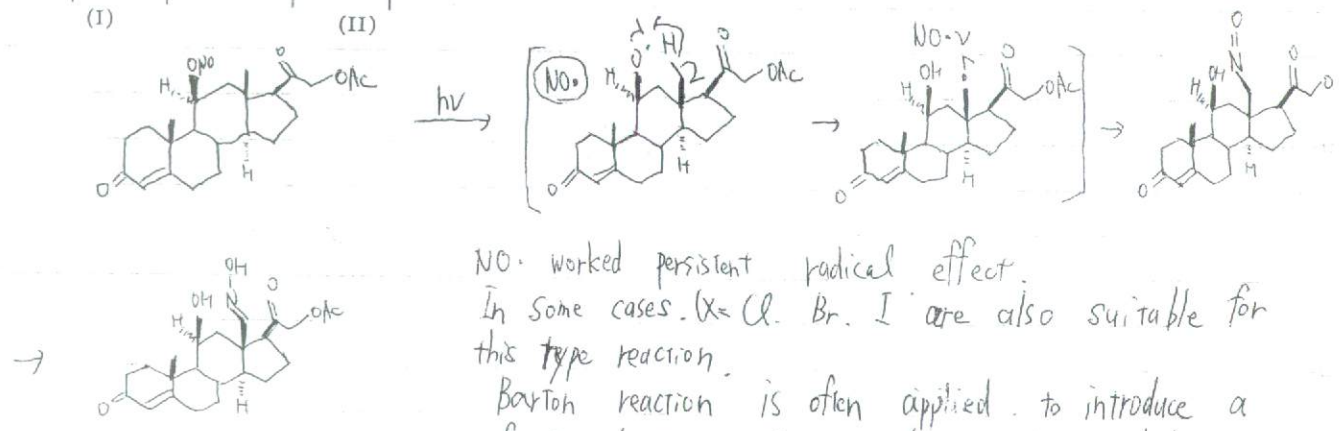
$$Ph_3C-CHPh_2 + O_2 \xrightarrow{100°C} Ph_3C-O-O-CHPh_2$$
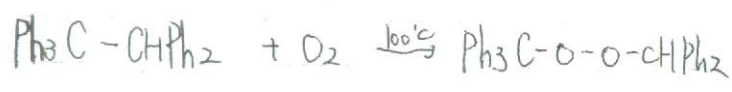
Old example of useful reaction using persistent radical effect.

J. Am. Chem. Soc. 1960. 82. 2640

A NEW PHOTOCHEMICAL REACTION
(Barton reaction)

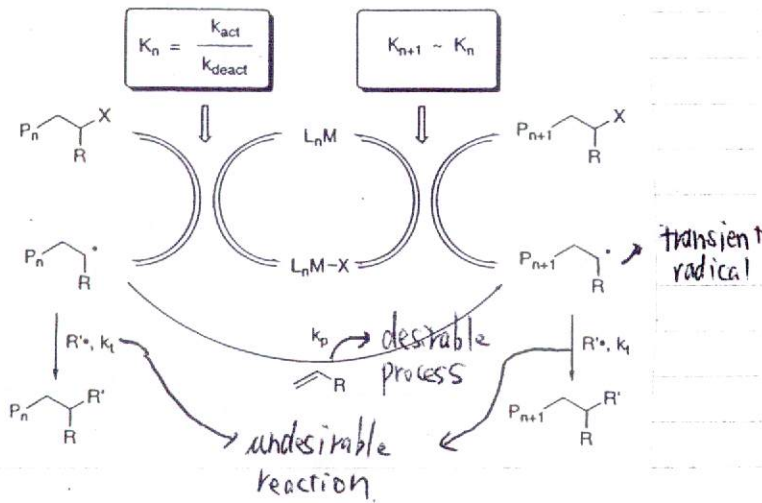D. H. R. BARTON
J. M. BEATON
L. E. GELLER
M. M. PECHET

NO· worked persistent radical effect.
In some cases (X = Cl. Br. I are also suitable for this type reaction.
Barton reaction is often applied to introduce a functional group into less reactive methyl group.

Typical examples using the Persistent Radical Effect
— Living radical polymerizations —

① Metal catalyzed a on transfer radical polymerization

General Mechanism for Atom Transfer Radical Polymerization (ATRP)

$$K_n = \frac{k_{act}}{k_{deact}}$$

$$K_{n+1} \sim K_n$$

$P_n \overset{X}{\underset{R}{\diagdown}}$ L_nM $P_{n+1} \overset{X}{\underset{R}{\diagdown}}$

$P_n \overset{\bullet}{\underset{R}{\diagdown}}$ L_nM-X $P_{n+1} \overset{\bullet}{\underset{R}{\diagdown}}$ → transient radical

$R'^\bullet, k_t$ k_p → desirable process $R'^\bullet, k_t$

$P_n \overset{R'}{\underset{R}{\diagdown}}$ → undesirable reaction ← $P_{n+1} \overset{R'}{\underset{R}{\diagdown}}$

L_nM-X complex supports persistent radical effects

Cu (I) complex   Matyjaszewski et al
J. Am. chem. Soc. 1995. 117. 5614
Macromolecules 1995. 28. 7901

$\overset{Cl}{\diagup}$ + n (styrene) $\xrightarrow[130\,°C]{CuCl / 2\ bipy}$ (polymer)
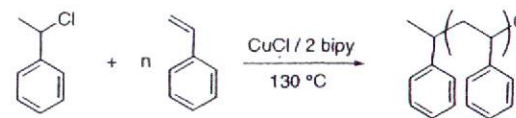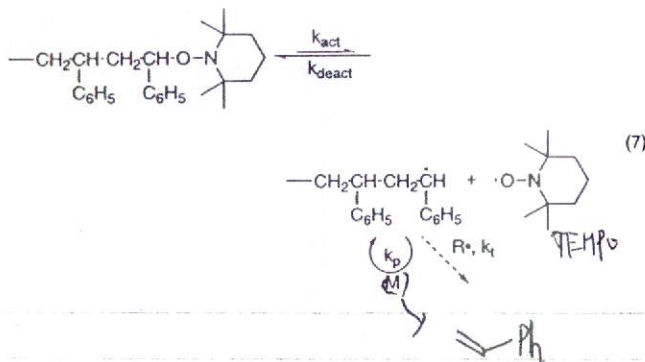
Ru (II) complex   Sawamoto et al.
Macromolecules 1995, 28, 1721
Macromolecules 1996, 29, 1070
Ni (II) complex   Granel et al.
Macromolecules 1996, 29, 8576
Fe (II) complex   Sawamoto et al
Macromolecules 1997 30 4507

② Nitroxide mediated radical polymerizations

$-CH_2CH\cdot CH_2CH\text{-}O\text{-}N\langle\ \rangle$ $\underset{k_{deact}}{\overset{k_{act}}{\rightleftharpoons}}$
$\quad\ \ \overset{|}{C_6H_5}\ \ \overset{|}{C_6H_5}$

$-CH_2CH\cdot CH_2\overset{\bullet}{C}H\ +\ \cdot O\text{-}N\langle\ \rangle$ (7)
$\quad\ \ \overset{|}{C_6H_5}\ \ \overset{|}{C_6H_5}$ TEMPO
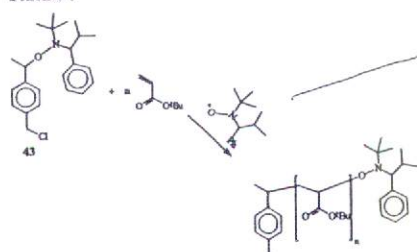 (k_p) $R^\bullet, k_t$
  (M)
  $\diagup\!\diagdown$ Ph

TEMPO works as persistent radical

George et al.
Macromolecules 1993. 26. 2987

Development of a Universal Alkoxyamine for "Living" Free Radical Polymerizations

Didier Benoit,[†] Vladimir Chaplinski,[‡] Rebecca Braslau,[*,‡] and Craig J. Hawker[*,†]

Scheme 7

Hawker developed library of alkoxy amine.

