Novel Radical Chain Substitution Reaction Involving Single Electron Transfer Processes

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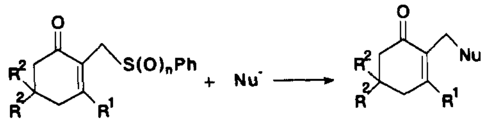
Summary: β-Substituted α-[(phenylsulfonyl)methyl]- and α-[(phenylthio)methyl]cyclohexenones **1**–**4** underwent regioselective replacement of the sulfonyl and sulfenyl groups by stabilized carbanions such as $LiCMe_2NO_2$ mainly by a radical chain mechanism, which was confirmed by investigating the effects of photoirradiation, radical scavengers, and reaction solvents and by the ESR and spectroscopic studies.

Allylic compounds exemplified as $-CR^1{=}C(EWG)CR^2(X)-$ (EWG, electron-withdrawing groups; X, leaving groups) undergo substitution reactions by various nucleophiles to provide the S_N2' or the S_N2 product, depending on the nature of the nucleophile and the substrate. The reaction has been generally believed to proceed in a S_N2' fashion[1] or via two consecutive S_N2' reactions.[2] Here we describe evidence that the substitution reaction between certain allylic substrates of the above type and stabilized carbanions proceeds mainly by a radical chain pathway.

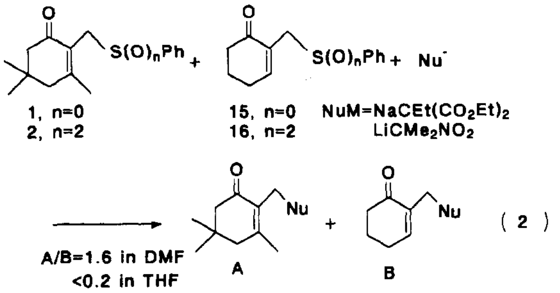
β-Substituted α-[(phenylsulfonyl)methyl]- and α-[(phenylthio)methyl]cyclohexenones **1**–**4** were subjected to substitution reaction with two sets of congener carbanions [$NaCEt(CO_2Et)_2$ and $NaCH(CO_2Et)_2$, $LiCMe_2NO_2$ and $LiCHMeNO_2$] in DMF (0.20 M of enones and 0.30 M of carbanions) at 25 °C to produce the S_N2-type alkylation products regioselectively (eq 1 and Table I). From the results shown in Table I, the following points deserve attention. (i) Reaction rates were distinctly dependent on the nature of the nucleophile, i.e., the more bulky or basic the nucleophile, the faster the substitution.[3] (ii) Only C-alkylation with nitronate anions was observed.[4] (iii) The sulfonyl group was a better leaving group than the sulfenyl one.[5] (iv) The tosyloxy group remains present in the products **7**, **10**, and **13**. Interestingly, kinetic competition reaction between **1** and **15**, or **2** and **16**, toward $NaCEt(CO_2Et)_2$ or $LiCMe_2NO_2$ in DMF showed that the more substituted enone **1** or **2** reacts ca. 1.6 times faster than the simple enone **15** or **16**, respectively, in all four cases (eq 2). Conversely, in THF, **15** or **16** reacts with $NaCEt(CO_2Et)_2$ much faster than **1** or **2** by more than 5 times, respectively. These results strongly suggested that the substitution reaction of the β-substituted enones in DMF (eq 1 and Table I) has radical character.[6,7] Therefore, we investigated the effects of photoirradiation and radical inhibition on the substitution reaction and found that, particularly, the reaction of **1** or **2** with $LiCMe_2NO_2$ was quite sensitive to such factors that affect radical reactions.[8]



(1)

5 - 14

1, n=0; $R^1=R^2=Me$
2, n=2; $R^1=R^2=Me$
3, n=2; $R^1=OEt$, $R^2=H$
4, n=2; $R^1=OTs$, $R^2=H$



1, n=0
2, n=2
15, n=0
16, n=2
$NuM=NaCEt(CO_2Et)_2$, $LiCMe_2NO_2$

(2)

