A Dimethyl Sulfoxide-mediated Oxidation of Arylalkyl and Alkyl Alcohols to Corresponding Aldehydes and Ketones *via* Tropolonyl Ethers

Hitoshi TAKESHITA,* Hiroaki MAMETSUKA, and Norihide MATSUO†

Research Institute of Industrial Science, 86, Kyushu University, Hakozaki, Higashi-ku, Fukuoka 812

†*Graduate School of Engineering Sciences, 39, Kyushu University, Hakozaki, Higashi-ku, Fukuoka 812*

(Received July 9, 1981)

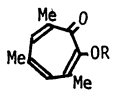
The arylmethyl and diarylmethyl ethers of tropolones were oxidized to the corresponding carbonyl derivatives by heating in dimethyl sulfoxide. The free alcohols were oxidized at a much slower rate, suggesting that some sort of DMSO-linked intermediates are responsible for the oxidation. Inertness of free alcohols was proven by means of the cross-over experiments, including deuterium-labelling. This oxidation was applicable to alkyl ethers, but not to alkenyl ethers, which are known to cause the Claisen-rearrangement.

Recently, dimethyl sulfoxide (DMSO)-oxidation of alcohols or organic halides has been shown to be useful in organic synthesis.[1] We have found that several tropolonyl ethers, of which the preparations are tabulated in Table 1, are also capable of forming carbonyl compounds in a manner to be described in this paper. The investigations of non-benzenoid aromatic compounds have been hitherto focussed on the peculiarity of their chemical properties, and there seems to have been no attempt to utilize them as a reagent or catalyst.

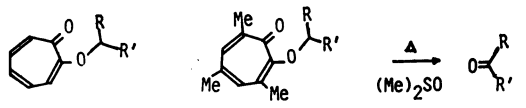
When a mixture of 2-benzyloxytropone (**1a**)[2] and DMSO in a sealed tube was heated at 180 °C for 2 h, a clean reaction occurred to give tropolone (**2**), dimethyl sulfide, and benzaldehyde (**3a**) in good yields. Although their isolated yields were in the range of 60 to 85%, the NMR spectrometry of **3a** in the reaction mixture proved a nearly quantitative formation. Some other (arylmethoxy)tropones also gave aroyl derivatives, including 2-(diphenylmethoxy)tropone (**1g**) and 2-(1-naphthylmethoxy)tropone (**1h**) to benzophenone (**3g**) and 1-naphthaldehyde (**3h**).

However, the reaction was not applicable to the alkanals, *i.e.*, the yield of hexanal (**4a**) obtained from 2-(hexyloxy)tropone (**5a**) was less than 3% when heated in DMSO. This was at least partly due to the secondary reaction of the aldehyde with regenerated **2**.[3] This was also the case when 2-[4-(methoxycarbonyl)-butoxy]tropone (**5b**) gave ethyl 4-oxobutyrate (**4b**), in a trace amount. Alkanones, inert to tropones under these conditions, were prepared in a moderately good yield; 2-isopropoxytropone (**5c**) gave acetone (**4c**) in a 55% yield.