This nitroxide improved substrate generality and efficiency
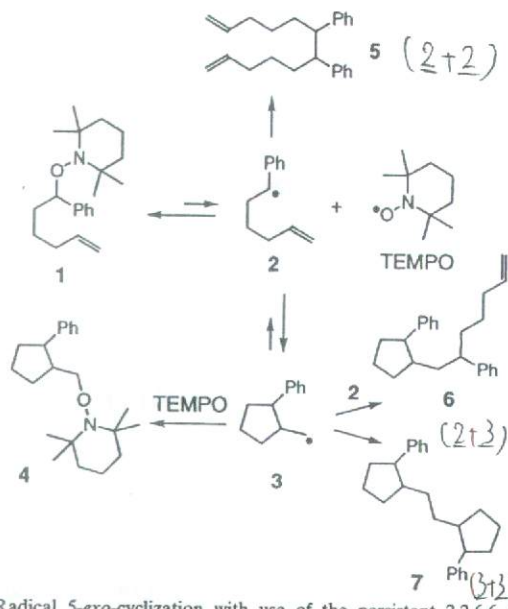↳ not only styrene but also acrylate.

[2] Application to organic synthesis using the Persistant Radical Effect of Alkyoxy amine.

(1) Application 1

Tin-Free Radical Cyclization Reactions Using the Persistent Radical Effect**
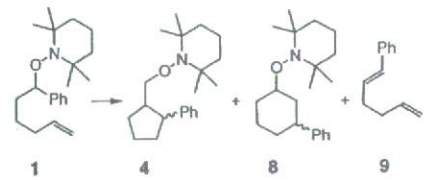
Armido Studer*

Angew. Chem. Int. Ed. 2000, 39, 1108

· Strategy

Scheme 1. Radical 5-exo-cyclization with use of the persistent 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) radical.

· Results and Solvent effects.

Table 1. Isomerization of **1** under different conditions (130–132°C, sealed tube).

Entry	Solvent	Conc. [M]	t [h]	4 [%]	8 [%]	9 [%]
1	tBuPh	0.1	22	< 2[a]	< 2[a]	20
2	DMPU	0.1	14	< 2[a]	< 2[a]	< 2[a]
3	DMF	0.1	16	56	10	< 2[a]
4	tBuOH	0.1	16	n.d.[b]	n.d.[b]	< 2[a]
5	tBuOH	0.01	36	n.d.[c]	n.d.[c]	< 2[a]
6	tBuOH	0.01	24[d]	53	10	< 2[a]
7	tBuOH	0.02	24[d]	70	13	2

[a] In the 300-MHz ^{1}H NMR spectrum of the crude product, no signals of the corresponding compound were observed. [b] After 16 h, 62% of the starting material remained. Products **4** and **8** were not isolated. [c] After 36 h, about 10% of starting material remained. Products **4** and **8** were not isolated. [d] 10% CSA was added.

↳ the rate of C–O bond cleavage is increasing upon increasing the polarity

· Scope and Limitation.

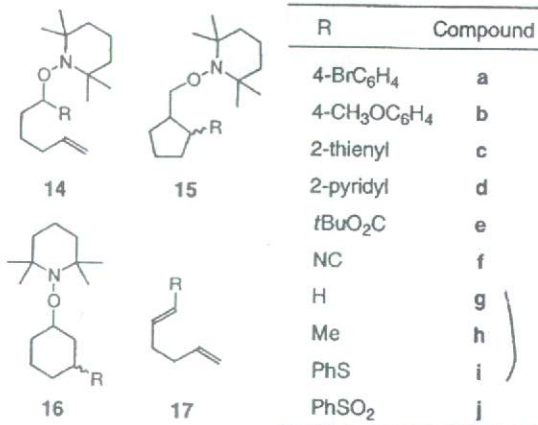| R	Compound
4-BrC$_6$H$_4$	a
4-CH$_3$OC$_6$H$_4$	b
2-thienyl	c
2-pyridyl	d
tBuO$_2$C	e
NC	f
H	g
Me	h
PhS	i
PhSO$_2$	j

Table 2. Isomerization of **14a–f** under optimized conditions (tBuOH, 0.02M, 24 h, 130–132°C, 10% CSA, sealed tube). Yields refer to chromatographically (SiO$_2$) purified compounds.

Entry	Starting material	15 [%]	d.r. (15) (trans:cis)	16 [%][a]	17 [%]
1	14a	71	2.7:1	8	< 2[b]
2	14b	46	2.8:1	8	10
3	14c	67	2.1:1	11	5
4	14d	57	1.6:1	12	5
5	14e	67	1:1	< 2[b]	10
6	14f	61	1.1:1[c]	7	< 2[b]

[a] The 6-endo product was formed as a 1:1 mixture of the diastereoisomers. [b] In the 300-MHz ^{1}H NMR spectrum of the crude product, no signals of the corresponding compound were observed. [c] The relative configuration of the two isomers was not assigned.
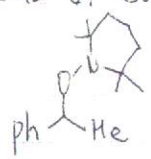
C–O bonds of 14g–i too strong to be effectively cleaved.

In case of 14j, elimination of PhSO$_2$H proceeded.
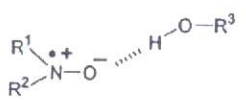
Effects of solvents. and CSA.

(1) Effects of polarity

in tBuPh $k_{(393)} = 5.2 \times 10^{-4} s^{-1}$
CℓPh $k = 1.2 \times 10^{-3} s^{-1}$ } 2.3 times faster in polar solvent

↳ the results were shown in the J. org. chem.
2001. 66. 1146 Studer et al.

(2) Effects of protic source

$R^1, R^2 - \overset{+}{N} - O^- \cdots H - O - R^3$ → Polar protic solvents intermolecular H-bonding may also accelerate the C-O bond cleavage.

(3) Effects of CSA

Influence of Acids on Reaction Rates of Free Radical Scavenging by TEMPO. Relevance to "Living" Free Radical Polymerizations

M. V. Baldoví, N. Mohtat, and J. C. Scaiano*
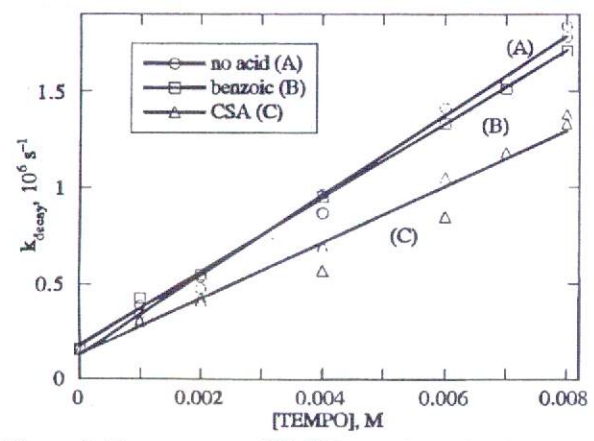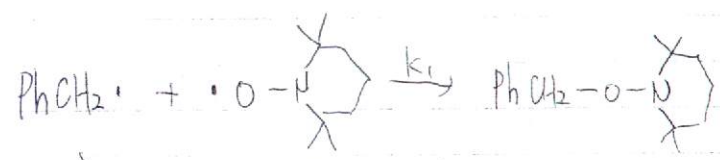
macromolecules. 1996. 29. 5497

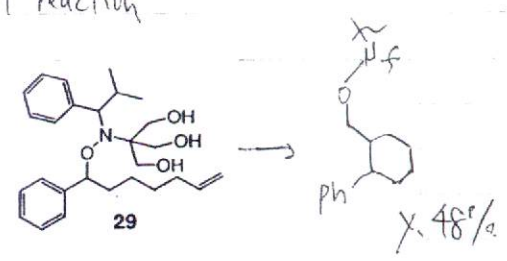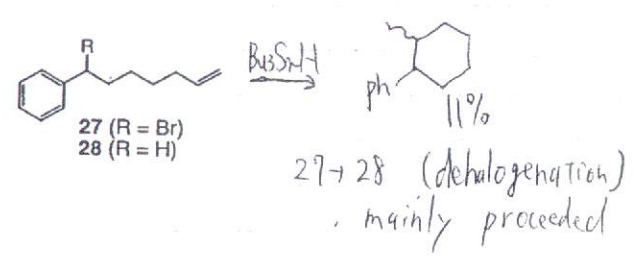Figure 1. Representative TEMPO quenching plots for benzyl radicals generated from DBK in the absence and presence of 40 mM acid, in dry THF at room temperature.