The reaction of **1** or **2** with $LiCMe_2NO_2$ in DMF was greatly accelerated by irradiation with visible light (400-W tungsten lamp; through a Pyrex-brand flask), more distinctly at 0 °C than at 25 °C.[9] For instance, yields of the product **11** in the reaction between **2** and $LiCMe_2NO_2$ in DMF at 0 °C for 6 h were 8% and 25% in the dark (wrapped in aluminum foil) and in the presence of light, respectively. We observed two absorption bands at 510 and 450 nm in the course of the reaction (Figure 1 in the supplementary material).[10] The former band appeared as soon as **2** and $LiCMe_2NO_2$ was mixed (red color de-

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[1] (a) Nelson, R. P.; McEuen, J. M.; Lawton, R. G. *J. Org. Chem.* **1969**, *34*, 1225. For recent examples: (b) Takahashi, T.; Hori, K.; Tsuji, J. *Tetrahedron Lett.* **1981**, *22*, 119; *Chem. Lett.* **1981**, 1189. (c) Donaldson, R. E.; Saddler, J. C.; Byrn, S.; Mckenzie, A. T.; Fuchs, P. L. *J. Org. Chem.* **1983**, *48*, 2167. (d) Seebach, D.; Knochel, P. *Helv. Chim. Acta* **1984**, *67*, 261. (e) Knochel, P.; Seebach, D. *Tetrahedron* **1985**, *41*, 4861. (f) Auvray, P.; Knochel, P.; Normant, J. F. *Tetrahedron* **1988**, *44*, 4495, 4509. (g) Brocchini, S. J.; Eberle, M.; Lawton, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 5211. (h) Okamoto, S.; Kobayashi, Y.; Kato, H.; Hori, K.; Takahashi, T.; Tsuji, J.; Sato, F. *J. Org. Chem.* **1988**, *53*, 5590. (i) Tamura, R.; Tamai, S.; Katayama, H.; Suzuki, H. *Tetrahedron Lett.* **1989**, *30*, 3685. (j) Najera, C.; Mancheno, B.; Yus, M. *Tetrahedron Lett.* **1989**, *30*, 3837. (k) Amri, H.; Rambaud, M.; Villieras, J. *Tetrahedron* **1990**, *46*, 3535. (l) Ghera, E.; Yechezkel, T.; Hassner, A. *J. Org. Chem.* **1990**, *55*, 5977. (m) Tamura, R.; Watabe, K.; Katayama, H.; Suzuki, H.; Yamamoto, Y. *J. Org. Chem.* **1990**, *55*, 408.

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[3] The basicity or nucleophilicity of the nucleophile is an important factor in determining the rate of addition of the nucleophile to carbon free radicals. (a) Bowman, W. R. *Chem. Soc. Rev.* **1988**, *17*, 283. (b) Russell, G. A. *Adv. Phys. Org. Chem.* **1987**, *23*, 271.

[4] O-Alkylation is usually a predominant path in the S_N2 reaction with nitronate anions. Kornblum, N. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 734.

[5] Carbon–sulfur bonds could be cleaved under $S_{RN}1$ conditions. (a) Rossi, R. A.; Bunnett, J. F. *J. Org. Chem.* **1973**, *38*, 1407; *J. Am. Chem. Soc.* **1974**, *96*, 112. (b) Cheng, C.; Stork, L. M. *J. Org. Chem.* **1991**, *56*, 2436.

[6] Solvent plays a pivotal role in determining the reduction potentials of organic substrates, see: Lipshutz, B. H.; Wilhelm, R. S.; Nugent, S. T.; Little, R. D.; Baizer, M. M. *J. Org. Chem.* **1983**, *48*, 3306.

[7] Solvent affects the reaction pathway in a nucleophilic substitution reaction, see: Ashby, E. C.; Argyropoulos, J. N. *J. Org. Chem.* **1985**, *50*, 3274.

