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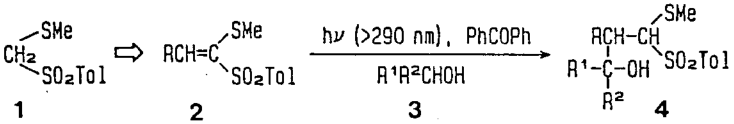
AN EFFICIENT ACCEPTOR OF 1-HYDROXY(OR ALKOXY)ALKYL RADICALS
-- KETENE DITHIOACETAL S,S-DIOXIDE --

Katsuyuki OGURA,* Atsushi YANAGISAWA, Takeo FUJINO, and Kazumasa TAKAHASHI
Department of Synthetic Chemistry, Faculty of Engineering,
Chiba University, 1-33 Yayoicho, Chiba 260, Japan

Summary: Irradiation of a ketene dithioacetal S,S-dioxide (2) in alcohols or ethers containing benzophenone gave an adduct which was formed by addition of 1-hydroxy- or 1-alkoxyalkyl radicals to 2 followed by hydrogen transfer.

In organic synthesis, one of current topics is formation of carbon-carbon bond by addition of free radicals to alkenes.[1] However, little attention has been paid on utilization of sulfur functionalities for increasing the reactivity of alkenes to radicals. During our investigation to develop synthetic utility of methylthiomethyl p-tolyl sulfone (1),[2] we have found that a ketene dithioacetal S,S-dioxide (2), easily obtainable from 1,[3,7] serves as an acceptor of 1-hydroxyalkyl radicals and 1-alkoxyalkyl radicals. This provides a novel method for functionalizing the α-position of alcohols and ethers.



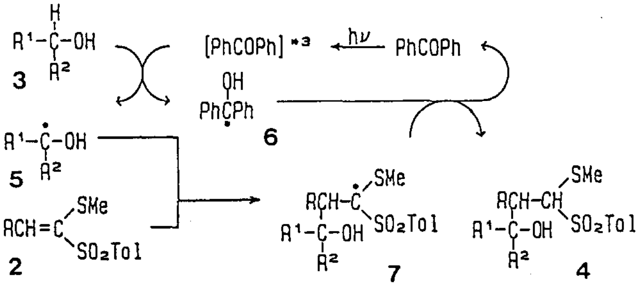
When a solution of 2 (ca. 2 mmol) in an alcohol (3) (70 ml) containing benzophenone (one mol-equiv) was irradiated with a high pressure Hg lamp (100 W) through a Pyrex filter under internally cooling with a water jacket, a smooth reaction took place. Evaporation followed by column chromatography on silica gel gave an adduct (4) as a mixture of its diastereomers. The results are summarized in Table 1, indicating that all of the yields are excellent except for irradiation of 2 (R=Ph) in methanol (run 3). Since no reaction was observed on irradiation in the absence of benzophenone, benzophenone is indispensable to the present reaction. As the reaction proceeded, benzophenone was consumed to afford benzopinacol (see Table 1). However, runs 6 and 7 of Table 1 indicate that one mol-equiv of benzophenone was not necessary to the completion of the reaction. From these observations, photochemical production of 4 from 2 and 3 may be explained by the pathways depicted in Scheme 1. Since ultraviolet absorption of 2 is very weak, if any, in the region of longer wavelength than 290 nm, irradiation through a Pyrex filter almost exclusively excites benzophenone, and fast intersystem crossing gave the $^3(n,\pi^*)$ state of benzophenone, which abstracts the α-hydrogen of 3 to produce

Table 1. Irradiation of **2** in an Alcohol (**3**)[a]

run	**2**		**3**		PhCOPh / mmol	time	**4**		benzopinacol
	R	amount/mmol	R^1	R^2			yield / %		yield / %
1	Me	1.0	H	H	1.0	0.5 h	96	[52:48][c]	62[d]
2	$n\text{-}C_{11}H_{23}$	0.6	H	H	1.0	1 h	~96	[60:40][c]	67[d]
3	Ph	1.6	H	H	1.0	7 h	55 (67)[b]	[30:70][c]	21[e]
4	Ph	1.6	Me	H	1.0	2 h	89	[12:28:22:38][c]	~95[d]
5	Ph	1.0	Me	Me	1.0	1 h	90	[20:80][c]	90[d]
6	Ph	1.0	Me	Me	0.5	2 h	98	[22:78][c]	92[d, f]
7	Ph	1.0	Me	Me	0.2	3 h	87 (91)[b]	[22:78][c]	75[d]
8	Ph	1.0	Et	Me	1.0	3 h	92 (99)[b]	[16:19:28:37][c]	94[d]

[a] Irradiation of **2** in an alcohol (**3**; 70 ml) with a 100 W high-pressure Hg lamp (Pyrex filter) under cooling with water and bubbling with nitrogen. [b] ( ) = the yield based upon the unrecovered. [c] The diastereomeric ratio of **4** determined by ^{1}H-NMR. [d] A small amount of PhCOPh was detected. [e] PhCOPh (~ 79 %) was recovered. [f] Benzhydrol (trace) was detected.

a 1-hydroxyalkyl radical (5) and a hydroxydiphenylmethyl radical (6).[10] The radical (6) is so stable that it cannot add to 2, but addition of 5 to 2 afforded an intermediary radical (7). The subsequent transfer of hydrogen from 6 to 7 produces 4 and benzophenone. If the radical (6) dimerizes or abstracts hydrogen, benzophenone is not recovered.