TABLE 1. PREPARATIONS AND CHARACTERIZATIONS OF TROPOLONYL ETHERS

	Ethers	Yield/%	Mp θ_m/°C	Found(%)[a] C	Found(%)[a] H	Calcd(%) C	Calcd(%) H (Compositions)	Ref.
	**1a**: R=CH_2Ph	76	82—83	79.27	5.80	79.22	5.70 ($C_{14}H_{12}O_2$)	
	1b: R=$CH_2C_6H_4Cl(p)$	83	109—110	68.06	4.68	68.16	4.49 ($C_{14}H_{11}O_2Cl$)	
	1c: R=$CH_2C_6H_4Br(p)$	79	105—106	57.67	4.09	57.75	3.81 ($C_{14}H_{11}O_2Br$)	
	1d: R=$CH_2C_6H_4Me(p)$	85	114—115	79.53	6.46	79.62	6.24 ($C_{15}H_{14}O_2$)	
	1e: R=$CH_2C_6H_4Me(o)$	61	89—91	79.63	6.28	79.62	6.24 ($C_{15}H_{14}O_2$)	
	1f: R=$CH_2C_6H_4OMe(p)$	69	124—125	74.53	6.11	74.36	5.83 ($C_{15}H_{14}O_3$))	
	1g: R=$CHPh_2$	33	137—138	288.1152		288.1150	($C_{20}H_{16}O_2$)	
	1h: R=$CH_2C_{10}H_7(1)$	79	121—123	82.21	5.48	82.42	5.38 ($C_{18}H_{14}O_2$)	
	5a: R=$(CH_2)_5Me$	77	Liquid	206.1287		206.1307	($C_{13}H_{18}O_2$)	
	5b: R=$(CH_2)_3COOEt$	45	Liquid	236.1057		236.1049	($C_{13}H_{16}O_4$)	
	5c: R=$CHMe_2$	20	Liquid	164.0830		164.0837	($C_{10}H_{12}O_2$)	
	5d: R=CH_2COPh	50	136—137	74.70	4.96	74.99	5.03 ($C_{15}H_{12}O_3$)	
	7a: R=$CH_2CH=CH_2$	79						6
	7b: R=$CH_2C(Me)=CH_2$	69	Liquid	176.0841		176.0837	($C_{11}H_{12}O_2$)	
	7c: R=$CH_2C(Cl)=CH_2$	17						6
	7d: R=$CH_2CH=CMe_2$	58						11
	10a: R=CH_2Ph	68	Liquid	254.1302		254.1307	($C_{17}H_{18}O_2$)	
	**10d**: R=$CH_2C_6H_4Me(p)$	41	Liquid	268.1454		268.1463	($C_{18}H_{20}O_2$)	
	10e: R=$CH_2C_6H_4Me(o)$	40	Liquid	268.1459		268.1463	($C_{18}H_{20}O_2$)	
	11a: R=$CH_2CH=CH_2$	63						10
	13a: R=$(CH_2)_5Me$	47	Liquid	248.1797		248.1776	($C_{16}H_{24}O_2$)	
	13b: R=$(CH_2)_9Me$	70	Liquid	304.2406		304.2402	($C_{20}H_{32}O_2$)	
	13d: R=CH_2COPh	38	Liquid	282.1254		282.1254	($C_{18}H_{18}O_3$)	

a) Certain tropolonyl ethers were characterized by high-resolution mass-spectra for the samples of more than 99%-purity in respect of high-pressure liquid chromatography (micropolasil-ethyl acetate and hexane).



Scheme 1.

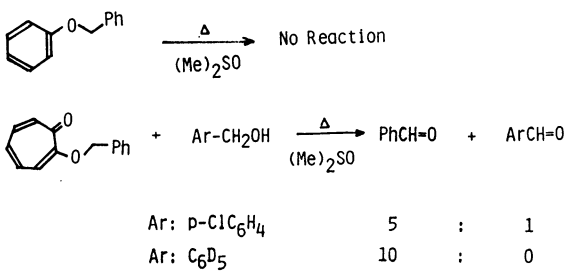
Table 2. DMSO-oxidation of troponyl ethers

Starting materials	Conditions T/°C	Conditions t/h	Products: R, R′	Yield/%
1a:	180	2	**3a**: Ph, H	82
10a:	180	1	**3a**: Ph, H	64
1b:	180	2	**3b**: *p*-ClC_6H_4, H	85
1c:	180	2	**3c**: *p*-BrC_6H_4, H	83
1d:	180	3	**3d**: *p*-MeC_6H_4 H	76
10d:	180	1	**3d**: *p*-MeC_6H_4 H	80
1e:	180	2	**3e**: *o*-MeC_6H_4, H	60
10e:	180	1	**3e**: *o*-MeC_6H_4, H	75
1f:	180	2	**3f**: *p*-$MeOC_6H_4$, H	67
1g:	180	4	**3g**: Ph, Ph	77
1h:	180	1	**3h**: 1-$C_{10}H_7$,H	60
5a:	180	17	**4a**: C_5H_{11}, H	+
13a:	180	12	**4a**: C_5H_{11}, H	55
5b:	180	21	**4b**: C_2H_4COOEt, H	+
5c:	180	5	**4c**: Me, Me	70
5d:	180	20	**4d**: PhCO, H	—a)
13d:	180	20	**4d**: PhCO, H	—a)
13b:	180	5	**14b**: C_9H_{19}, H	31

a) Me_2S was undetectable.