[8] $LiCMe_2NO_2$ is an excellent nucleophile in $S_{RN}1$ reactions. For reviews on $S_{RN}1$ reactions, see: (a) Kornblum, N. In *Supplement F: The chemistry of Amino, Nitroso and Nitro Compounds and Their Derivatives*; Patai, S., Ed.; Wiley: New York, 1982; Part 1, Chapter 10. (b) Kornblum, N. *Aldrichimica Acta* **1990**, *23*, 71. Also see refs 3a, 3b, and 4.

[9] Photochemical activation was similarly observed in the reaction of **2** with $LiCHMeNO_2$. But only slight photostimulation was noted in the reaction of **1** or **2** with $NaCEt(CO_2Et)_2$. These results are in good agreement with the recent report that photostimulation is required for SET in reactions with nucleophiles of low basicity. (a) Bordwell F. G.; Clemens, A. H. *J. Org. Chem.* **1981**, *46*, 1035. (b) Bordwell, F. G.; Bausch, M. J. *J. Am. Chem. Soc.* **1986**, *108*, 1985. (c) Bordwell, F. G.; Bausch, M. J.; Wilson, C. A. *J. Am. Chem. Soc.* **1987**, *109*, 5465. (d) Bordwell, F. G.; Wilson, C. A. *J. Am. Chem. Soc.* **1987**, *109*, 5470.

[10] Aliquots were taken from the reaction flask to obtain absorption spectra.

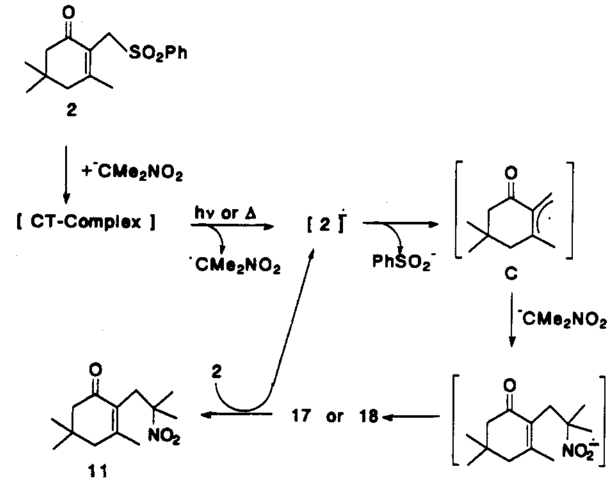
0022-3263/91/1956-5743$02.50/0

Table I. Radical Chain Substitution Reaction[a]

entry	nucleophile	enone	n	R^1	R^2	time, h	product[b]	yield, %
1	$NaCEt(CO_2Et)_2$	1	0	Me	Me	24	5	72
2		2	2	Me	Me	2	5	83
3		3	2	OEt	H	3	6	75
4		4	2	OTs	H	3	7	60
5	$NaCH(CO_2Et)_2$	1	0	Me	Me	168	8	72
6		2	2	Me	Me	7	8	76
7		3	2	OEt	H	24	9	71
8		4	2	OTs	H	3	10	43
9	$LiCMe_2NO_2$	1	0	Me	Me	48	11	62
10		2	2	Me	Me	48	11	86
11		3	2	OEt	H	48	12	85
12		4	2	OTs	H	48	13	66
13	$LiCHMeNO_2$	1	0	Me	Me	48	14	48
14		2	2	Me	Me	48	14	59

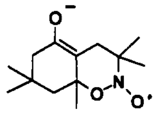
[a] All reactions were run under argon atmosphere using 0.20 M of enones and 0.30 M of carbanions in DMF at 25 °C. The reaction was quenched by adding water, and the product was extracted with ether and purified by column chromatography on silica gel (hexane–ethyl acetate). [b] All new products were fully characterized by means of infrared and ^1H NMR spectra and elemental analyses.

