Synthesis of 1,2,4-Trioxans

By MASAHIRO MIURA, MASATOMO NOJIMA,* and SHIGEKAZU KUSABAYASHI

(*Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka* 565, *Japan*)

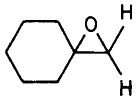
Summary The reaction of a mixture of α-hydroxydecyl hydroperoxide [or bis-(α-hydroxyalkyl)peroxides] and epoxides in the presence of tungstic anhydride and catalytic amounts of chlorosulphonic acid gave the corresponding 1,2,4-trioxans in 7—63% yield.

BECAUSE of the unique properties of 1,2,4,5-tetroxans[1] and 1,2-dioxans[2] the syntheses of these compounds have been well studied.[2–5] In contrast, a limited number of synthetic methods have been reported for the relevant 1,2,4-trioxans.[6–9] While developing a new, general synthetic method for cyclic peroxides with α-hydroxy hydroperoxides,[10] we discovered that the reaction of α-hydroxydecyl hydroperoxide (**1**) [or the related peroxides (**2a**) and (**2b**)] and the epoxides methylenecyclohexane oxide (**3a**), cyclohexene oxide (**3b**), styrene oxide (**3c**), or diphenylethylene oxide (**3d**), in the presence of tungstic anhydride and catalytic amounts of chlorosulphonic acid gave the corresponding 1,2,4-trioxans (**4a**)—(**4h**), as shown in the Table.[†] The following experimental procedure illustrates the method.

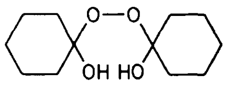
[†] In some cases, configurationally isomeric products can be formed. However, only one isomer was isolated in all the reactions. The configuration of the trioxan (**4a**) is reasonably assigned as *trans* on the basis of ^{1}H n.m.r. signals of 3-H [δ 5·13 (1 H, t, *J* 4·5 Hz)], 5-H [δ 3·69 (1 H, d × d, *J* 12·0 and 13·5 Hz) and 4·20 (1 H, d × d, *J* 12·0 and 3·0 Hz)], and 6-H [δ 6·16 (1 H, d × d, *J* 13·5 and 3·0 Hz)] (see the discussion in ref. 5). Because of the stability, the configuration of the trioxan (**4f**) must also be *trans*. Similarly, the substituents of the trioxans (**4b**), (**4e**), (**4g**), and (**4h**) at C-3 are expected to occupy the equatorial positions.

$C_9H_{19}CH(OH)OOH$

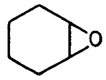
(1)



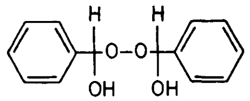
(3a)



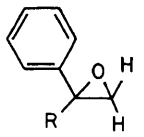
(2a)



(3b)

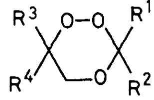


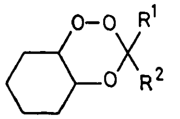
(2b)



(3c) R = H

(3d) R = Ph





(4a) $R^1 = C_9H_{19}, R^2 = R^4 = H, R^3 = Ph$

(4b) $R^1 = C_9H_{19}, R^2 = H, R^3 = R^4 = Ph$

(4c) $R^1, R^2 = R^3, R^4 = -[CH_2]_5-$

(4d) $R^1, R^2 = -[CH_2]_5-$

(4e) $R^1 = Ph, R^2 = H, R^3, R^4 = -[CH_2]_5-$

(4g) $R^1 = Ph, R^2 = H$

(4f) $R^1 = R^3 = Ph, R^2 = R^4 = H$

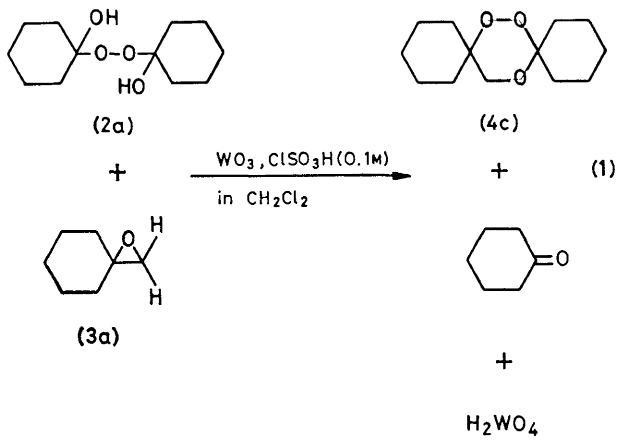
(4h) $R^1 = R^3 = R^4 = Ph, R^2 = H$

TABLE. Synthesis of 1,2,4-trioxans.

