Electrophile-induced Rearrangement of 1,2,4-Trioxanes. Formation of 1-Benzofuran and 2*H*-1-Benzopyrans

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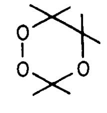
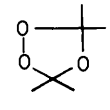
3,3,6,10b-Tetramethyl-4a,10b-dihydronaphtho[2,1-*e*][1,2,4]trioxane and its 3,3-spirocyclic cyclopentane analogue on treatment with an excess of trimethylsilyl trifluoromethanesulphonate for 10 min at 24 °C rearrange to give 2-(2-oxopropyl)-3-methyl-1-benzofuran in high yield; in similar fashion the 3-methyl, n-butyl, and phenyl derivatives of 3,10b-epidioxy-2,3,4a,10b-tetrahydro-6-methyl-1*H*-naphtho[2,1-*b*]pyran give the 3-oxobutyl, 3-oxoheptyl, and 3-phenyl-3-oxopropyl derivatives of 2-formyl-3-methyl(2*H*)-1-benzopyran.

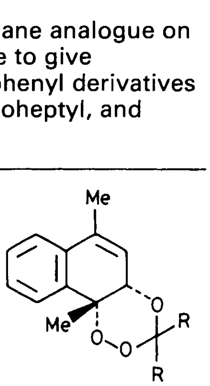
1,2,4-Trioxanes (**1**), unlike their lower homologues, the secondary ozonides (**2**), are relatively unknown. Since the first mention of a 1,2,4-trioxane in 1957,[1] little has been reported.[2] However, many derivatives are now available for study thanks to new synthetic methods.[3] They already show promise as synthons. Certain 1,2,4-trioxanes[4] and 1,2,4-trioxan-5-ones[5] react with base to give 1,2-diol monoesters and α-keto acids respectively. We now report that electrophiles cause suitably substituted 1,2,4-trioxanes to rearrange to furans and pyrans.



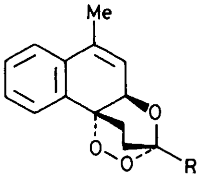
(**1**)



(**2**)



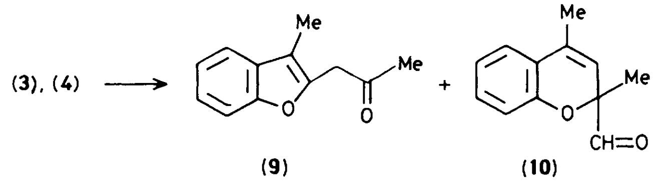
(**3**) R = Me
(**4**) R ,R = $-[CH_2]_4-$
(**5**) R = H



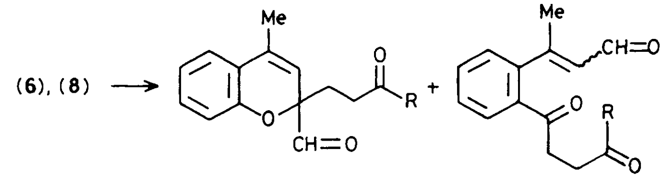
(**6**) R = Me
(**7**) R = Bu^n
(**8**) R = Ph

Two series, having *cis*- (**3**)—(**5**)[3a] and *trans*-fused trioxane rings (**6**)—(**8**)[6] respectively, provide apt illustrations. Treatment of (**3**) with trimethylsilyl trifluoromethanesulphonate (TMSOTf) (1.2 mol equiv.) in dichloromethane for 10 min at 24 °C followed by chromatography over Florisil afforded (**9**) in essentially quantitative yield. Under milder conditions (0.07 mol equiv. of TMSOTf) the amount of (**9**) diminished, but was compensated by formation of its 2*H*-1-benzopyran isomer (**10**).† The spirocyclic trioxane (**4**) behaved analogously, giving the same furan (**9**) and pyran (**10**), whereas the parent trioxane (**5**) proved inert under mild conditions, even after several hours.