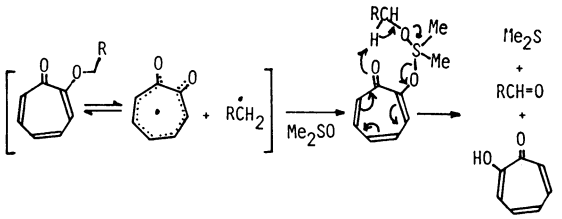
To determine the responsibility of the troponyl ethers, the reaction was checked by phenyl benzyl ether (**A**); but it was completely recovered unchanged. In addition, a 1 : 1-mixture of **1a** and *p*-chlorobenzyl alcohol (**6b**) gave aromatic aldehydes which consisted of **3a** : **3b** in a ratio of 5 : 1. Furthermore, **1a** and benzyl-2,3,4,5,6-d_5 alcohol (**6a**-d_5), prepared from benzoic-d_5 acid (**B**-d_5),[4] resulted in the overwhelming formation of the deuterium-free aldehyde (**3a**): In the NMR spectrum of the reaction mixture in DMSO-d_6, the intergral ratio for the signals ascribable to aldehydic protons and to 2,6-protons of **3a** was exactly 1 : 2. Even more convincingly, the mass-spectral analysis of the resultant **3a** showed less than 3% of **3a**-d.[5] Thus, within experimental error, hydrolyzed alcohols, if any, are not primarily responsible for the aldehyde formation. Therefore, the present oxidation can be termed a novel DMSO-mediated reaction of tropolonyl ethers.

As in the recently-found radical rearrangement: 2-(arylmethoxy)tropones to 3- and 5-(arylmethyl)-tropolones,[2] the present radical-induced oxidation also revealed a sensitization effect when analyzed kinetically;



Scheme 2.

throughout the oxidation up to 70% conversion of **1a** in DMSO-d_6, the rate enhancement by addition of the radical sensitizer, benzoyl peroxide (BP, 0.5 mol equiv.), k_{BP}/k_o, was *ca.* 2.7 at 180 °C ($k_o=2.3\times10^{-2}$, $k_{BP}=6.1\times10^{-2}$/min mol). In addition to this, the rate was also increased by addition of 2,4,6-tri-*t*-butylphenol (TB, 0.5 mol equiv.), *i.e.*, $k_{TB}/k_o=1.7$ at 140 °C ($k_{TB}=3.1\times10^{-3}$, $k_o=1.8\times10^{-3}$/min mol). The observed rate increase by introduction of TB, generally regarded as a radical scavenger, may indicate an intermediate formation of some condensate which can be homolyzed to regenerate the benzyl radical. However, these thermodynamic parameters might not be accurate enough to calculate $\Delta S^{\ddagger}$. But 2-(2-alkenyloxy)tropones, feasible for concerted intramolecular 3,3-sigmatropy, must not yield the oxidation products. Indeed, 2-allyloxytropone (**7a**) and some other analogs (**7b** and **7c**)[6] gave only the Claisen rearrangement products (**8a**—**c**).[7] But 2-(3-methyl-2-butenyloxy)-tropone (**7d**), the Claisen rearrangement product of which should suffer serious steric hindrance, failed to give either oxidation product or Claisen rearrangement product. The identified compounds were regenerated **2** together with isoprene.[8]



Scheme 3.

As an alternative of **2**, 3,5,7-trimethyltropolone (**9**)[9] can be used; 2-benzyloxy-3,5,7-trimethyltropone (**10a**) gave **3a** in 64% yield after silica-gel chromatographic work up. However, again 2-allyloxy-3,5,7-trimethyltropone (**11a**) gave only a Claisen rearrangement product: 3-allyl-3,5,7-trimethyl-4,6-cycloheptadiene-1,2-dione (**12a**),[10] and no oxidation occurred. On the other hand, the oxidation of 2-alkoxy-3,5,7-trimethyltropones (**13**) proceeded, after an induction period, to give the corresponding aldehydes in good yields; *i.e.*, from 2-hexyloxy-3,5,7-trimethyltropone (**13a**), **4a** was obtained in a 55% yield. This might be a result of blocking of the *o*- and *p*-position with methyl groups to prevent electrophilic attack of the resultant aldehydes. Similar features were observed in several derivatives, as shown in Table 2, and the reaction thus became applicable for the preparation of saturated aldehydes in general.

Related studies are in progress, and will be reported in future.

Experimental

Preparation of Tropolonyl Ethers (General Method). A hexamethylphosphoric triamide (HMPA) solution of tropolones and sodium hydride (1.2 mol equiv.) was treated with alkyl, allyl, or arylmethyl halides until the starting troponoids disappeared. In the cases of alkyl and arylmethyl derivatives, the mixture had to be heated as high as 120 °C,

but allyl and other thermally-sensitive derivatives gave good results when the mixture was kept at room temperature. After dilution with water, the mixture was extracted with ether, dried on $MgSO_4$, and chromatographed on a silica-gel column, if necessary. Yields varied depending on the steric circumstances of the halides, as compiled in Table 1; these are not optimized results.

