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1,3-DIOXEPIN

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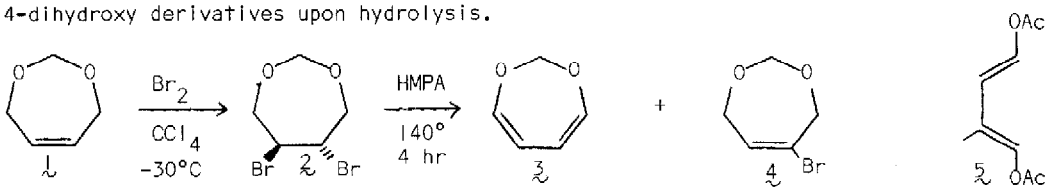
Dioxygenated 1,3-butadienes are of considerable interest as the diene components in stereoselective syntheses involving the Diels-Alder reaction.[2] 1,3-Dioxepin (3) attracted our attention since 3 might be more reactive in a Diels-Alder reaction than the open chain 1,4-dioxygenated dienes owing to the requisite s-cis conformation of the 1,3-diene system in 3. The reaction of 3 with certain dienophiles might also lead to adducts, the stereochemistry of which at the 1 and 4 positions may be opposite to that of adducts derived from the open chain E,E 1,4-diacetoxy-1,3-butadiene. Moreover, the acetal linkage in adducts derived from 3 should readily afford cis 1,4-dihydroxy derivatives upon hydrolysis.



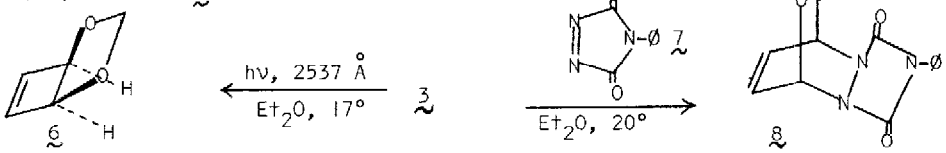
1 2 3 4 5

1,3-Dioxepin (3) was prepared as follows. A stirred solution of 6.08 g of dibromide 2,[3] mp 40-41°, in 17.8 g of dry HMPA was heated (N_2) for 4.0 hr at 140°.[4] The dark mixture was cooled, poured into chilled sat. aq. $NaHCO_3$ (45 ml) and extracted with ether (5x10 ml). Removal of the solvent at -10°/15 mm from the washed and dried (Na_2SO_4) ether layer afforded 1.22 g of a viscous orange oil. Evaporative distillation (bath 70°, 11 mm, receiver -78°) afforded 260 mg (12% yield[5]) of essentially pure diene 3.[6] Continued distillation afforded 320 mg (8% yield) of essentially pure vinyl bromide 4[7] (bp 70°/11 mm).

Whereas diene 3 was unreactive (by nmr) toward N-phenylmaleimide or p-benzoquinone in benzene-d_6 at 80° for 2 hr, addition of 1 equiv of the more reactive dienophile 4-phenyl-1,2,4-triazoline-3,5-dione (7) to an ether solution of 3 at 20° afforded analytically pure adduct 8[8] (>95%). By contrast, E,E diacetoxydiene 5 readily reacts with p-benzoquinone in benzene at 80°.[2c]

Although a Dreiding molecular model of 3 suggests that a twisted (probably unreactive) conformation may be the preferred one, by analogy to the rather well studied 1,3-cycloheptadiene[9] one would expect the requisite planar (except for C_2) conformation of 3 to be easily accessible. For whatever reason, the reduced reactivity of 3 is consistent with the known decrease in cyclic diene reactivity in the Diels-Alder reaction as ring size increases.[10]

When a 23-mg sample of 3 dissolved in 0.60 ml of ether was irradiated for 7.5 hr at 17° with 2537 Å light, cyclobutene 6 was formed.[11]



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References and Notes

1. Alfred P. Sloan Fellow; Recipient of an NIH Research Career Development Award.

2. a) S. Danishefsky and T. Kitahara, J. Am. Chem. Soc., 96, 7807 (1974); b) H. H. Inhoffen, J. Heimann-Trosien, H. Muxfeldt and H. Kramer, Chem. Ber., 90, 187 (1957); c) J. F. W. Keana and P. E. Eckler, in press, J. Org. Chem.; d) M. E. Jung, J. Chem. Soc. (D), 956 (1974).

3. a) K. C. Brannock and G. R. Lappin, J. Org. Chem., 21, 1366 (1956); b) D. B. Pattison, J. Org. Chem., 22, 662 (1957).

4. See R. Hanna, Tetrahedron Letters, 2105 (1968).

5. Treatment of an ether solution of an aliquot of the orange oil before distillation with a slight excess of dienophile 7 (see below) afforded adduct 8 in an amount corresponding to a 22% yield of diene 3. Thus, much 3 is lost during the distillation process.

6. Preparative vpc (SE-30/Chromosorb W, 5' x 1/4", 80°, Rt=5.6 min) afforded the analytical specimen of 3 as a very pale yellow colored volatile air sensitive oil: uv max (cyclohexane) 264 nm (7,000); nmr ($CDCl_3$) δ 5.03 (m, 2, H-5,6), 5.25 (s, 2, H-2), 6.61 (m, 2, H-4,7); Found: C, 61.38; H, 5.88. Calcd for $C_5H_6O_2$: C, 61.22; H, 6.17. Hydrogenation of 3 over 10% Pd/C in benzene produced 1,3-dioxepane identical by nmr to that obtained by hydrogenation of olefin 1.

7. Bromide 4 has been reported[3a] without analytical data. Preparative vpc (130°, Rt=6.9 min) afforded the analytical sample of 4 as a colorless oil: Found: C, 33.49; H, 4.00. Calcd for $C_5H_7BrO_2$: C, 33.54; H, 3.94.

8. Adduct 8: mp 183-186° d; nmr ($CDCl_3$) δ 4.72 (a, b-q, 2), 6.28 (m, 2), 6.55 (m, 2), 7.5 (bs, 5); Found: C, 57.29; H, 3.95; N, 15.13. Calcd for $C_{13}H_{11}N_3O_4$: C, 57.14; H, 4.06; N, 15.39.

9. N. L. Allinger and J. T. Sprague, Tetrahedron, 29, 3811 (1973).

10. R. Huisgen, R. Grashey and J. Sauer in The Chemistry of Alkenes, S. Patai, Ed., Interscience Publishers, New York, N.Y., 1964, p.887.

11. 2,4-Dioxabicyclo[3.2.0]hept-6-ene (6): Preparative vpc (100°, Rt=2.8 min) afforded the analytical specimen as a very pale yellow oil: nmr ($CDCl_3$) δ 5.07 (m, 1, H-3), 5.15 (m, 2, H-1,5), 5.34 (m, 1, H-3), 6.22 (m, 2, H-6,7); Found: C, 61.36; H, 6.11. Calcd for $C_5H_6O_2$: C, 61.22; H, 6.17.