$PhCH_2 \cdot + \cdot O - N \xrightarrow{k_1} PhCH_2 - O - N$

↳ CSA causes a reduction in the rate of this process.

Comparison to Bu$_3$SnH mediated radical reaction

27 (R = Br)
28 (R = H)

Bu$_3$SnH

11%

27 → 28 (dehalogenation)
. mainly proceeded

29

X. 48%

Improvement and Mechanis Studies.
1. Structure effects of alkoxy Amines.

Factors Influencing the C–O–Bond Homolysis of Trialkylhydroxylamines

Sylvain Marque,[†] Christophe Le Mercier,[‡] Paul Tordo,[‡] and Hanns Fischer*,[†]

↳ Determination of k_d values of Alkoxy amines

① In case of Nitroxide radicals which have long half lives

$$\ln\left(\frac{[\text{nitroxide}]_\infty - [\text{nitroxide}]_t}{[\text{nitroxide}]_\infty}\right) = -k_d t \qquad (5)$$
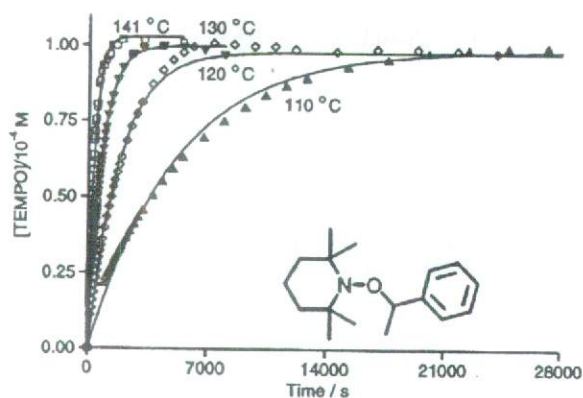

Figure 2. Time dependence of the TEMPO concentration during thermolysis of TEMPO–PhEt in the presence of excess scavengers: 141 °C, galvinoxyl; 130, 120, and 110 °C, TMIO–$^{15}ND_{12}$. Lines are fits of eq 5 to the data.
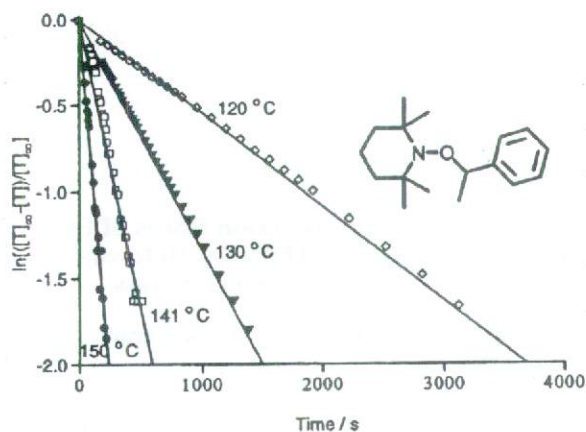

Figure 3. First-order plot (data partially shown in Figure 2) according to eq 5.

② In case of Nitroxide radicals which have short. half lives

$$[\text{nitroxide}]_t / [\text{nitroxide}]_\infty = k_d t \qquad (6)$$

→ The initial Slope of the signal rise at less than 20% conversion was evaluated according to eq 6
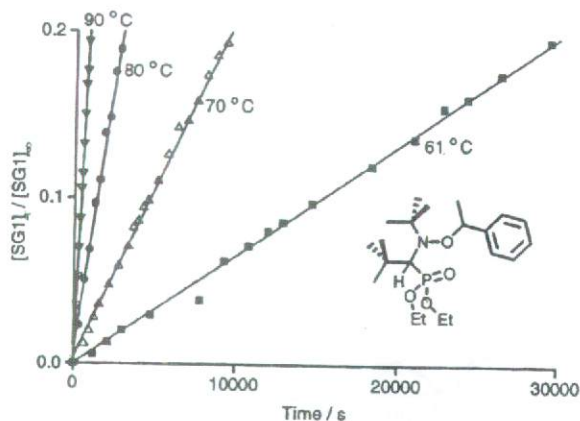
Figure 4. Time dependence of the SG1 concentration during the thermolysis of SG1–PhEt in the presence of excess scavengers: 90, 70, and 61 °C, galvinoxyl; 80 °C, TMIO–$^{15}ND_{12}$. Lines are fits of eq 6 to the data.

~ Appendix ~

①
$$[\text{nitroxide}]_t = [\text{nitroxide}]_\infty - [\text{nitroxide}]_\infty e^{-kt}$$

$$e^{-kt} = \frac{[\text{nitroxide}]_\infty - [\text{nitroxide}]_t}{[\text{nitroxide}]_\infty}$$

$$-k_d t = \ln\left(\frac{[\text{nitroxide}]_\infty - [\text{nitroxide}]_t}{[\text{nitroxide}]_\infty}\right)$$

② $t \approx 0$
$$e^{-k_d t} \doteq 1 - k_d t$$

$$k_d t = \frac{[\text{nitroxide}]_t}{[\text{nitroxide}]_\infty}$$

Determined k_d values are not dependent on kinds of scavengers.

Table 2. C−O Bond Homolysis Rate Constants of Alkoxyamines (10^{-4} M) Obtained with Different Scavengers

| scavenger	k_d/s^{-1}				
	TEMPO−Cum 90 °C	TEMPO−PhEt 140 °C	TEMPO−Bz 130 °C	SG1−PhEt 110 °C	DBNO−PEst 80 °C
galvinoxyl	4.3×10^{-3} [a]	3.3×10^{-3}	2.1×10^{-5} [b]	2.3×10^{-3} [b]	7.6×10^{-3}
TMIO−^{15}ND$_{12}$	5.3×10^{-3}	3.7×10^{-3}	4.0×10^{-5} [b]	2.5×10^{-3}	7.2×10^{-3}
air	7.0×10^{-3} [c]	3.8×10^{-3}			7.1×10^{-3}

[a] [TEMPO−Cum] = 2×10^{-3} M. [b] Calculated with eq 6. [c] 93 °C.

Table 5. Experimental and Estimated[a] Rate Constants (s^{-1})
for the Dissociation of Trialkylhydroxylamines at 120 °C

	TEMPO	SG1	DBNO
Cum−	8.5×10^{-2}	*1.7*	*2.7*
PCN−	0.13	*0.7*	*1.2*
PEst−	2.2×10^{-2}	*0.5*	*0.31*
PhEt−	5.2×10^{-4}	5.5×10^{-3}	1.4×10^{-2}
EEst−	3.4×10^{-5}	3.0×10^{-3}	1.1×10^{-3}
Bz−	1.1×10^{-5}	3.3×10^{-4}	1.9×10^{-4}
MEst−	8.1×10^{-8}	*2.2×10^{-6}*	*1.8×10^{-6}*
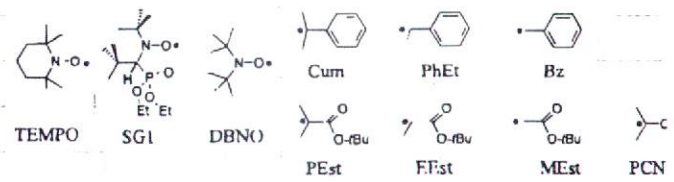
[a] Estimated rate constants in italics, obtained with $A = 2.6 \times 10^{14}$ s^{-1}

and the average activation energies

k_d values of SG1 and DBNO are apparently larger than TEMPO.
Isomerization promoted by 18 or 19 is faster than TEMPO.

