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CONVERSION OF 3-CYCLOPENTENYL HYDROPEROXIDE INTO 5-SUBSTITUTED-2,3-DIOXABICYCLO[2.2.1]HEPTANES

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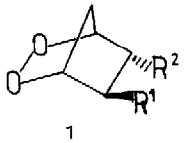
Summary. 3-Cyclopentenyl hydroperoxide 8 has been prepared from cyclopentadiene via hydroboration and autoxidation. Bromination of 8 followed by treatment with an appropriate silver salt has afforded the 5-substituted-2,3-dioxabicyclo[2.2.1] heptanes 11 (endo-bromo), 13 (exo-bromo), and 12 (exo-trifluoroacetoxy).

In the search for bicyclic peroxides that might serve as simple chemical models for the prostaglandin endoperoxides 1 [e.g. $R^1 = \overset{E}{CH}{=}CHCH(OH)C_5H_{11}$, $R^2 = CH_2\overset{Z}{CH}{=}CH(CH_2)_3CO_2H$], 2,3-dioxabicyclo[2.2.1]heptane 2^1 and its derivatives 3 - 6^1 and 7^2 have been prepared during the past three years. Where the model compounds contain substituents they are at the bridgehead or 7-position, unlike the prostaglandin endoperoxides in which substitution is at the 5- and 6-positions of the [2.2.1] skeleton. We now report a convenient synthesis of 3-cyclopentenyl hydroperoxide and its conversion into the first simple 5-substituted-2,3-dioxabicyclo[2.2.1]heptanes.



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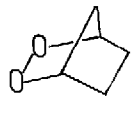

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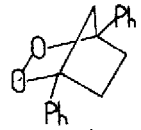

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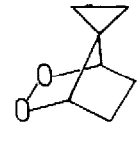

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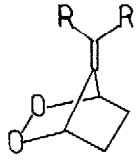
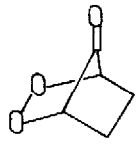


5 (R = Me or Ph)



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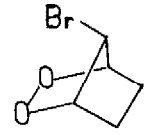

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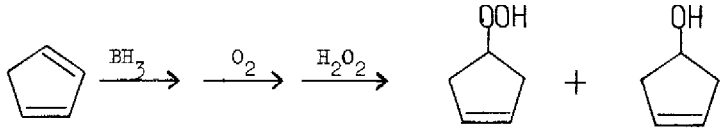
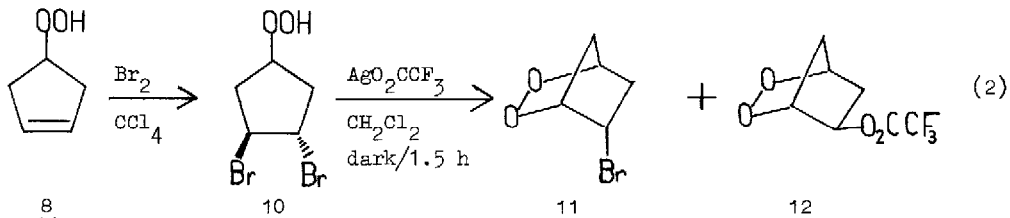
3-Cyclopentenyl hydroperoxide 8 has been prepared previously from the corresponding alcohol 9 by conversion to methanesulphonate followed by solvolysis with basic hydrogen peroxide.[3] This S_N2-route is not very satisfactory for secondary alkyl peroxides in general, and in this case requires the initial preparation of 9 via hydroboration and oxidation of cyclopentadiene.[4] We have now shown that autoxidation of the tri(3-cyclopentenyl)borane affords appreciable quantities of 8 directly; we find the sequence shown in equation (1) a convenient route to a mixture of 8 and 9, from which 8[5] is readily isolated via its sodium salt



(1)

8 9

Bromination of 8 proceeded smoothly at 0 °C to afford 10[5] and treatment of 10 with AgO_2CCF_3 gave a mixture containing 3-bromo-4-trifluoroacetoxycyclopentyl hydroperoxide and the bicyclic peroxides 11 and 12.

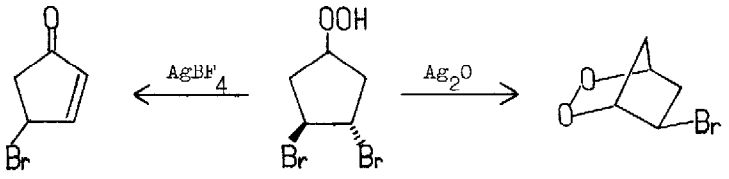


(2)

8 10 11 12

Isolation of 11[5] (6%) and 12[5] (14%) was effected by column chromatography ($SiO_2/CH_2Cl_2/-15\ ^{o}C$). In an independent experiment it was shown that 11 is rapidly and quantitatively converted into 12 by reaction with AgO_2CCF_3.