The bridged bicyclic trioxanes (**6**)—(**8**) also rearranged, giving the corresponding benzopyrans (**11**)—(**13**) in 63—87% yields,† accompanied by decreasingly minor amounts of the isomers (**14**)—(**16**).‡



(**9**) (**10**)



(**11**) R = Me
(**12**) R = Bu^n
(**13**) R = Ph

(**14**) R = Me
(**15**) R = Bu^n
(**16**) R = Ph

Both sets of trioxanes undoubtedly undergo electrophile-induced rupture of the oxygen–oxygen bond. The geometry in both the *cis*- and *trans* series is ideal for the concerted shift of the phenyl substituent as the bond breaks.[9] In the bridged bicyclic skeleton (*trans* series), the vinyl group is also correctly placed for migration. The action of electrophile on (**6**)—(**8**) triggers the double 1,2 transposition to the oxonium cation (**17**) resulting in isomerization to the aldehydic benzopyrans (**11**)—(**13**) [Scheme 1(a)]. A competitive, but minor event is the unravelling of the trioxane ring [Scheme 1(b)]. Cleavage of the intracyclic bond generates the medium ring oxonium cation (**18**) which collapses to products (**14**)—(**16**).

In the decalin-like skeleton (*cis* series) the vinyl group is less well placed, therefore allowing the benzohomopyrylium cations, *e.g.* (**19**), produced from (**3**) or (**4**), to eliminate ketone (Scheme 2). The resulting epoxide (**20**) then opens to