18 (3hr)   19 (4.5hr)
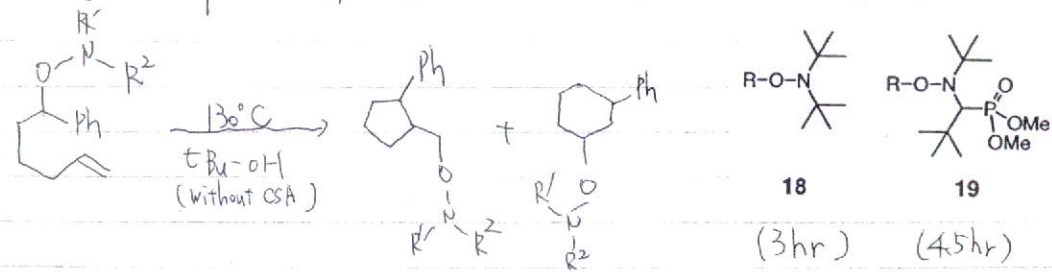
Factors Influencing the C−O Bond Homolysis of Alkoxyamines:
Effects of H−Bonding and Polar Substituents

J. Org. Chem. 2001. 66

Sylvain Marque,*,† Hanns Fischer,† Elisabeth Baier,‡ and Armido Studer*,§
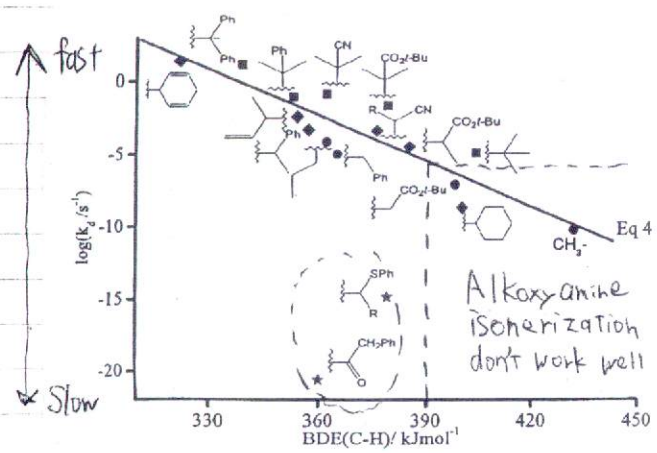
$$\log(k_d/s^{-1}) = 35.5(\pm 5.5) - 0.11(\pm 0.02)\text{BDE(C−H)} \qquad r^2 = 0.80$$
(4)

○ A linear correlation was obtained (Rate constant log(kd) for the C−ON bond cleavage)

○ In case of substrates shown as ★, Delocalization of lone pair of oxygen into n* or π* prevents the cleavage.

Alkoxyamine isomerization don't work well

Figure 3. Rate constants $\log(k_d)$ for the C−ON bond cleavage of TEMPO derivatives of trialkylhydroxylamines vs BDE-(C−H) of the corresponding hydrocarbon: (■) tertiary alkoxyamines, (♦) secondary alkoxyamines, (●) primary alkoxyamines, (★) other alkoxyamines.

(2, Application ②
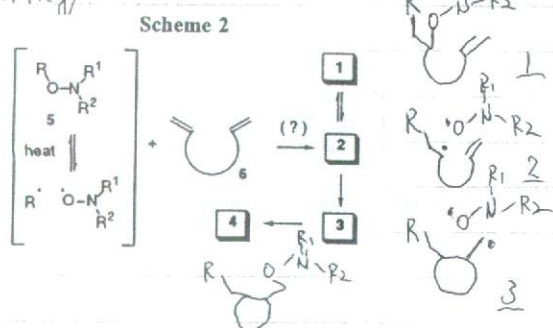
Alkoxyamine-Mediated Radical Cyclizations

Corinne Leroi,[†] Bernard Fenet,[‡] Jean-Luc Couturier,[§] Olivier Guerret,[§] and Marco A. Ciufolini[*,†]
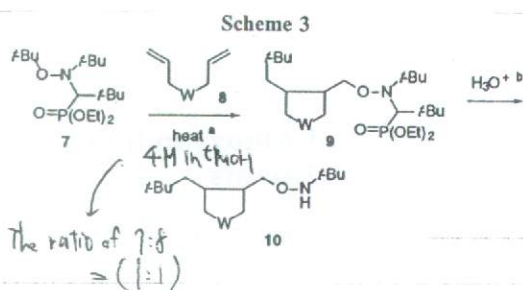
· Strategy.

Scheme 2

Intermediate **1** arise through binolecular addition of an alkoxyamine to bis olefin.

↓

· To promote the initial addition step via binolecular reaction. might be problematic.

· To prevent side reaction mediated by **5** or intermediates

Merit · Halogenated substrates and tin or silicon hydride reagents are not required

· Introduction of oxygenated functionality

· Results.

Scheme 3

The ratio of 7:8 ≥ (1:1)

· Selection of radical source might be key
  > tBu radical is highly reactive.
  Nitroxy radical (SG1) is stable

Table 1. Conjunctive Radical Cyclization of Substrates 8 with Alkoxyamine 7

$$8 \xrightarrow{7} 9 \xrightarrow{HCl} 10$$

entry	W	react. time[c]	yield of 9[d]	yield of 10[d]	cis/trans ratio[e]
a	CH₂	60	25	99	69:31
b	O	40	23	83	70:30
c	C(COOEt)₂	30	51	90	85:15
d	N-Cbz	65	29	83	60:40
e	N-SO₂C₆H₄-4-Br	30	42	74	66:33

[a] 4 M in t-BuOH, 120 °C. [b] 4 M HCl, dioxane, rt. [c] Hours. [d] Chromatographed yields. [e] Determined by 1-D and 2-D ¹H NMR.

Scheme 5

8l W = SO₂
8j W = P(O)(OEt)
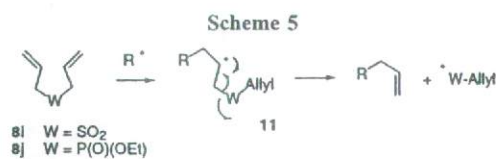
In case of substrates where in SO₂ or POli fragmentation occured.

5-hembered rings were obtained in moderate yield.

3, Application ③ (handwritten)

Intermolecular Radical Addition and Addition/Cyclization Reactions of Alkoxyamines onto Nonactivated Alkenes

Christian Wetter, Katja Jantos, Katharina Woithe, and Armido Studer*

Strategy (handwritten)

Scheme 2. PRE in Intermolecular Addition Reactions

4   TEMPO   5   6

① Reversible thermal C-O bond homolysis of an alkoxyamine. (handwritten)
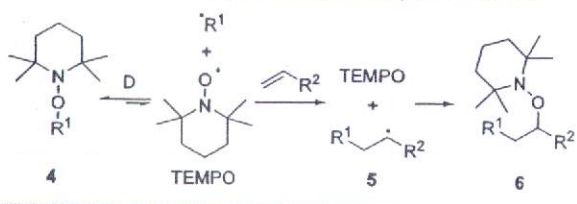② Reaction of R' with olefin afford radical adduct (handwritten)
③ Trapping by TEMPO (handwritten)

→ Carbohydroxylation (handwritten)

Examination of R_1 (handwritten)

7 ($R^1 = CO_2Me$, $R^2 = H$, $R^3 = Me$)
8 ($R^1 = Ph$, $R^2 = H$, $R^3 = Me$)
9 ($R^1 = R^2 = R^3 = Me$)
10 ($R^1 = R^2 = CO_2Me$, $R^3 = H$)
11 ($R^1 = R^2 = CO_2t$-Bu, $R^3 = H$)

+ ⌇C_6H_{13} octene (handwritten)
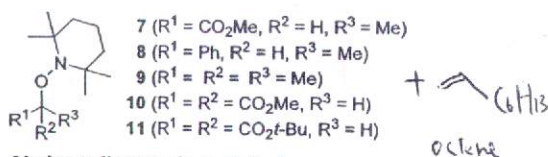
Figure 1. Various alkoxyamines studied.