Scheme I



veloped)[11] and disappeared on completion of the reaction. The intensity of the latter band increased as the reaction proceeded, then reached a steady state, and finally diminished on completion of the substitution. The observed photoacceleration can be rationalized by assuming that either or both of two new species corresponding to the above absorption bands are energized to make SET (single electron transfer) feasible (vide infra).[12] Addition of 20 mol % of *m*-dinitrobenzene (*m*-DNB), a known radical-anion scavenger,[8] substantially decreased the reaction rate between 2 and excess $LiCMe_2NO_2$ at 25 °C.[13] One molar equiv of di-*tert*-butyl nitroxide greatly inhibited the reaction of 2 with 2 equiv or more of $LiCMe_2NO_2$ at 25 °C,[8] although addition of catalytic amounts of the free radical scavenger only slightly reduced the reaction rate. These results suggest an intermediacy of radical chain processes of short chain length involving SET similar to $S_{RN}1$ reactions.[8]

Further, we could detect an ESR spectrum of fairly stable radical species in the course of the reaction of 2 and $LiCMe_2NO_2$ in DMF (1.0 M of 2 and $LiCMe_2NO_2$) at 25 °C (Figure 2 in the supplementary material). The intensity of the spectrum increased with the elapse of time and then disappeared on completion of the reaction through a steady state. From the *g* value ($g = 2.006$; reference: Fremy salt) and the hyperfine coupling constant of the equally spaced triplet structure ($a_N = 14.7$ G), the observed radical is considered to be a nitroxide radical bearing no hydrogen on the carbon atom linked to the nitrogen atom.[14] This spectrum was considerably, although not all, diminished immediately when the reaction mixture was irradiated with visible light (500-W Xe lamp with a filter cutting off UV and IR rays) and reappeared quickly in the absence of light. More importantly, an identical ESR spectrum was obtained by simply irradiating the isolated product 11 alone in DMF (1.0 M of 11) at 25 °C. Thus, the observed nitroxide radical seems to be an actual reaction intermediate, which is consumed under visible light irradiation during the reaction and possesses a structure very close to that of 11. We propose the structure of the observed radical as nitroxide radical-anion 17 or 18. The aforementioned absorption band at 450 nm might be assigned to 17 or 18, because di-*tert*-alkyl nitroxides usually exhibit an absorption band at 410–460 nm, ascribed to n–π* transitions,[15] and both the absorption band and ESR spectrum showed similar behavior with regard to the mode of the appearance, steady state, and vanishment. And another absorption band at 510 nm might correspond to a charge-transfer complex between 2 and $LiCMe_2NO_2$.



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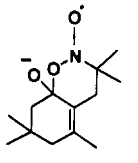

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From these results, we postulate the reaction mechanism between 2 and $LiCMe_2NO_2$ shown in Scheme I. The charge-transfer complex between 2 and $LiCMe_2NO_2$ was thermally or photochemically stimulated to induce SET to produce radical-anion of 2, which liberated $PhSO_2^-$ to give transient free radical C, followed by coupling with $^-CMe_2NO_2$ to generate radical anion 17 or 18, which has a fairly long lifetime in the dark as already mentioned. Photochemically induced SET from 17 or 18 to 2[16] afforded the product 11 and the radical-anion of 2 which entered the chain process.

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[11] The initial red-orange color development on mixing starting materials was observed uniformly in each combination of β-substituted enones 1–4 and four carbanions used in Table I.

[12] Neither the enone 2 nor $LiCMe_2NO_2$ absorbs visible light.

[13] *m*-DNB also exhibited great suppression effects in the reaction between 1 and $NaCEt(CO_2Et)_2$ or 2 and $LiCHMeNO_2$ IN DMF.

[14] An analogous ESR spectrum differing only in the a_N value (a_N = 15.50 G) was detected in the reaction between 2 and $LiCMe_2NO_2$.

[15] Rozantsev, E. G.; Sholle, V. D. *Synthesis* 1971, 190.

