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CYCLOBUTENONES: THE SYNTHESIS AND DIELS ALDER REACTIVITY OF 4,4-DIMETHYLCYCLOBUTENONE

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In conjunction with another project it recently became necessary to develop a synthon which would be synthetically equivalent to terelactone (1)[1] but more reactive than 1 as a dienophile in the Diels Alder reaction. 4,4-Dimethylcyclobutenone (2) appeared to be an attractive candidate since it seemed that the relief of angle strain[2] resulting from the rehybridization of the olefinic carbons from "sp^2" to "sp^3" during the course of the Diels Alder reaction would

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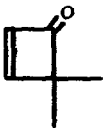

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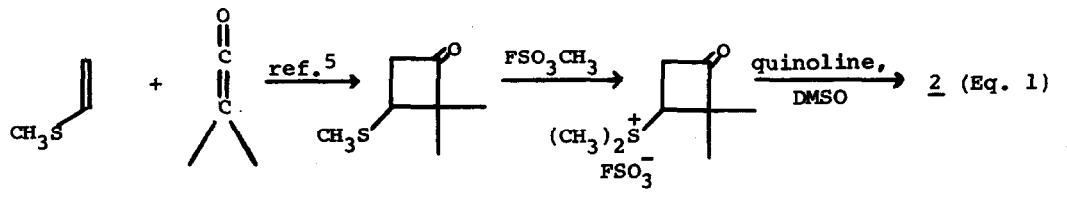
provide substantial driving force for the desired cycloaddition. An examination of the literature revealed, however, that despite this apparent potential of cyclobutenones for enhanced dienophilicity no Diels Alder reaction of a cyclobutenone had been recorded. Furthermore 2 was not a known compound and no convenient, general method for the synthesis of simple cyclobutenones existed.[3,4]

We now wish to report the results of studies which, although still preliminary in nature, provide (a) the first demonstration of Diels Alder reactivity of a cyclobutenone and (b) a short, potentially general synthesis of cyclobutenones.[3,4]

4,4-Dimethylcyclobutenone‡ (2) was prepared in an overall, isolated yield of forty percent from the known, readily available[5] 3 by the route outlined in Equation 1. Alkylation of 3 with methyl fluorosulfonate in methylene chloride

‡ Warning: 2 is a potent lachrymator.

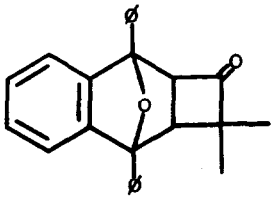
affords the sulfonium salt 4. The latter undergoes rapid elimination of dimethyl sulfide when treated at room temperature for 2-3 hours with quinoline



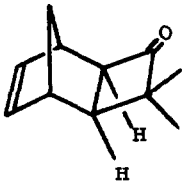
3 4

in dimethylsulfoxide to give 2[6], bp ~ 80-90° (~20 mm), $\nu_{max}^{CDCl_3}$: 2980, 1762, 1075, 870, 805 cm^{-1}; $\lambda_{max}^{absEtOH}$: 217 nm (ε = 2000); NMR ($CDCl_3$): 1.26(6H,s), 6.05 (1H, d, J ≈ 4Hz), 8.20 (1H, d, J ≈ 4Hz). In contrast to cyclobutenone[3] itself 2 is stable for prolonged periods at -10°.

The superior (with respect to 1) dienophilicity of 2 was first established by reaction with 1,3-diphenylisobenzofuran (5)[7]. Thus while reaction of 2 with 5 in deuterochloroform (five days at room temperature) gives 5a (stereochemistry unassigned), mp 136-8°, in sixty-two percent yield, terelactone (1) does not react with 5 either at room temperature or in refluxing chloroform.



5a



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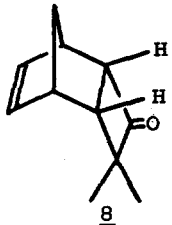