Reaction of ***1a*** *with DMSO.* A DMSO solution (2 cm³) of **1a** (50 mg) was heated in a sealed tube for 6 h at 180 °C (refluxing *o*-dichlorobenzene bath). After dilution with water, the mixture was extracted with diethyl ether and chromatographed on a silica-gel column to give a colorless oil, **3a**, which was directly identified to be benzaldehyde. The isolated yield was 65%, but the latter fractions of chromatography contained colorless needles, which was identified to be benzoic acid (**B**).

Attempted Reaction of Phenyl Benzyl Ether (A) in DMSO-d_6. A DMSO-d_6 solution (0.5 cm³) of **A** (50 mg) was heated in a sealed tube at 180 °C for 15 h. The NMR spectroscopy revealed that the reaction did not proceeded at all.

The NMR Analysis of the Reaction of ***1a*** *with DMSO-*d_6 *in a Presence of* p*-Chlorobenzyl Alcohol (****6b****).* A DMSO-d_6 solution (0.5 cm³) of **1a** (25 mg) and **6b** (12 mg) was heated in a sealed tube (in refluxing *o*-dichlorobenzene bath) for 3 h. The mixture was then directly analyzed by an FT-NMR spectrometer: the result was **3a** : **3b**=5 : 1. If we judge only from the NMR spectrum, the reaction was very clean; there are no signals other than those of **1a**, **3a**, **3b**, regenerated **2**, and **6b**.

Reaction of ***1a*** *with DMSO in a Presence of Benzyl-*d_5 *Alcohol (****6a****-*d_5). A DMSO solution (2 cm³) of **1a** (90 mg) and **6a**-d_5 (50 mg)[4] was heated in a sealed tube at 180 °C for 2 h. The product isolated by the usual manner was a colorless oil, **3a**, from which autoxidized benzoic acid (**B**), colorless needles, mp 122—123 °C, were obtained in a pure form, 10 mg (20%). Its mass-spectrum [Found: *m/e*, 122 : 123 : 124 : 125 : 126 : 127=100.0 : 8.1 : 0.7 : 0.2 : 0.6 : 1.3] confirmed that there was only a negligible incorporation of deuterium atoms.[5]

Kinetic Analysis of the Reaction of ***1a*** *in DMSO-*d_6 *in a Presence of BP or TB.* Each DMSO-d_6 solution (0.4 cm³) of **1a** (each 30 mg) with various amounts of BP or TB (0 to 50 mg) was heated in a sealed tube at a constant temperature (140—160 °C), and the rates of formation of **3a** were measured.

Attempted Reaction of 2-(Alkenyloxy)tropones with DMSO. a): A DMSO solution (0.5 cm³) of 2-allyloxy tropone (**7a**, 25 mg) was heated in a sealed tube at 180 °C for 30 min. The product isolated after preparative silica-gel column chromatography was a pale yellow oil, 21 mg (84%), **8a**.[6]

b): A DMSO solution (0.3 cm³) of 2-(2-methyl-2-propenyloxy)tropone (**7b**, 30 mg) was heated in refluxing *o*-dichlorobenzene for 1.5 h. The mixture was then extracted by ether and water, and the organic extract was chromatographed on a silica-gel column to give a colorless oil, which was identified to be the Claisen product (**8b**), 21 mg (70%) [Found: *m/e*, 176.0824 (M^+). Calcd for $C_{11}H_{12}O_2$: 176.0837. δ: 1.33 (3H, d, J=7 Hz), 4.31 (1H, dqt, J=7, 5, 1.5 Hz), 5.13 (1H, dt, J=10, 1.5 Hz), 5.15 (1H, dt, J=17, 1.5 Hz), 5.99 (1H, ddd, J=17, 10, 4 Hz), 6.97 (1H, ddd, J=10, 7, 4 Hz), 7.27 (2H, m), 7.41 (1H, dt, J=10, 1 Hz), and 8.8—9.6 (1H, OH)].

c): A DMSO solution (0.3 cm³) of **7c** (50 mg) was heated in a sealed tube at 180 °C for 1 h. Silica-gel column chromatography of the mixture afforded a colorless oil (**8c**), 48 mg (96%), which was identical with the authentic sample.[6]

d): A DMSO solution (0.3 cm³) of **7d** (50 mg) was heated in a sealed tube at 180 °C for 30 min. Silica-gel column chromatography of the mixture gave only **2**, 31 mg (97%), together with isoprene, which was identified by NMR spectroscopy.

