duced pressure and the residue distilled, giving benzaldehyde dimethyl acetal (4.5 g., 61.6%), b.p. 196° (reported[11] b.p. 198–199°).

Anal. Calcd. for $C_9H_{12}O_2$: C, 71.0; 7.9. Found: C, 71.2; H, 8.1.

This acetal was hydrolyzed by boiling with 2% hydrochloric acid, yielding benzaldehyde, which was identified as its 2,4-dinitrophenylhydrazone, m.p. 237°, undepressed on admixture with an authentic specimen.

Electrolysis of α-methoxydiphenylacetic acid. The solution of α-methoxydiphenylacetic acid (4.6 g.) in methanol (100 ml.) was electrolyzed. During the electrolysis an insoluble colorless solid was deposited at the bottom of the vessel. The methanol was evaporated under reduced pressure and the residue dissolved in ether. The ethereal solution, washed successively with saturated sodium carbonate solution, dried and evaporated, afforded, after recrystallization from methanol, benzophenone dimethyl acetal (3.2 g., 74%) m.p. 105–107°. A m.p. of 106.5–107° has been reported[12] for this acetal.

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.9; H, 7.0. Found: C, 79.2; H, 6.8.

Addition of concd. sulfuric acid to this acetal afforded benzophenone, m.p. 47–49°, undepressed on admixture with an authentic specimen.

Electrolysis of α-ethoxyphenylacetic acid. The solution of α-ethoxyphenylacetic acid (3.8 g.) in methanol (90 ml.) was electrolyzed. The methanol was evaporated under reduced pressure and the residue distilled. A colorless liquid was collected as the main fraction (2.5 g., 71.4%), b.p. 205°, $n_D^{19.0}$ 1.4878.

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.3; H, 8.4. Found: C, 72.5; H, 8.6.

This acetal was hydrolyzed by boiling with 2% hydrochloric acid, yielding benzaldehyde, which was identified as its 2,4-dinitrophenylhydrazone, m.p. 237°, undepressed on admixture with an authentic specimen.

Electrolysis of α-ethoxydiphenylacetic acid. The solution of α-ethoxydiphenylacetic acid (5.5 g.) in methanol (150 ml.) was electrolyzed. During the electrolysis an insoluble colorless solid was deposited at the bottom of the vessel. The methanol was evaporated under reduced pressure and the residue disolved in ether. The ethereal solution was washed successively with saturated sodium carbonate solution, dried, and evaporated. The residue, distilled under reduced pressure, yielded as a main fraction a colorless liquid (3.05 g., 74%), b.p. 133–135°, $n_D^{22.5}$ 1.9432. The liquid solidified when refrigerated overnight and, after crystallization from methanol, melted at 32–33°.

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.3; H, 7.4. Found: C, 79.3; H, 7.1.

This substance, when treated with concd. sulfuric acid, gave benzophenone, m.p. 48°, undepressed on admixture with an authentic specimen.

Acknowledgment. The authors wish to thank the Rockefeller Foundation and the Brazilian "Conselho Nacional de Pesquisas" for grants and also for a scholarship awarded to A. M. J. Ayres.

DEPARTAMENTO DE QUÍMICA
FACULDADE DE FILOSOFIA, CIÊNCIAS E LETRAS
UNIVERSIDADE DE SÃO PAULO
SÃO PAULO, BRAZIL

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Periodate Oxidation of Sulfides to Sulfoxides. Scope of the Reaction

NELSON J. LEONARD AND CARL R. JOHNSON[1]

Received July 12, 1961

Since the first recorded synthesis of a sulfoxide by Märcker[2] in 1865, numerous methods have been developed for the transformation of sulfides to sulfoxides,[3] utilizing reagents such as nitric acid,[2,4] hydrogen peroxide,[5] dinitrogen tetroxide,[6] chromic acid,[7] ozone,[8] peracids,[9] hydroperoxides,[10] manganese dioxide,[7a] selenium dioxide,[11] and iodosobenzene.[12] We wished to synthesize a particular sulfoxide, 1-thiacyclooctan-5-one 1-oxide (I), from the corresponding sulfide in order to investigate its chemical and physical properties,[13] in continuation of our study of transannular effects in mesocyclic systems.[14] Difficulties experienced earlier in this laboratory in obtaining the sulfoxide (I) free from contaminating sulfide and/or sulfone by the usual oxidation methods were resolved when we turned to sodium metaperiodate as the oxidant.