On irradiation in methanol, 2 (R=Ph) reacted slowly and the yield of the corresponding 4 was relatively low. At the present time, we have no evidence to explain this phenomenon, but it seems to be one possible explanation that, since the α-hydrogen of methanol is less reactive to the $^3(n,\pi^*)$ state of benzophenone, quenching of $^3(n,\pi^*)$ benzophenone with 2 (R=Ph) which has a conjugated phenyl group occurs in competition with slow hydrogen abstraction by $^3(n,\pi^*)$ benzophenone in methanol.

The key step of the present reaction is regiospecific addition of 1-hydroxyalkyl radical (5) to the C-C double bond of 2. The radicals which intermolecularly and efficiently add to 2 seem to be restricted to ones with an electron-releasing group, because n-hexyl radical and benzyl radical do not exhibit such reactivity to 2 (R=Ph): When n-hexyl bromide and 2 (R=Ph) was treated with tributyltin hydride and AIBN (a catalytic amount) in refluxing benzene, n-hexyl bromide was consumed, but 2 (R=Ph) remained completely unchanged. On irradiation of 2 (R=Ph) in toluene in the presence of benzophenone, the expected 1-methylthio-2,3-diphenyl-1-(p-tolylsulfonyl)propane was not formed, but 1,2-diphenylethane was obtained along with the starting material (2; R=Ph).

Furthermore, the present method was extended to functionalizing the α-position of an ether (8). When a solution containing 2 and benzophenone in the ether (8) was irradiated under the conditions similar to those of the irradiation in alcohols, we also obtained an adduct (9) as a mixture of its diastereomers in a good to high yield as summarized in Table 2.

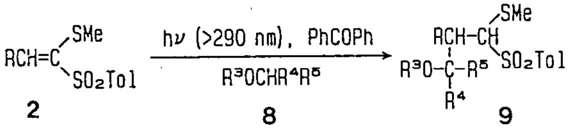
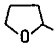
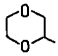
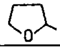
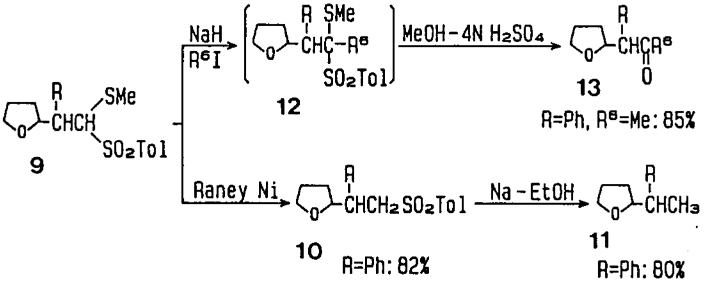


Table 2. Irradiation of **2** in an Ether (**8**)[a]

run	**2**	$R^3O\underset{\mathrm{H}}{C}R^4R^5$	PhCOPh / mol-equiv	time	**9**		benzopinacol
	R				$R^3OCR^4R^5$-	yield / %	yield / %
1	Ph		1	1.0 h		90 [28:24:27:21][c]	53[e, f]
2	Ph		1	2.5 h		80 (92)[b] [28:24:20:28][c]	56[e]
3	Ph	^{i}PrOCHMe$_2$	1X4[d]	15 h	^{i}PrOCMe$_2$-	62 (76)[b] [54:46][c]	25[e]
4	H	^{i}PrOCHMe$_2$	1	0.5 h	^{i}PrOCMe$_2$-	96 ——	~34[g]
5	Me		1	1.0 h		88 [24:29:21:25][c]	52[e, f]

[a] Irradiation of **2** (1 mmol) in an ether (**8**; 70 ml) with a 100 W high-pressure Hg lamp under cooling with water and bubbling with nitrogen. [b] The yield based upon the unrecovered. [c] The diastereomeric ratio of **9** determined by HPLC. [d] PhCOPh (4 mol-equiv) was added in four portions. [e] A small amount of PhCOPh was detected. [f] -C(OH)Ph$_2$ was also isolated (28~33%). [g] PhCOPh (~66%) was recovered.

Thus, we have exploited a novel method for introducing 1-methylthio-1-(p-tolylsulfonyl)-2-alkyl group into the α-positions of the alcohol (3) or the ether (8). Finally, we would like to briefly describe on the conversion of the thus introduced dithioacetal S,S-dioxide group to other functionalities. On treatment with Raney Ni in ethanol, the methylthio group of 9 (R=Ph, $R^3+R^4=(CH_2)_3$, $R^5=H$) was reductively desulfurized and a sulfone (10) was obtained. Further reduction of 10 with sodium in ethanol brought about the formation of 2-(1-phenylethyl)tetrahydrofuran (11).



We have already established an efficient method for transforming an aldehyde dithioacetal S,S-dioxide to a ketone by alkylation and the subsequent acid-hydrolysis.[5] This can be applied to the conversion of 9 (R=Ph, R^3+R^4=$(CH_2)_3$, R^5=H) to the corresponding α-(2-tetrahydrofuranyl) ketone (13).

Hitherto the combined action of an electron-withdrawing substituent and electron-donating substituent on a radical center has been well established to lead to an enhanced stabilization.[11] Since the intermediary radical (7) has an electron-withdrawing sulfonyl group and an electron-donating thio group on its radical center, 7 is considered to be thermodynamically stable. The stability of 7 seems to reflect the decrease of activation energy which might be taken into consideration as a driving force for the addition of radicals to 2. Now we are investigating whether a combination of p-tolylsulfonyl group and methylthio group is crucial to the reactivity of the ketene dithioacetal S,S-dioxide (2) to radicals.[12] The result of our investigation on these problems will be reported in due course.

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