		1,2,4-Trioxan[a]	
Peroxide	Epoxide	Yield/mol %	M.p./°C
(**1**)	(**3c**)	(**4a**) 15	145—147
(**1**)	(**3d**)	(**4b**) 28	53—54
(**2a**)	(**3a**)	(**4c**) 35	34—35
(**2a**)	(**3b**)	(**4d**) 7	33—34
(**2b**)	(**3a**)	(**4e**) 42	68
(**2b**)	(**3b**)	(**4f**) 37	149
(**2b**)	(**3c**)	(**4g**) 63	65—66
(**2b**)	(**3d**)	(**4h**) 41	169—170

[a] All the products gave satisfactory spectral and elemental analysis data.

A mixture of the hydroperoxide (**2a**) (2 mmol), the oxide (**3a**) (2 mmol), and tungstic anhydride (2 mmol) in dichloromethane (10 ml) was stirred at 20 °C for 3 h. A solution of chlorosulphonic acid (0·2 mmol) in dichloromethane (2 ml) was added and the mixture was stirred for a further 2 h. After conventional work-up the neutral products were isolated by column chromatography on silica gel using benzene–light petroleum as eluant. The first fraction contained dispiro{cyclohexane-1,3′-[1.2.4]trioxan-6′,1″-cyclohexane} (**4c**) (35%); i.r. ν_{max} (KBr) 1445, 1360, 1330, 1270, 1155, 1080, and 920 cm^{-1}; ^{1}H n.m.r. δ (CCl_4) 1·12—1·46 (20 H, m) and 3·44 (2 H, br. s); *m/e* 226 (M^+). From the second fraction cyclohexanone was obtained in a yield of 95% [equation (1)].



This procedure, as a widely applicable synthetic route to 1,2,4-trioxans, is advantageous in some respects compared with the reported methods in which *vic*-hydroperoxy-alcohols, prepared by the reaction of epoxides with 98% hydrogen peroxide[6] or generated *in situ* by the reaction of alkenes with 34% hydrogen peroxide in the presence of tungstic acid,[7] were treated with acetone; 98% hydrogen peroxide is somewhat dangerous and, moreover, generation of *vic*-hydroperoxy-alcohols *in situ* is accompanied by the production of the 1,2-diols in a considerable amount.[7] By contrast, the pure peroxides (**1**), (**2a**), and (**2b**) can be prepared very easily by the reaction of the corresponding carbonyl compounds with 30% hydrogen peroxide.[11]

(*Received*, 19*th March* 1981; *Com.* 308.)

---

[1] K. J. McCullough, A. R. Morgan, D. C. Nonhebel, and P. L. Pauson, *J. Chem. Res.*, 1980, (*S*) 35, (*M*) 0629; (*S*) 36, (*M*) 0651.
[2] W. Adam and N. Duran, *J. Am. Chem. Soc.*, 1977, **99**, 2729.
[3] K. J. McCullough, A. R. Morgan, D. C. Nonhebel, P. L. Pauson, and G. J. White, *J. Chem. Res.*, 1980, (*S*) 34, (*M*) 0629.
[4] A. J. Bloodworth and J. A. Kahan, *J. Chem. Soc., Perkin Trans.* 1, 1980, 2450.
[5] M. Miura and M. Nojima, *J. Am. Chem. Soc.*, 1980, **102**, 288.
[6] W. Adam and A. Pios, *Chem. Commun.*, 1971, 822.
[7] G. B. Payne and C. W. Smith, *J. Org. Chem.*, 1957, **22**, 1682.
[8] H. Yamamoto, M. Akutagawa, H. Aoyama, and Y. Omote, *J. Chem. Soc., Perkin Trans.* 1, 1980, 2300.
[9] K. Maruyama, M. Muraoka, and Y. Naruta, *J. Chem. Soc., Chem. Commun.*, 1980, 1282.
[10] M. Miura, A. Ikegami, M. Nojima, and S. Kusabayashi, *J. Chem. Soc., Chem. Commun.*, 1980, 1279.
[11] D. Swern, 'Organic Peroxides,' Interscience, New York, 1970, vol. 1.