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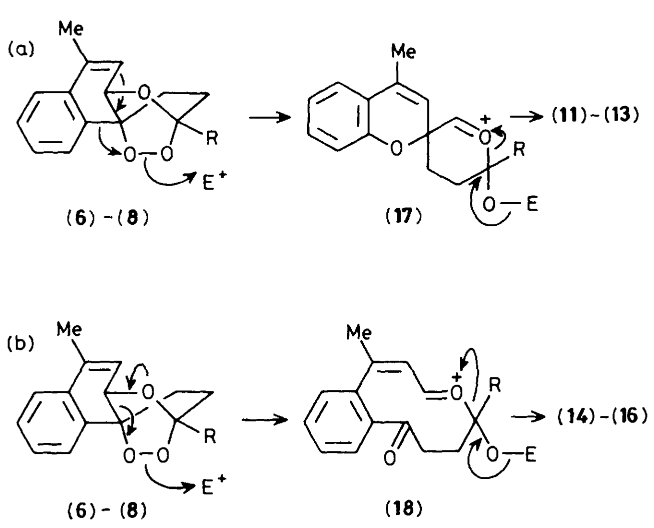
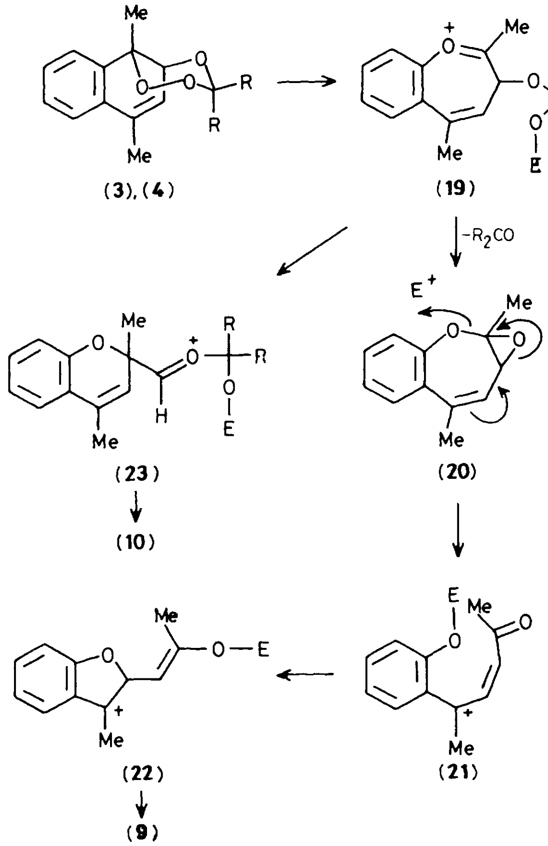
† Trifluoroacetic and trifluoromethanesulphonic acid also brought about the same rearrangements of (**3**) and (**4**), but were less effective than TMSOTf. All new compounds gave satisfactory elemental analyses and spectral data. Some typical values follow. Benzofuran (**9**): orange oil; ^{1}H n.m.r. (360 MHz, $CDCl_3$) 2.22 (s, 3H), 2.23 (s, 3H), 3.83 (s, 2H), 7.28 (m, 2H), 7.44 (m, 1H), 7.50 (m, 1H); ^{13}C n.m.r. (50 MHz, $CDCl_3$) 7.97 (q), 29.31 (q), 41.93 (t), 110.90 (d), 112.94 (s), 119.19 (d), 122.41 (d), 124.05 (d), 129.91 (s), 146.61 (s), 154.22 (s), 203.75 (s); i.r. (CCl_4) 1728 cm^{-1}; *m/z* 188 (24, *M*$^+$), 145 (100). The substitution pattern on the furan ring was confirmed by comparison of the n.m.r. data with that of the 2- and 3-methyl-1-benzofurans.[7] Benzopyran (**11**): pale yellow oil; ^{1}H n.m.r. (360 MHz, $CDCl_3$) 2.04 (d, *J* 1.5 Hz, 3H), 2.09 (t, *J* 8 Hz, 2H), 2.10 (s, 3H), 2.59 (m, 2H), 5.30 (q, *J* 1.5 Hz, 1H), 6.94 (m, 2H), 7.18 (m, 2H), 9.68 (s, 1H); ^{13}C n.m.r. (50 MHz, $CDCl_3$) 18.19 (q), 29.42 (t), 30.05 (q), 37.08 (t), 84.39 (s), 115.91 (d), 117.42 (d), 121.56 (d), 121.63 (s), 123.95 (d), 130.01 (d), 133.62 (s), 152.45 (s), 198.73 (s), 207.42 (s); i.r. (CCl_4) 1740, 1725 cm^{-1}; *m/z* 244 (5, *M*$^+$), 215 (100). The parent aldehyde related to (**11**) is reported to be unstable.[8]

‡ Compound (**16**) was not detected, while (**14**) and (**15**) were observed as pairs of geometric isomers in a 3 : 1 ratio.



Scheme 1. (a) Major and (b) minor scission of the *trans*-trioxanes catalysed by electrophiles (E).



Scheme 2. Major eliminative scission of the *cis*-trioxanes catalysed by electrophiles (E).

cation (**21**) which by re-cyclization to (**22**) and elimination yields furan (**9**). Nonetheless, cation (**19**) still has time for some vinylic rearrangement to (**23**), which subsequently divests itself of ketone and electrophile so creating the tertiary aldehyde (**10**).

Proof for the fate of the peroxide link was provided by the electrophile-induced rearrangement of ^{18}O-labelled (**3**). Only one labelled oxygen atom was retained within the rings of (**9**) and (**10**).§

Lastly, it is worth noting that TMSOTf is not only the catalyst of choice for preparing trioxanes[3a] at −78 °C, but also for rearranging them at 24 °C.

We believe that these rearrangements are novel and have synthetic relevance as they open a new avenue to fused pyrans and furans which are of interest in view of their widespread natural occurrence.[10]

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§ ^{18}O-labelled trioxane (**3**) has been prepared by the route described in ref. 3a using $^{18}O_2$. The labelling in the rearranged products (**9**) and (**10**) was ascertained from their mass spectral data.