Reaction of 2-(Benzyloxy)-3,5,7-trimethyltropone with DMSO. A DMSO solution (0.3 cm³) of **10a** (50 mg) was heated in a sealed tube in a refluxing decalin bath. Preparative thin-layer chromatography of the mixture yielded benzaldehyde (**3a**), 13 mg (64%).

*Attempted Oxidation of 2-(Allyloxy)-3,5,7-trimethyltropone (****11a****)*[10] *with DMSO.* A DMSO solution of **11a** (50 mg) was heated in a secaled tube at 180 °C for 20 min. After dilution with water, the mixture was extracted with ether to give a colorless oil, 29 mg (58%), whose NMR spectrum was identical with the Claisen rearrangement product (**12a**) described previously:[10] δ: 1.28 (3H, s), 1.91 (3H, d, J=2 Hz), 1.99 (3H, d, J=2 Hz), 2.50 (2H, m), 4.99 (1H, m), 5.12 (1H, m), 5.60 (1H, m), 5.65 (1H, *q*, J=2 Hz), and 6.58 (1H, q, J=2 Hz). No other product was identified.

*Reaction of 2-Alkoxy-3,5,7-trimethyltropones (****13****). a)*: A DMSO solution (2 cm³) of 2-(hexyloxy)-3,5,7-trimethyltropone (**13a**, 50 mg) was heated in a sealed tube at 180 °C for 8 h. The product isolated after silica-gel column chromatography was hexanal (**4a**) [δ: 0.89 (3H, tm, J=7 Hz), 1.2—1.7 (6H, m), 2.38 (2H, td, J=7, 2 Hz) and 9.66 (1H, t, J=2 Hz). δ (C): 14.0, 22.5, 23.3, 31.5, 43.8, and 201.1], 11 mg (55%).

b): A DMSO solution (0.4 cm³) of 2-(decyloxy)-3,5,7-trimethyltropone (**13b**, 50 mg) was similarly heated in a sealed tube at 180 °C for 5 h. Eight mg of decanal (**14b**) was obtained (31%) [δ: 0.87 (3H, tm, J=7 Hz), 1.26 (12H, m), 1.60 (2H, m), 2.38 (2H, td, J=7, 2 Hz), and 9.67 (1H, t, J=2 Hz). δ (C): 14.1, 22.2, 22.8, 29.4 (2C), 29.7 (2C), 32.0, 43.9, and 201.6].

References

1) M. Fieser, "Reagents in Organic Synthesis," Wiley-Interscience Publ., New York (1980), Vol. 8, p. 199. See also previous Vols. 1—7.

2) H. Takeshita, H. Mametsuka, A. Chisaka, and N. Matsuo, *Chem. Lett.*, **1981**, 73.

3) Indeed, by heating of **2** and **4a** in DMSO at 180 °C for 2 h, a decrease of the NMR signals of both compounds occurred by formation of an intractable condensate mixture.

4) The sample of pentadeuteriobenzoic acid kindly provided by Prof. Masashi Tashiro, Research Institute of Industrial Science, Kyushu University, had the following isotope distributions: d_5=70%, d_4=23%, and d_3=7%. However, the deuterium content of 2- and 6-positions is practically 100%. We thank him for the generous gift.

5) Based on the deuterium distributions of the starting **6a—d**, the observed *m/e*: 123 (8.1) must be interpreted as the $(M+1)^+$ peak, but not as the **3a**-d_1.

6) H. Takeshita, I. Kouno, and K. Miyake, *Kyushu Daigaku Seisan Kagaku Kenkyusho Hokoku*, **66**, 1 (1977).

7) In our previous study,[6] Claisen rearrangements on some of these (alkenyloxy)tropones were unsuccessful.

8) Previously, **7d** was converted to the *o*- and *p*-Claisen rearrangement products (33% and 28%) by heating at 150 °C.[11]

9) T. Nozoe, T. Mukai, and K. Takase, *Sci. Reports Tohoku Univ., Ser. I*, **36**, 40 (1952).

10) The Claisen rearrangement product of **11a** (**12a**) is known to cause a further intramolecular Diels-Alder reaction. See R. M. Harrison, J. D. Hobson, and M. M. Al Holly, *J. Chem. Soc., C*, **1971**, 3084.

11) R. M. Harrison and J. D. Hobson, *J. Chem. Soc., Perkin Trans. 1*, **1973**, 1958.