[16] The half-wave potentials ($E_{1/2}$ vs SCE) of 2 and 11 in DMF at 25 °C were −1.93 and −1.68 V, respectively, indicating the significance of photoactivation for SET from 17 or 18, the radical-anion of 11, to 2. Meanwhile, the $E_{1/2}$ value of 5 was −2.01 V, showing the ease of SET from the radical-anion of 5 to 2.

Thus, we have shown that β-substituted cyclohexenones such as 1–4 bearing sulfur leaving groups at the β′ position undergo substitution reactions with stabilized carbanions mainly by a radical mechanism. Especially in the case with $LiCMe_2NO_2$, distinct photochemical stimulation and radical inhibition were observed, and a very interesting radical-anion intermediate was detected.

Registry No. 1, 126319-19-5; **2**, 135823-73-3; **3**, 135823-74-4; **4**, 135823-75-5; **5**, 135852-94-7; **6**, 135823-76-6; **7**, 135852-95-8; **8**, 135823-77-7; **9**, 135823-78-8; **10**, 135823-79-9; **11**, 135823-80-2; **12**, 135823-81-3; **13**, 135823-82-4; **14**, 135823-83-5; **15**, 76047-55-7; **16**, 125066-15-1; *m*-DNB, 99-65-0; $NaCEt(CO_2Et)_2$, 18995-13-6; $NaCH(CO_2Et)_2$, 996-82-7; $LiCMe_2NO_2$, 3958-63-2; $LiCHMeNO_2$, 28735-55-9; $(CH_3)_3CNO$, 2406-25-9.

Supplementary Material Available: Complete experimental details and spectral data (5 pages). Ordering information is given on any current masthead page.

Novel Photochemical Ring Contraction of 1-Naphthols Promoted by Aluminum Halides

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Summary: Irradiation of 1-naphthol (**1a**) and its 2-alkyl and 6-methoxy derivatives **1b–d** with 5 equiv of $AlCl_3$ or $AlBr_3$ in CH_2Cl_2 gave (chloromethyl)indanones **4a–d** in 41–72% yields. Irradiation of **1a** with $AlBr_3$ in CH_2Br_2 afforded (bromomethyl)indanone **5a** in 54%. 3-Methyl derivative **1e** was unreactive and 4-methyl derivative **1f** underwent isomerization to **1e**.

In the presence of Lewis or Brønsted acid, alkyl-substituted phenols have been shown to form C4-protonated species,[1,2c,d] which can be envisaged as AlX_3-coordinated or protonated cyclohexa-2,5-dienone. Childs has shown that these C4-protonated species undergo photochemical rearrangement to bicyclo[3.1.0]hex-3-en-2-ones,[2] which is analogous to the well-known lumiketone rearrangement of cyclohexa-2,5-dienones themselves.[3] Indeed, protonated cyclohexa-2,5-dienones are also known to undergo similar isomerization.[4] From synthetic points of view, this skeletal transformation is of great interest since it represents an aromatic to alicyclic transformation and it provides a useful way to prepare the bicyclo[3.1.0]hexenone system from readily available phenol derivatives. 1-Naphthol (**1a**) is also reported by Koptyug to form C4-protonated species **2** with $AlBr_3$.[1a,c] Since **2** is a 2,3-benzo homologue of the AlX_3 complex of C4-protonated phenol, it may well be anticipated to undergo a similar photochemical rearrangement leading to benzobicyclo[3.1.0]hexenone (**3a**) (Scheme I).[5,6] We report here that this is not the case but 1-naphthols **1a–d** undergo a novel photochemical ring contraction promoted by AlX_3 (X = Cl, Br) leading to the