→ 7 – 9 less (handwritten)

→ 10, 11 Malonyl radicals are suitable for this alkoxyamine mediated reaction. (handwritten)

CO_2R ⌇ CO_2R ↑ + (handwritten structure) $\xrightarrow{CuCl_2}$ 10 or 11 (handwritten)

Results and solvent effects (handwritten)

Table 1. Reaction of 10 and 11 with Various Olefins (5 equiv) at 135 °C for 3 days

10,11 $\xrightarrow[\text{or 11 in } t\text{-BuOH}]{\text{10 in ClCH}_2\text{CH}_2\text{Cl}}$ 12-20
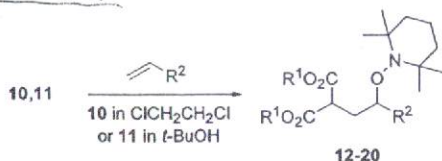
run	R^1	R^2	compd	solvent	yield (%)
1	Me	C_6H_{13}	12	t-BuOH	35[a]
2	Me	C_6H_{13}	12	MeOH	25
3	Me	C_6H_{13}	12	CH_3CO_2Et	55
4	Me	C_6H_{13}	12	DMF	46
5	Me	C_6H_{13}	12	C_6H_5Cl	63
6	Me	C_6H_{13}	12	$C_6H_5CF_3$	64
7	Me	C_6H_{13}	12	$ClCH_2CH_2Cl$	66
8	t-Bu	C_6H_{13}	13	t-BuOH	54
9	t-Bu	C_6H_{13}	13	t-BuOH	72[b]
10	t-Bu	C_6H_{13}	13	t-BuOH	76[c]
11	Me	CH_2CH_2Ph	14	$ClCH_2CH_2Cl$	49
12	Me	OBu	15	$ClCH_2CH_2Cl$	78
13	t-Bu	OBu	16	t-BuOH	69[b]
14	Me	$(CH_2)_3OCO_2Me$	17	$ClCH_2CH_2Cl$	42
15	t-Bu	$(CH_2)_3OCO_2Me$	18	t-BuOH	38[b]
16	Me	$(CH_2)_3OTBDMS$	19	$ClCH_2CH_2Cl$	70
17	t-Bu	$(CH_2)_3OTBDMS$	20	t-BuOH	55[b]

[a] Transesterification product formed in 36%; see text. [b] Reaction for 5 days. [c] Performed with 10 equiv of 1-octene.

(run 1) 35% of $R_1 = {}^t$Bu (transesterification) product was obtained (handwritten)

(run 7) ⌐ClCH₂CH₂Cl gave best result in case of $R_1 = Me$ (handwritten)

(run 9) ^{t}BuOH was suitable for $R_1 = {}^t$Bu (handwritten)

(run 11-17) substrate generality (handwritten)

→ 10 eq of olefin (handwritten) Reaction to terminally substituted olefin was also promoted (handwritten)

Scheme 3. Thermal Addition of 10 to Cyclohexene

10 $\xrightarrow[\text{ClCH}_2\text{CH}_2\text{Cl, 135 °C}]{\text{cyclohexene}}$ 21
(58%, *trans:cis* = 2.1:1)
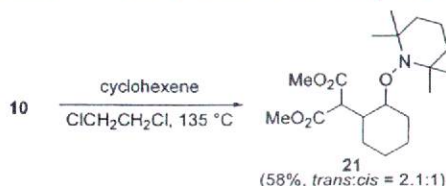
Application to cyclization

Scheme 4. Addition/Cyclization Reactions
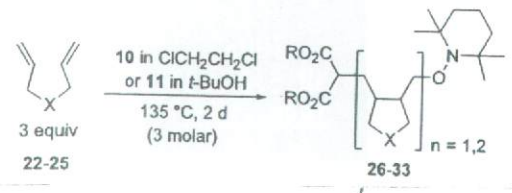
Telomerization was observed as a side reaction

Telomerization could compete with TEMPo trapping of the primary C-radical formed after cyclization

Table 2. Intermolecular Addition/Cyclization Reactions

starting material	X	R	product (n = 1)	(%)	cis:trans[a]
22	C(CO$_2$Me)$_2$	Me	26	68	
22	C(CO$_2$Me)$_2$	t-Bu	27	40[b]	2.2:1
23	O	Me	28	33[c]	1.8:1
23	O	t-Bu	29	37[d]	1.7:1
24	NTos	Me	30	49	1.3:1
24	NTos	t-Bu	31	42[e]	1.5:1
25	C(CH$_2$CH$_2$O)$_2$CMe$_2$	Me	32	36	2.3:1
25	C(CH$_2$CH$_2$O)$_2$CMe$_2$	t-Bu	33	34[f]	2.1:1

[a] Determined by HPLC or NMR. [b] Consisted of 10% telomer was isolated as a side product. [c] Performed with 6 equiv of 23. [d] Consisted of 12% telomer was isolated as a side product. [e] Consisted of 23% telomer was isolated as a side product. [f] Consisted of 12% telomer was isolated as a side product.

Deprotection

Scheme 6. Reductive N—O Bond Cleavage with Subsequent Lactonization

40 (73%, dr = 1:1)

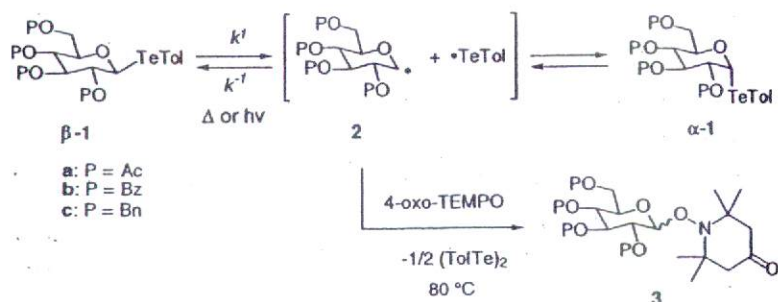→ amino hydroxy product can be converted to alcohol

[3] Radical coupling reactions with organotellurium compounds.
(1) Introduction

Reversible Generation of Glycosyl Radicals from Telluroglycosides under Photochemical and Thermal Conditions

Tetrahedron Lett. 1999, 40, 23??

Shigeru Yamago*, Hiroshi Miyazoe and Jun-ichi Yoshida*

(1)

Telluroglycoside **1** generates glycosyl radical **2** under photolysis or thermolysis by homolitic C-Te bond cleavage.
While the glycosyl radical so generated predominantly returned to the starting telluroglycoside without trapping reagents.

> Telluroglycoside shows persistent radical effects.

After irradiation by some light sources Both stereochemically pure α-, β- glycosides were isomerized to the mixture of α and β isomers in the same ratio.

Table 1. Photochemical and Thermal Isomerization of Telluroglycosides.

Entry	Telluroglycoside	λmax (nm)[a]	hv[b]	Time (h)[c]	α:β[d]	% Recovery[d]
1	β-1a	324	A	2	84:16	76
			A[e]	2	70:30	100
			B	2	81:19	79
			C	5	69:31	90
			D	8	69:31	28
2	α-1a	326	A	0.5	83:17	100
3	β-1b	324	A	2	86:14	91
4	α-1b	325	A	0.6	87:13	87
5	β-1c	327	A	1	88:12	83
			D	10	89:11	92
6	β-4	324	A	2	89:11	99
7	β-5	324	A	2	83:17	32
8	α-6	(302)[f]	A	40	27:73	77

[a] UV absorption corresponding to the tellurium moiety. [b] Photochemical reaction was carried out in C₆D₆ at 40 °C with irradiation by various light sources. A: Rayonet RMR-3000Å (3.9 W x 8) was used. B: Rayonet RMR-3500Å (4.5 W x 8) was used. C: Xe lamp (5.4 W) was used. D: The reaction under the dark at 140 °C. [c] The time required for the complete equilibration as monitored by ¹H NMR. [d] Determined by ¹H NMR. [e] The reaction was carried out in CD₃CN. [f] No characteristic UV absorption corresponding to the tellurium moiety was observed.