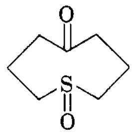

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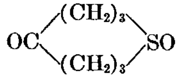
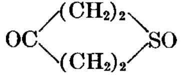
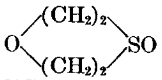
TABLE I

Sulfoxides Produced by Sodium Metaperiodate Oxidation of the Corresponding Sulfides

Name	Structure	Yield, %	M.P. (B.P.)		ν_{max}S=O, cm.$^{-1}$	Formula	C, %		H, %		Other Identifying Properties, Remarks
			Found	Reptd.			Calcd.	Found	Calcd.	Found	
1-Thiacyclooctan-5-one 1-oxide		91	91–92	—	1049[a]	$C_7H_{12}O_2S$	52.48	52.46	7.55	7.86	$\nu^a_{C=O}$ 1710 cm.$^{-1}$; extremely hygroscopic
1-Thiacyclohexan-4-one 1-oxide		97	109–110	113[c]	1055[a]	$C_5H_8O_2S$	45.43	44.72[d]	6.10	6.19	$\nu^a_{C=O}$ 1725 cm.$^{-1}$
Methyl 4-ketopentyl sulfoxide	$CH_3SO(CH_2)_3COCH_3$	98	22.5–23.5 (99–101/ 0.12 mm.)	—	1058[b]	$C_6H_{12}O_2S$	48.66	48.86	8.17	8.25	n^{25}_D 1.4873, $\nu^b_{C=O}$ 1718 cm.$^{-1}$
Phenyl sulfoxide	$(C_6H_5)_2SO$	98	69–71	69–71[e,f]	1033[b]	$C_{12}H_{10}OS$	—	—	—	—	$\lambda^{C_2H_5OH}_{max}$ 274 mμ (log ε 3.2) 233 mμ (log ε 4.1)[g]
Methyl phenyl sulfoxide	$CH_3SOC_6H_5$	99	29–30 (83–85/0.1 mm.)	29.5 (104.5/0.7 mm.)[h,i]	1050[a]	C_7H_8OS	59.90	59.75	5.71	6.18	Very hygroscopic
Thian 1-oxide	$(CH_2)_5SO$	99	67–68.2	60–61.5[j]	1045[a]	$C_5H_{10}OS$	—	—	—	—	Liquifies immediately on exposure to the atmosphere
1,4-Oxathian 4-oxide		83[k]	46–47.2	44.5–45[l]	1026[a]	$C_4H_8O_2S$	—	—	—	—	Hygroscopic
Bis(2-diethylaminoethyl) sulfoxide	$[(C_2H_5)_2N(CH_2)_2]_2SO$	85[m]	Dipicrate, 146–148	—	—	Dipicrate, $C_{24}H_{34}N_8O_{15}S$	40.80	40.98	4.86	5.16	
1-Benzylsulfinyl-2-propanone	$C_6H_5CH_2SOCH_2COCH_3$	89	126–126.5	125[n]	1046[b]	$C_{10}H_{12}O_2S$	61.17	61.33	6.16	6.22	$\nu^b_{C=O}$ 1705 cm.$^{-1}$
Acetoxymethyl methyl sulfoxide	$CH_3COOCH_2SOCH_3$	72	(85–90/0.1 mm.)	—	1044[a]	$C_4H_8O_3S$	35.28	35.17	5.92	5.80	n^{25}_D 1.4798; $\nu^a_{C=O}$ 1762 cm.$^{-1}$
Phenylsulfinylacetic acid[o]	$C_6H_5SOCH_2COOH$	99	118–119.5	113–115[p]	1015[q]	$C_8H_8O_3S$	—	—	—	—	$\nu^q_{C=O}$ 1732 cm.$^{-1}$
Benzyl sulfoxide[r]	$(C_6H_5CH_2)_2SO$	96	135–136	132–133[f]	1025[a]	$C_{14}H_{14}OS$	73.00	73.12	6.13	6.06	Analytically pure after single crystallization from ethanol
Ethyl sulfoxide	$(C_2H_5)_2SO$	65[s]	(45–47/0.15 mm.)	(88–89/15 mm.)[t]	1047[a]	$C_4H_{10}OS$	—	—	—	—	n^{25}_D 1.4676

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[a] Carbon tetrachloride solution. [b] Chloroform solution. [c] G. M. Bennett and W. B. Waddington, *J. Chem. Soc.*, 2829 (1929) reported m.p. 113°, but were unable to repeat their preparation. [d] Repeated purification procedures did not improve analysis. [e] H. H. Szmant and R. L. Lapinski, *J. Am. Chem. Soc.*, **78**, 458 (1956). [f] R. L. Shriner, H. C. Struck, and W. J. Jorison, *J. Am. Chem. Soc.*, **52**, 2060 (1930). [g] $\lambda^{C_2H_5OH}_{max}$ 274 mμ (log ε 3.3), 233 (4.2), H. P. Koch, *J. Chem. Soc.*, 2892 (1950). [h] Ref. 6b. [i] C. C. Price and J. J. Hydock, *J. Am. Chem. Soc.*, **74**, 1943 (1952). [j] M. Tamres and S. Searles, Jr., *J. Am. Chem. Soc.*, **81**, 2100 (1959). [k] Yield based on technical thioxane. [l] French patent **859,866**; *Chem. Abstr.*, **42**, 3783 (1948). [m] Crude yield. No formal purification of free base was made. Characterized as the dipicrate. [n] C. Wahl, *Ber.*, **55**, 1449 (1922). [o] Isolated by lyophillization of reaction mixture, followed by extraction with hot ethyl acetate. [p] A. Tananger, *Arkiv. Kemi Mineral. Geol.*, **24A**, No. 10 (1947). [q] Nujol mull. [r] Oxidation by 0.25*M* sodium metaperiodate in 50% methanol. [s] Lower yield due to incomplete extraction. Ethyl sulfone (5%) was formed during heating used to concentrate reaction mixture prior to extraction. [t] R. Pummerer, *Ber.*, **43**, 1401 (1910).