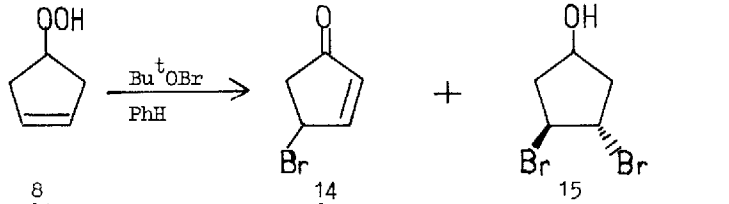
The use of other silver salts was investigated in an attempt to avoid the bromide displacement that accompanies and competes with the dioxabicyclization. Thus treatment of 10 with Ag_2O slowly (63 h) afforded 13[5] (19%; isolated as for 11), but with $AgBF_4$, extensive decomposition took place, no endoperoxide was detected, and 4-bromocyclopent-2-en-1-one 14 was the major product identified.



14 10 13 (3)

We assume that in the Ag_2O reaction the endo-bromide 11 is formed initially but is transformed into the thermodynamically favoured exo-compound 13 by equilibration with the liberated AgBr. It is tempting to suggest that 14 is derived from 11 via acid-catalysed rearrangement to 4-bromo-3-hydroxycyclopentanone followed by dehydration.

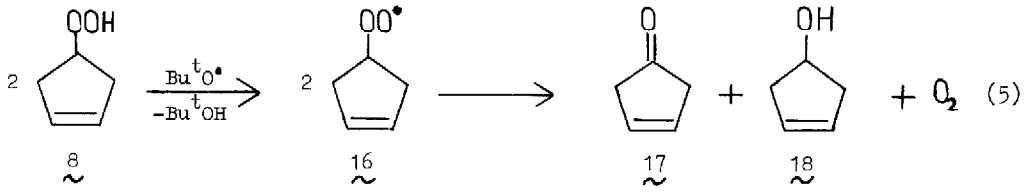
We attempted to prepare 5-bromo-2,3-dioxabicyclo[2.2.1]heptane independently by the reaction of 8 with t-butyl hypobromite. We hoped that, in a free radical chain process, the 3-cyclopentenyl peroxy radical 16 would be generated, undergo intramolecular addition to the double bond,[3] and the resulting alkyl radical would abstract bromine from the hypobromite. However instead of 11 and 13 the main products were 14 and 15 (equation 4).



8 14 15 (4)

We believe that the peroxy radical 16 is formed, but that disproportionation[6] is preferred to the desired intramolecular cyclization. Such a reaction (equation 5)

would liberate oxygen and gas evolution was observed, and would afford 17 and 18 which are reasonable precursors for the observed 14 and 15.



(5)

8 16 17 18

In a separate experiment the peroxy radical 16 was generated by photolysis of a mixture of 8 and di-t-butyl peroxide in cyclopropane at -120 °C and was observed by ESR spectroscopy.[7] No evidence for the desired cyclization could be found over the temperature range -120 to +20 °C.

We thank the S.R.C. for financial support.

References and Notes

1. W. Adam and A.J. Bloodworth, Ann. Reports B, (1978)342, and references therein.

2. A.J. Bloodworth and H.J. Eggelte, Chem. Comm., (1979)741.

3. N.A. Porter, M.O. Funk, D. Gilmore, R. Isaac, and J. Nixon, J. Amer. Chem. Soc., 98(1976)6000.

4. E.L. Allred, J. Sonnenberg, and S. Winstein, J. Org. Chem., 25(1960)26.

5. Compound 8.[3] ^{1}H NMR (60 MHz; CCl_4): δ 2.5d(J = 4.5 Hz; 4H), 4.8 m approximating quintet (1H), 5.65 s (2H), 9.37 br s (1H). ^{13}C NMR (20 MHz; $CDCl_3$): δ 37.74, 84.74, 128.31. Compound 10. ^{1}H NMR: δ 2.1 - 3.3 m (4H), 4.3 - 4.65 m (2H), 4.65 - 5.1 m (1H), 8.7 s (1H). ^{13}C NMR: δ 39.18, 40.04, 52.78, 54.39, 84.36. Compound 11. ^{1}H NMR: δ 1.8 - 2.9 m (4H), 4.12 m (1H), 4.73 m (2H). ^{13}C NMR: δ 40.66, 42.63, 43.81, 78.28, 81.67 IR:633 cm^{-1} (νC-Br). Compound 12. ^{1}H NMR: δ 1.75 m (1H), 2.2 - 2.75 m (3H), 4.76 m (2H), 5.07 m (1H). ^{13}C NMR: δ 38.19, 41.14, 74.94, 76.77, 77.45. IR: 1780 cm^{-1} (νC=O). Compound 13. ^{1}H NMR: δ 1.8 - 2.7 m (4H), 4.2 m (1H), 4.6 br s (2H). ^{13}C NMR: δ 40.74, 43.67, 47.13, 78.74, 81.24.

6. R. Hiatt, T. Mill, K.C. Irwin, and J.K. Castleman, J. Org. Chem., 33(1968)1428.

7. Radical 16. a(1H) = 7.7 G, g = 2.0152; we thank Mr. Jalal Hawari for carrying out this experiment.

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