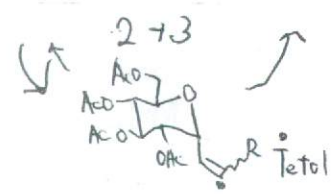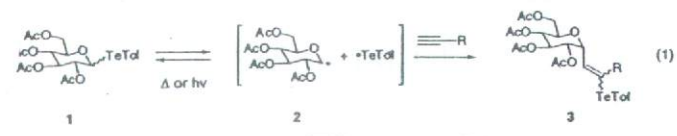(2) Application ① Glycosyl radical addition to alkynes

Synthesis of Vinylic *C*-Glycosides from Telluroglycosides. Addition of Photochemically and Thermally Generated Glycosyl Radicals to Alkynes

Shigeru Yamago*, Hiroshi Miyazoe and Jun-ichi Yoshida*

Tetrahedron Lett. 1999. 40. 2343

(1)

2 + 3

Aryl and heteroaryl-substituted alkynes were good acceptor. (entry 1~5)

Acetylene carboxylic ester and Alkyl-substituted alkynes were not so reactive.

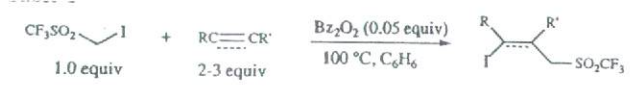α-Isomers were preferentially obtained in all cases. (anomeric effect)

The E:Z ratio is not high.

Table 1. Telluroglycoside Addition to Alkynes.[a]

Entry	Telluroglycoside	Alkyne	Major product	%Yield[b]	α(E:Z):β[c]
1	1	≡—⟨⟩—X	3a	93	75(61:39):25
		X = H		81[d]	78 (64:36):22
				87[e]	83 (54:46):17
				89[f]	78 (47:53):22
2		X = CO₂Me	3b	79	77(58:42):23
3		X = OMe	3c	70	75(61:39):25
4		≡—⟨pyridyl⟩		78	80 (59:41):20
5		≡—⟨furyl⟩		48	79 (67:33):21
6[g]		≡—CO₂Me		38 (50)[h]	69 (49:51):31
7		≡—n-C₆H₁₃		11 (23)[h]	74 (45:55):26
				24[e] (56)[h]	72 (51:49):21
8[g]		≡—⟨steroid⟩		41	76 (63:37):24
9	AcO...TeTol	≡—⟨⟩		94	90 (50:40):10
10	AcO...TeTol			55	90 (53:37):10

[a] The reaction was carried out by UV irradiation of neat telluroglycoside and 5 equiv. of alkynes at 120 °C for 20 h. [b] Isolated yield. [c] Isomeric ratio was determined by the ¹H NMR analysis of the crude reaction mixture. The β-isomer consisted of a ca. 1:1 mixture of the *E*- and *Z*-isomers. [d] The reaction was carried out in the dark at 120 °C for 20 h. [e] The reaction was carried out in the presence of 10 mol% of AIBN at 80 °C in the dark for 20 h. See ref. 6c. [f] The reaction was carried out in the presence of 10 mol% of AIBN at 120°C in the dark for 20 h. [g] The reaction was carried out at 100 °C. [h] Yield based on the converted telluroglycosides. [i] Reaction was carried out with 5 equiv. of 1 in toluene, and the yield was based on the alkyne.

• "I atom transfer mediated C radical additions. were well known. ⟶ for example But to prepare glycosyl iodide is difficult. J. Am. Chem. Soc 1995. 117. 3272

CF₃SO₂—I   +   RC≡CR'   —Bz₂O₂ (0.05 equiv)→   R—C=C(R')—SO₂CF₃ (with I)
1.0 equiv   2-3 equiv   100 °C, C₆H₆

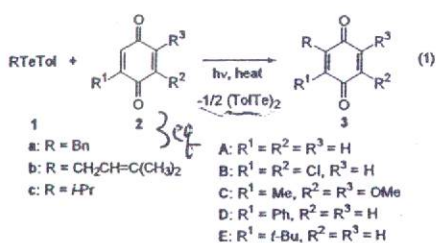• Tin radical (Bu₃SnH) reacts alkyne faster than glycosil radical precursor

• The stability of Csp₂—Te promoted this reaction.

3) Application ② Alkyl radical additions to quinones

Radical-Mediated Synthesis of Substituted Quinones with Organotellurium Compounds

Shigeru Yamago,* Masahiro Hashidume, and Jun-ichi Yoshida*

Chem. Lett. 2000. 1235

$$RTeTol + \text{(quinone)} \xrightarrow[\text{-1/2 (TolTe)}_2]{hv, heat} \text{(product)} \quad (1)$$

1
a: R = Bn
b: R = CH$_2$CH=C(CH$_3$)$_2$
c: R = i-Pr

2 3 eq

A: R^1 = R^2 = R^3 = H
B: R^1 = R^2 = Cl, R^3 = H
C: R^1 = Me, R^2 = R^3 = OMe
D: R^1 = Ph, R^2 = R^3 = H
E: R^1 = t-Bu, R^2 = R^3 = H

Table 1. Synthesis of substituted quinones [a]

Entry	RTeAr	Quinone	Time/h	Product	Yield/%
1	1a	2A	1	3aA	57
2		2B	1	3aB	71
3		2C	2	3aC	53
4		2D	2.5	3aD	57
5		2E	1		55
					23
6		4	1		87
7			1.5		64
8	1b	2C	2	3bC	41
9		4	2		61
10	1c	2A	3	3cA	44

[a] See Ref. 11 for the experimental procedures. Two equivalents of quinone were used in all cases.

In case of ordinary radical reaction. radical promoters (Bu$_3$Sn H $\cdots$) react prior to other radical.

Organotellurium Compounds reversibly generate carbon centered radicals. these radicals react with ketones.
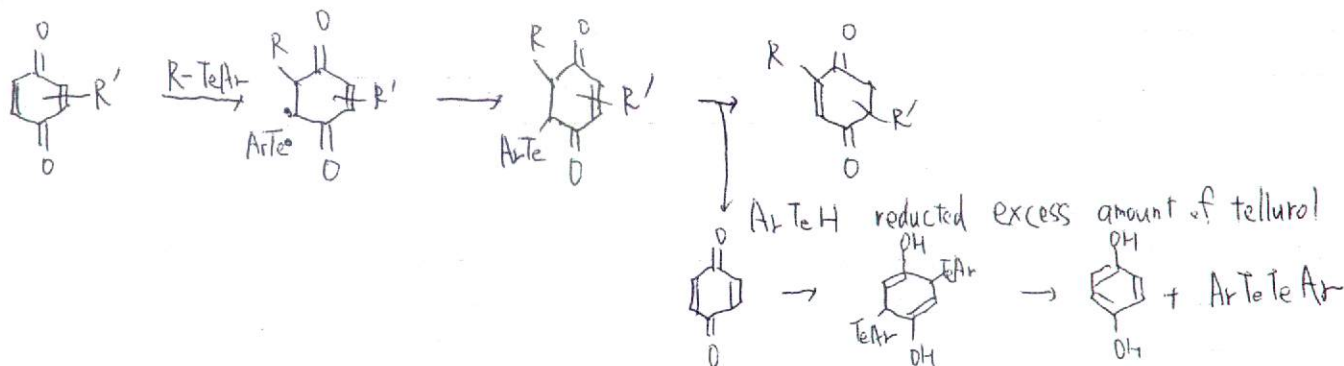
After reaction, diaryldaitelluride generated. (½ eq)

Ph group effects the regioselectivity

regioselectivity was poor

Speculated mechanism

Ar Te H reduced excess amount of tellurol

Application ③ Group-Transfer Imidoylation of Organotellurium Compounds

Synthetic and Theoretical Studies on Group-Transfer Imidoylation of
Organotellurium Compounds. Remarkable Reactivity of Isonitriles in
Comparison with Carbon Monoxide in Radical-Mediated Reactions

J. Am. Chem. Soc.
2001, 123, 3696

Shigeru Yamago,* Hiroshi Miyazoe, Ryuta Goto, Masahiro Hashidume,
Takashi Sawazaki, and Jun-ichi Yoshida*

Carbonylation

$$R\cdot \ + \ \overset{O}{\underset{\cdot\cdot}{C}} \ \rightleftharpoons \ R\overset{O}{\underset{\cdot}{C}}\cdot \quad (1)$$

→ This process proceeded under high pressure of CO.
→ Stable radicals (benzyl-, α-carbonyl) can't apply this reaction.