During the extensive penicillin effort of the 1940's, sodium metaperiodate had been reported by Sykes and Todd[15] to oxidize the sulfide function of benzylpenicillin methyl ester and related systems to sulfoxide,[16] but the method had not found general application. In our hands an adaptation of the sodium metaperiodate procedure of Sykes and Todd to the oxidation of 1-thiacycloöctan-5-one afforded the desired sulfoxide (I) in 91% yield. Encouraged by the success of this conversion, we have now provided additional examples of the oxidation, sufficiently varied (Table I) to demonstrate the generality and selectivity of the method.

On a preparative scale the oxidation is conveniently carried out by addition of the sulfide to a slight excess of 0.5*M* aqueous sodium metaperiodate at ice-bath temperature.[17] The reaction, complete in three to twelve hours, affords pure sulfoxide, usually in better than 90% yield. It appears expedient to use a mixed solvent system—*e.g.*, methanol-water—in those cases where solubility of the sulfide in water is slight. Lower yields may result when water solubility of the product diminishes the efficiency of extraction. The extent and rate of the

$$R_2S + NaIO_4 \longrightarrow R_2SO + NaIO_3 \qquad (1)$$

reaction (1) may be followed quantitatively by the titration methods commonly used in the Malaprade procedure for the periodate oxidation of glycols.[15,18]

When considered with the array of reagents available for the oxidation of sulfides to sulfoxides, sodium metaperiodate possesses certain advantages: over-oxidation can be avoided; mild conditions are employed; the reagent is readily available and is safely and easily handled; and excellent yields are obtainable, even when other functionality is present (periodate-susceptible groupings such as α-glycols being excepted).

EXPERIMENTAL

General method of oxidation. To 210 ml. (0.105 mole) of a 0.5*M* solution of sodium metaperiodate at 0° was added 0.1 mole of sulfide. The mixture was stirred at ice-bath temperature, usually overnight. The precipitated sodium iodate was removed by filtration, and the filtrate was extracted with chloroform. The extract was dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. The sulfoxide was purified by distillation, crystallization, or sublimation.

The Noyes Chemical Laboratory
University of Illinois
Urbana Ill.

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We wish to thank Dr. Peter Sykes, Cambridge University, for suggesting the application of periodate to our problem.

[16] E. H. Flynn, Eli Lilly and Co., Indianapolis, Ind., has recently applied periodate to the synthesis of other sulfoxides in the penicillin series (private communication).

[17] Temperature control is important during the reaction (Table I, footnote *s*). Some over-oxidation was experienced in the case of ethyl sulfide; W. A. Bonner and R. W. Drisko [*J. Am. Chem. Soc.*, **73**, 3699 (1951)] found ethyl sulfide to be oxidized to the sulfone by periodic acid at 60°. Moreover, Sykes and Todd[15] reported that *S*-benzylpenicillamine is oxidized to the corresponding sulfone by sodium metaperiodate at 60°.

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Hydrogenation of Substituted Pyridines with Rhodium on Carbon Catalyst[1]

Morris Freifelder, Ralph M. Robinson, and George R. Stone

Received August 4, 1961

Recently we investigated the action of ruthenium dioxide in the hydrogenation of pyridines.[2] While this procedure gives excellent results, it requires pressures in the range of seventy atmospheres. In laboratories where heavier equipment is not available, there is a need for a low pressure method which would eliminate some of the disadvantages of hydrogenation in the presence of platinum catalysts.

The presence of acid is required when Adams' catalyst is used to convert pyridines to piperidines.[3] If the desired base is water soluble, continuous extraction must be employed in order to get good yield. In addition, there are discouraging reports where hydrogen uptake is slow and where more catalyst must be added.[4]

In a description of some hydrogenations with ruthenium and rhodium catalysts, there is a mention of the reduction of pyridine with an equal weight of 5% rhodium on alumina.[5] When we repeated this reaction with a more normal amount of catalyst, we found that, while initial uptake of hydrogen was quite rapid, it slowed down considerably and was 90% complete in 15 hours. In addition, the catalyst was irrevocably poisoned after the reduction and could not be regenerated. We had noted in some previous work that hydrogenation with rhodium on alumina is inhibited by a strong base.[6] Piperidine after conversion from pyridine apparently has a similar effect on this catalyst. This retardation is even more pronounced in the

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[1] Presented at the 140th meeting, American Chemical Society, Chicago, Ill., September 1961.

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