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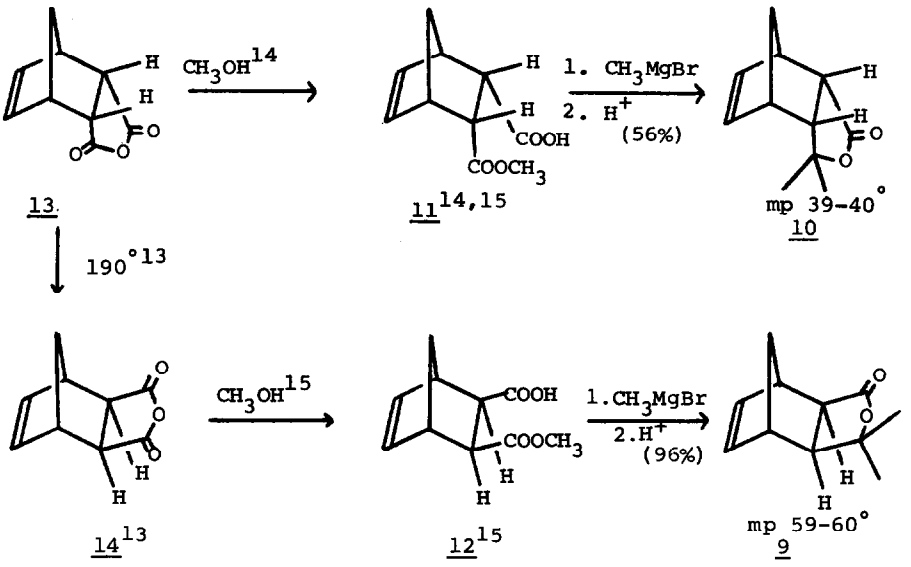
Addition of 2 to cyclopentadiene (6) at 25° and 100° is not competitive with dimerization of 6 under ordinary conditions but cycloaddition does occur in good yield at 25° when three equivalents of 6 is added over three hours to a solution of 2 in CCl_4 containing a trace of $BF_3 \cdot Et_2O$[8]. The reaction proceeds with high stereoselectivity to give the exo adduct 7. Little, if any,[9] of the corresponding endo adduct (8) is formed.

The assignment of exo stereochemistry to 7, which is strongly suggested[10] by the NMR spectrum of 7 was rigorously confirmed by Baeyer-Villager oxidation of 7 with alkaline hydrogen peroxide[11] to exo lactone 9 and comparison of the latter with samples of exo lactone 9 and endo lactone 10 prepared independently

by the routes shown in Scheme 1[12].

Terelactone (1) does not react with 6 at room temperature in the absence or presence of $BF_3 \cdot Et_2O$. Cycloaddition does occur (without added $BF_3 \cdot Et_2O$) in low yield at ~160° (refluxing dicyclopentadiene) to give a 2.9:1 mixture of 9 and 10.

Scheme 1



The extension of this work to the preparation and reactions of other cyclobutenones is presently under investigation.

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Footnotes and References

1. Prepared conveniently but in low yield from methyl hydrogen maleate or maleic anhydride and methyl magnesium bromide (unpublished results of John S. Jardin and Thomas A. Schmidt). For related reactions see, inter alia, M.S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice Hall, New York (1954); Chapter XI.

2. For a recent discussion of angle strain see P.v.R. Schleyer, J.E. Williams and K.R. Blanchard, J. Amer. Chem. Soc., 92, 2377(1970).

3. Cyclobutenone itself has been synthesized only recently (J.B. Sieja, ibid., 93, 2481 (1971)) by a relatively lengthy route.

4. After this work was in progress a potentially general synthetic approach to cyclobutenones which is complementary to the one described in this communication was reported: H.H. Wasserman, J.U. Piper and E.V. Dehmlow, J. Org. Chem., 38, 1451 (1973).

5. J.C. Martin, Ger. Offen. 1,213,398 (Chem. Abstr., 64, 19444e (1966)); U.S. Patent 3,345,402 (Chem. Abstr., 67, 116635y (1967)).

6. All new compounds with the exception of 4, which we were unable to purify, gave satisfactory analytical data. The spectra of all compounds (including 4) are consistent with the structures assigned.

7. J.A. Norton, Chem. Revs. 31, 319 (1942).

8. For an excellent review of catalyzed Diels Alder reactions see V.M. Andreev and L.K. Andreeva in B.A. Kazanskii, I.L. Knunyants, M.M. Shemyakin and N.N. Mel'nikov (Eds.), "Organic Compounds: Reactions and Methods," Vol. 21, IFI/Plenum, New York, 1973, pp. 41-91.

9. VPC analysis of the crude product indicated the presence of an unidentified minor (5-10%) component (i) which appears as a shoulder on the peak corresponding to 7 and which could not be separated. Although the product from the alkaline Baeyer Villager oxidation of crude 7 contained no endo lactone (9 and 10 are cleanly resolved by VPC (6' x 1/4" 20% SE-30 at 150°)) we cannot rigorously exclude the possibility that i is the endo adduct 8 since 8 may not yield 10 under the conditions which convert 7 to 9.

10. L.M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance in Organic Chemistry", 2nd Ed., Pergamon, New York, 1969, pp 288-89.

11. Y. Tsuda, T. Tanno, A. Ukai and K. Isobe, Tetrahedron Letters, 2009 (1971) B.M. Trost and M.J. Bogdanowicz, J. Amer. Chem. Soc., 95, 5321 (1973) and references therein.

12. The choice of reaction sequence and experimental conditions for the conversions 13 → 10 and 14 → 9 was greatly facilitated by previous work[1] in these laboratories on the synthesis of terelactone.

13. D. Craig, J. Amer. Chem. Soc. 73, 4889 (1951).

14. L.M. Rice and E.E. Reid, ibid., 74, 3955 (1952).

15. M. Mousseron, R. Jacquier and J. Soulier, Compt. rend. 247, 665 (1958).