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VERSATILE DIQUINANE INTERMEDIATES

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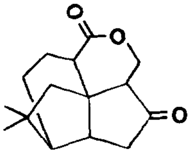
The preparation and chemical reactivity of two key diquinane intermediates are described.

Despite the existence of numerous polyquinane (1) natural products (e.g. quadrone **1** (2) and gymnomitrol **2** (3)), practical synthetic precursors to quinanes are rare (4). This is in sharp contrast to the polycyclic cyclohexanes for which such precursors abound (e.g. the Wieland-Miescher ketone **3** (5)).

We here disclose a convenient and inexpensive four-step procedure for the preparation of enone ketal **8** (6) (overall yield = 15%) from the readily available bicyclo[3.3.0]octane-3,7-dione **4**.



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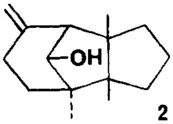

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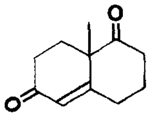

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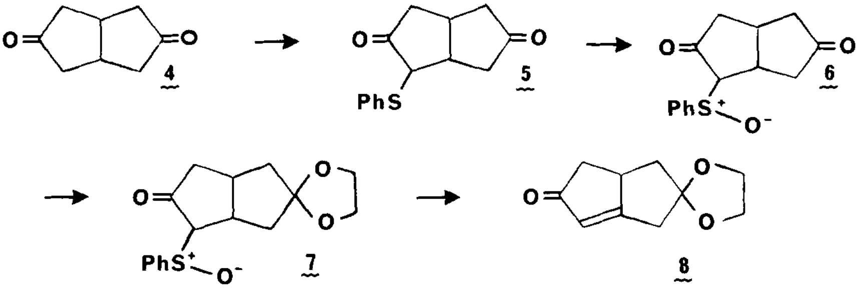

The enolate of dione **4** (7) is generated by slow addition of the dione to a preformed LDA solution (in THF at -55°). The enolate is not easily transferred due to its insolubility, thus precluding the usual (8) inverse addition to phenyl disulfide. A practical alternative is addition over 15 minutes of phenyl disulfide to a vigorously stirred suspension of the enolate (in THF at -55°) followed by warming to room temperature. After work-up (acidification/extraction/flash chromatography; EtOAc:ligroine; 1:1) pure monosulfide **5** can be obtained in 35-38% yield on a 10 mmole scale. Oxidation of **5** is accomplished by the dropwise addition of m-chloroperoxybenzoic acid in CH_2Cl_2 to a solution of **5** in CH_2Cl_2 held at -55° followed by washing with bisulfite and bicarbonate (yield ca. 90%). Monoketal **7** (m/e M^+ Calc'd: 306.0926; Fd: 306.0927) is prepared from sulfoxide **6** (m/e M^+ Calc'd: 262.0664; Fd: 262.0676) by transketalization (9) at room temperature using butanone ethylene ketal containing a trace of p-TsOH and ethylene glycol (yield ca. 70%). Both **6** and **7** are purified using flash chromatography (EtOAc:ligroine:CH_3OH; 150:150:1). Although thermally unstable, **6** (mp 168-169° d) and **7** (mp 157-158° d) readily crystallize from evaporating solutions of EtOAc-ligroine. Separation of the sulfoxide diastereoisomers prior to thermolysis is unnecessary. When a dilute CCl_4 solution of **7** is heated at reflux in the presence of an acid scavenger (e.g. $CaCO_3$ or $NaHCO_3$), slow elimination to the enone ketal occurs. Flash chromatography (EtOAc:ligroine; 1:4) followed by sublimation gives pure **8** (yield 64%; mp 66.5-67.5°; m/e M^+ Calc'd 180.0787; Fd: 180.0806 (10)).

Treatment of enone ketal **8** with $LiMe_2Cu$ (anhydrous ether; -60° to RT) affords the expected 1,4-addition product. Furthermore, sulfoxide ketal **7** can be converted to its ruby-red dianion (2^+ equiv. LDA; THF; -50° to 0° over 3 hrs. (11)) which undergoes facile reaction with 3-bromopropene. Application of these transformations to polyquinane syntheses will be reported in our full paper.

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References and Notes

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6. All compounds prepared have satisfactory analytical and spectroscopic data.
7. S.H. Bertz, G. Rihs, R.B. Woodward, Tetrahedron, **38**, 63 (1982).
8. B.M. Trost, T.N. Salzmann, J. Amer. Chem. Soc., **95**, 6840 (1973). The modest yield of **5** results from its statistical formation along with disulfenylation products and remaining unreacted **4**. On a 1 mmole scale, a (viscous) 0.08 M solution of the enolate in THF may be transferred by inverse addition to the phenyl disulfide. This affords a 47% yield of **5**. The 10 mmole scale reaction was the largest size still convenient for flash chromatography.
9. H.J. Dauben, B. Loken, H.J. Ringold, J. Amer. Chem. Soc., **76**, 1359 (1954); G. Rosenkranz, M. Velasco, F. Sondheimer, Ibid, **76**, 5024 (1954). Application of standard ketalization conditions (ethylene glycol, p-TsOH, refluxing benzene) to **5** gives, without appreciable selectivity, both possible monoketals and the bisketal. Thermolysis of **6** (CCl_4 at reflux) yields an air-sensitive yellow reaction mixture containing several components by TLC. This is consistent with the work of Bertz (12) and Docken; A. M. Docken, J. Org. Chem., **46**, 4096 (1981).
10. Spectral data: ^1H nmr (300 MHz, $CDCl_3$): δ 5.93 (s, 1H, vinyl proton), 3.96 (m, 4H, CH_2-CH_2), 3.18 (m, 1H, bridgehead proton), 2.91 (s, 2H, allylic CH_2), remaining four protons are multiplets centered at 2.64, 2.35, 2.12, and 1.55; ir ($CDCl_3$ solution) 1698 cm^{-1}.
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12. Compounds **5** and **6** of this paper were prepared independently by S. Bertz (Ph.D. dissertation; Harvard University (1978)). Private communication with S. Bertz.

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