Scheme I

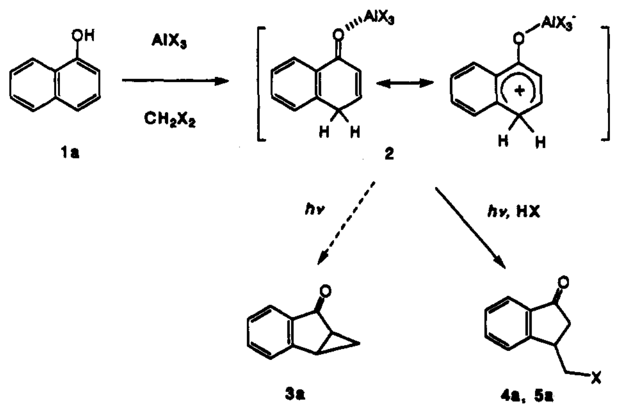

Table I. Product Distribution from Photoreaction of 1-Naphthols 1a–f in the Presence of AlX_3 in CH_2Cl_2

naphthol	AlX_3[a]	irradn time (h)	convn (%)	product (yield, %)[b]
1a	$AlCl_3$	2.5	95	**4a** (69)
	$AlBr_3$	2	85	**4a** (64), **5a** (trace)
	$AlBr_3$[c]	12.5	100	**5a** (54)
1b	$AlCl_3$	1.5	100	**4b** (72)
	$AlBr_3$	1	100	**4b** (41), **5b** (13)
1c	$AlCl_3$	6	100	**4c** (65)
	$AlBr_3$	6	100	**4c** (67)
1d	$AlCl_3$	10	91	**4d** (51)
	$AlBr_3$	7	93	**4d** (47), **5d** (trace)
1e	$AlCl_3$	7.5	0	no reaction
1f	$AlCl_3$	2	100	**1e** (81)

[a] 5 equiv of AlX_3 was used. [b] Yields are based on naphthols consumed. [c] In CH_2Br_2.

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(2) (a) Childs, R. F.; Parrington, B. D.; Zeya, M. *J. Org. Chem.* **1979**, *44*, 4912. (b) Baeckstrom, P.; Jacobsson, U.; Koutek, B.; Norrin, T. *J. Org. Chem.* **1985**, *50*, 3728. (c) Chadda, S. K.; Childs, R. F. *Can. J. Chem.* **1985**, *63*, 3449. (d) Childs, R. F.; George, B. E. *Can. J. Chem.* **1988**, *66*, 1343. Recently we have found that 3-methoxyphenol also undergoes similar photorearrangement promoted by $AlBr_3$: Kakiuchi, K.; Ue, M.; Yamaguchi, B.; Nishimoto, A.; Tobe, Y. *Bull. Chem. Soc. Jpn.* In press.

(3) (a) Zimmerman, H. E.; Schuster, D. I. *J. Am. Chem. Soc.* **1961**, *83*, 4486; (b) **1962**, *84*, 4527. For reviews, see: (c) Zimmerman, H. E. *Adv. Photochem.* **1963**, *1*, 183. (d) Chapman, O. L. *Adv. Photochem.* **1963**, *1*, 323. (e) Schaffner, K. *Adv. Photochem.* **1966**, *4*, 81. (f) Kropp, P. J. *Org. Photochem.* **1967**, *1*, 1. (g) Chapman, O. L.; Weiss, D. S. *Org. Photochem.* **1973**, *3*, 197. (h) Schaffner, K.; Demuth, M. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 3, p 281.

(4) Pauvlik, J. W.; Filipescu, N. *J. Am. Chem. Soc.* **1970**, *92*, 6062. Pavlik, J. W.; Pasteris, R. J. *J. Am. Chem. Soc.* **1974**, *96*, 6107.

(5) Although it has been reported that 4,4-disubstituted 2,3-benzocyclohexa-2,5-dienones reacted differently, i.e., migration of an aryl group on the 4-position to give 1-naphthol derivatives, we think that the aryl group on the 4-position plays a crucial role in its facile 1,2-migration. The situation for **2**, which does not possess the C4-substituents, may well be different from the 4,4-disubstituted benzocyclohexadienones: Zimmerman, H. E.; Hahn, R. C.; Morrison, H.; Wani, M. C. *J. Am. Chem. Soc.* **1965**, *87*, 1138. Zimmerman, H. E.; Rieke, R. D.; Scheffer, J. R. *J. Am. Chem. Soc.* **1967**, *89*, 2033.

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