Imidoylation

$$R\cdot \ + \ \overset{NR'}{\underset{\cdot\cdot}{C}} \ \rightleftharpoons \ R\overset{NR'}{\underset{\cdot}{C}}\cdot \quad (2)$$

isonitrile

→ The imidoyl radical is reactive.
→ The reverse reaction : don't proceed

Target reaction

$$R-TeAr \ + \ \overset{NAr'}{\underset{\cdot\cdot}{C}} \ \xrightarrow{h\nu/heat} \ R\overset{NAr'}{\underset{TeAr}{}} \quad (3)$$
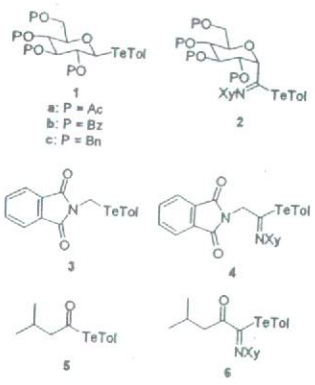
Table 1. Imidoylation under Various Conditions[a]

entry	substrate	solvent	$h\nu$[b]	temp (°C)	time (h)	product	yield (%)
1	1a	C_6D_6	A	100	10	2	65 (95)[c]
2	1a	C_6H_6	B	100	4	2	74
3	1a	C_6D_6	dark	140	50	2	43
4	3	C_6H_6	A	60	50	4	85
5	3	C_6H_6	B	80	2	4	91
6	3	C_6H_6	C	80	3	4	90
7	3	C_6H_6	C	80	6	4	91
8	3	hexane	C	80	3	4	67
9	3	$(CH_2Cl)_2$	C	80	3	4	85
10	3	THF	C	80	3	4	84
11	3	DMF	C	80	3	4	86
12	3	pyridine	C	80	3	4	80
13	3	CH_3OH	C	80	3	4	73
14	5	C_6D_6	A	100	12	6	74
15	5	C_6D_6	B	100	12	6	41
16	5	C_6D_6	dark	100	12	6	87
17	5	hexane	dark	100	12	6	83
18	5	CD_3CN	dark	100	12	6	73
19	5	EtOH	dark	100	12	6	80
20	5	H_2O	dark	100	12	6	87

[a] Two equivalents of xylylisonitrile were used except in entry 7, where 1.2 equiv of the isonitrile was used. [b] A: Rayonet RMR600 reactor equipped with a RMR-3500 Å lamp (4.5 W x 8) was used. B: USHIO Optical Modulex reactor equipped with a 250 W Hg lamp was used. C: a 100 W Hg lamp was used. [c] Yield based on the converted substrate.
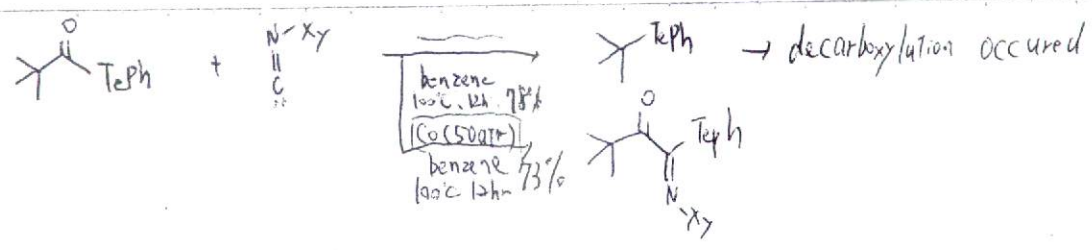
1
a: P = Ac
b: P = Bz
c: P = Bn

2

3

4

5

6

Proposed Mechanism

R—TeAr ⟶ hv or heat, -[ArTe·] ⟶ R·
path a / path b, +[ArTe·]
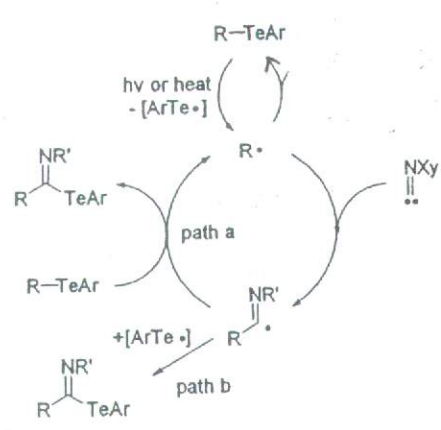
Entry 1-3 Glycosyl radical coupled with xylylisonitrile.
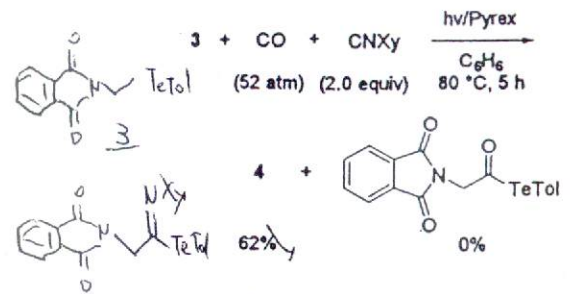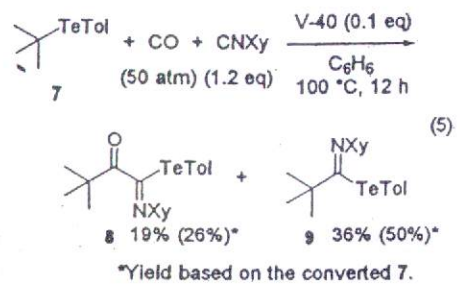   Stronger UV irradiation shortened reaction (B > A > dark)

Entry 4-13 N-phthalimide derivative coupled.
            Solvent effects are negligible (Entry 6-13)

Entry 14-20 acyl telluride was used
             UV irradiation promotes consumption 5, and decomposition
             (decarboxylation) of 6
             The better result obtained in dark.

(structure: tBu-C(=O)-TePh) Tephil + (structure: N=Xy, C)

benzene
100°C, 12h, 78%

(Co(50atm))
benzene
100°C, 12h, 73%

(structure: tBu-TePh) → decarboxylation occured

(structure with C=O, TePh, N-Xy)

· Mechanic studies.   (comparison CO vs isonitriles)

(structure: tBu-TeTol) + CO + CNXy → V-40 (0.1 eq)
(50 atm) (1.2 eq)   C₆H₆ 100 °C, 12 h

7

(structure with TeTol, NXy) + (structure with NXy, TeTol)   (5)

8 19% (26%)*   **9** 36% (50%)*

*Yield based on the converted 7.

(structure) **3** + CO + CNXy → hv/Pyrex
(52 atm) (2.0 equiv) C₆H₆ 80 °C, 5 h

4 + (phthalimide structure with TeTol)
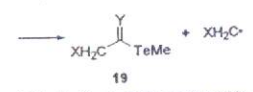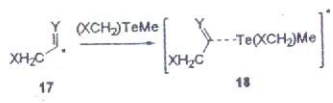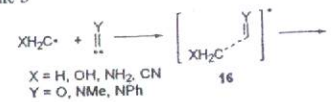
(structure with NXy, TeTol) 62%   0%

→ High reactive alkyl (tBu) radical
reacts with both CO and isonitrile

→ Stabilized radical don't react with CO.

Theoritical model

Scheme 3

XH₂C· + (Y structure) → [XH₂C···Y]· →
X = H, OH, NH₂, CN
Y = O, NMe, NPh   **16**

(structure) + (XCH₂)TeMe → [XH₂C···Te(XCH₂)Me]·
17   **18**

→ XH₂C-TeMe + XH₂C·
19
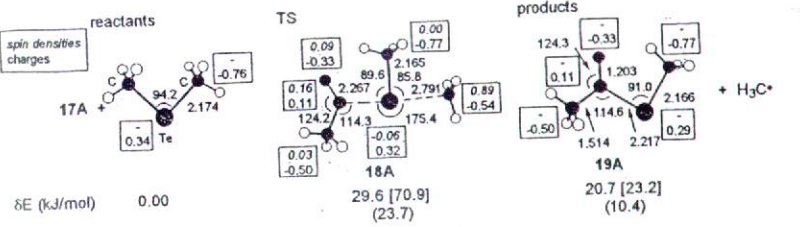A: X = H, Y = O, B: X = H, Y = NMe, C: X = H, Y = NPh
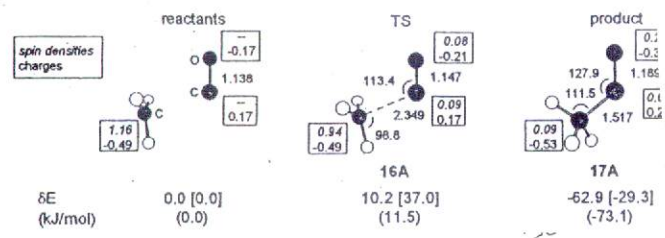
energies obtained by
B3LYP/631HW calculations

δE → [—]
Relative Gibbs
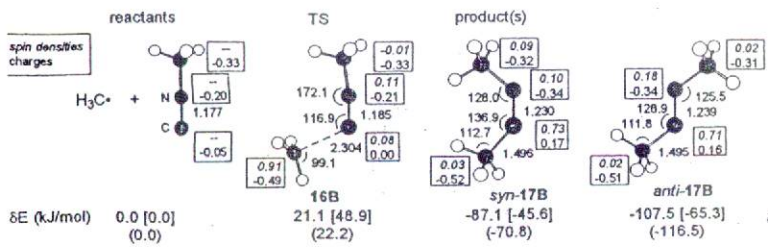energy at 298.15k

(—)
energies obtained by
B3LYP/631HW//631G/HW+ZPE

CH₃· and CO

spin densities / charges

reactants   TS   product

δE (kJ/mol)   0.0 [0.0]   10.2 [37.0]   -62.9 [-29.3]
              (0.0)   (11.5)   (-73.1)

16A   **17A**

spin densities charges   reactants   TS   products

17A +   **18A**   **19A** + H₃C·

δE (kJ/mol)   0.00   29.6 [70.9]   20.7 [23.2]
                      (23.7)   (10.4)

CH₃· and :C-N-Me

spin densities charges

reactants   TS   product(s)

H₃C· + (N,C structure)

δE (kJ/mol)   0.0 [0.0]   21.1 [48.9]   syn-17B   anti-17B
              (0.0)   (22.2)   -87.1 [-45.6]   -107.5 [-65.3]
                                          (-70.8)   (-116.5)

16B

anti-17B + Me₂Te   **18B**   **19B** + H₃C·

δE (kJ/mol)   0.00   40.0 [82.0]   33.0 [40.6]
                      (33.7)   (23.6)
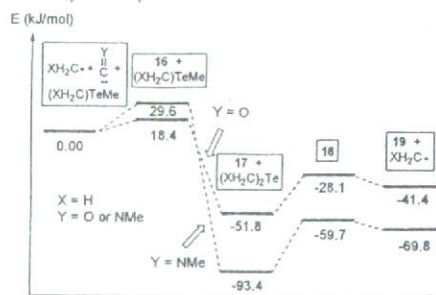
Energy profile.

E (kJ/mol)
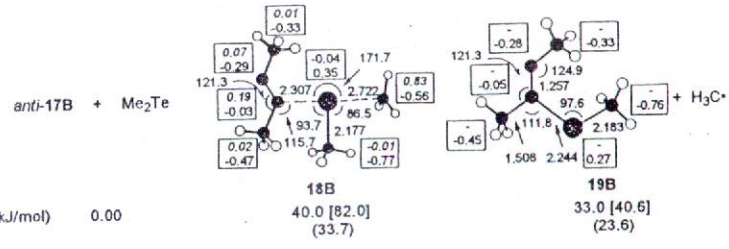
Figure 4. Energy profile of the group-transfer carbonylation and imidoylation reactions of methyl radical (X = H) and CO and methyl isonitrile with Me₂Te (X = H) obtained by B3LYP/6311HW//B3LYP/631HW + ZPE. The energy corresponding to the *anti*-imidoyl radical (*anti*-17B) is shown for Y = NMe.
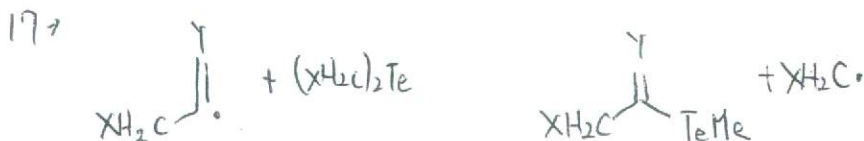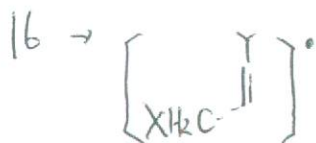
← The overall chain cycle is exothermic (41.4 kJ/mol - carbonylation. 69.8 kJ/mol - imidoylation

These results accord with the fact that competitive carbonylation and imidoylation of tBu-radical proceeded.

The imidoylation is more exothermic than carbonylation

X	Y	compd	total energy[a]		Gibbs energy[b]
			631HW	6311HW	631HW
		transition state 16			
H	O	16A	10.2	18.4	37.0
CH₃[c]	O	16D	8.7	16.8	42.9
OH[c]	O	16E	3.9	14.1	39.0
CN[c]	O	16F	3.9	42.9	68.3
H	NMe	16B	21.1	29.6	48.9
CH₃[c]	NMe	16G	22.2	31.5	58.3
OH[c]	NMe	16H	17.1	29.9	54.7
CN[c]	NMe	16I	18.7	28.3	59.1
H	NPh	16C	14.3	21.8	44.8

X	Y	compd	total energy		Gibbs energy
			631HW	6311HW	631HW
		product 17			
H	O	17A	-62.9	-51.8	-29.3
CH₃[c]	O	17D	-52.8	-40.4	-9.4
OH[c]	O	17E	-39.0	-26.4	1.9
CN[c]	O	17F	2.0	12.5	41.3
H	NMe	anti-17B	-107.5	-93.4	-65.3
CH₃[c]	NMe	anti-17G	-95.5	-80.5	-46.4
OH[c]	NMe	anti-17H	-87.7	-72.3	-41.8
CN[c]	NMe	anti-17I	-45.0	-38.3	-4.8
H	NPh	anti-17C	-114.5	-98.9	-74.1

X	Y	compd	total energy		Gibbs energy
			6311HW	631HW	631HW
		product 19			
H	O	19A	-42.2	-41.4	-6.1
·CH₃	O	19D	-49.2	-45.1	-5.2
OH	O	19E	-32.9	-29.5	11.6
CN	O	19F	-28.2	-23.6	14.8
H	NMe	syn-19B	-74.5	-69.8	-24.8
CH₃	NMe	syn-19G	-79.6	-72.6	-28.3
OH	NMe	syn-19H	-68.6	-62.1	-17.2

$$16 \rightarrow \left[XH_2C-\overset{Y}{\underset{}{C}} \right]^\bullet$$

$$17 \rightarrow XH_2C\overset{Y}{\underset{}{C}}\cdot + (XH_2C)_2Te$$

$$XH_2C\overset{Y}{\underset{TeMe}{C}} + XH_2C\cdot$$

The relative Gibbs free energies reveal that carbonylations of non-stabilized radicals (X=H, Me) are slightly exothermic, but stabilized radicals (X=OH, CN) are endothermic.

The results are consistent with the experimental results in that carbonylation takes place only with nonstabilized radical