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GENERAL APPROACH TO THE SYNTHESIS OF POLYQUINENES VII. SYNTHESIS OF A CENTRO-SUBSTITUTED TRIQUINACENE[1]

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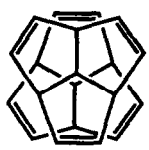
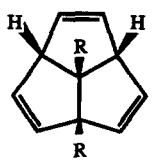
Summary: The synthesis of the 1,10-cyclohexanotriquinacene **3** has been accomplished *via* the Weiss reaction. The pivotal steps centered on the regiospecific mono-allylation of bisenol ether **7** to provide tetraester **8**, and the HMPA-mediated removal of three molecules of water from triol **12** to furnish **3**.

Serratosa *et al.*[2] have reported a new approach to the synthesis of dodecahedrane[3] related to the pericyclic route **1** originally proposed for this molecule by Woodward, Müller and Jacobson.[4] Difficulties encountered in the reaction of the two triquinacene **2** units in the desired fashion *via* their concave rather than convex faces have hampered previous attempts to execute this convergent, reflexive synthesis.[5] In keeping with our interest in the preparation of polyquinenes,[6,7,8] we wish to report the synthesis of tetracyclo[5.5.2.0.^{1,8}0^{4,8}]tetradeca-2,5,13-triene **3**[9] *via* the Weiss reaction.[10] This molecule **3** has embodied in its [4.3.3]propellane molecular structure a six-membered



1



2

3

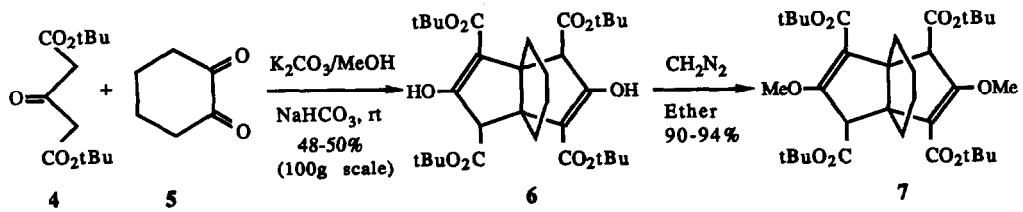
ring which shields the convex face of the triquinacene skeleton. This type of centro-substituted[9] triquinacene may prove to be useful in attempts to explore the "pericyclic" approach to dodecahedrane.[4]

Over the last several years an intense effort has been spent upon the synthesis of (m.n.p) propellanes which contain small rings and upon a study of the character of their central bond.[11] The approach, however, employed by Weiss and Edwards for the synthesis of [4.3.3]propellanedione[10] seemed appropriate for extension to **3**. Moreover, a procedure for the regiospecific monoalkylation of a *cis*-bicyclo[3.3.0]octane-3,7-dione

unit has been developed and employed in the preparation of a number of polyquinenes.[6,7] The combination of these two methods has resulted in the first synthesis of a centro-substituted triquinacene.

When two equivalents of di-*t*-butyl 3-ketoglutarate **4** were reacted with cyclohexane-1,2-dione **5** in an alkaline medium, the tetra-*t*-butyl propellanedione tetracarboxylate **6** was isolated in 50% yield (Scheme I). The tetraester **6** exists in solution entirely as the bisenol tautomer and can be converted into the desired bisenol ether **7** in >90% yield on treatment with ethereal diazomethane. The anti disposition of the double bonds in **7** was assigned on the basis of ^{1}H and ^{13}C NMR spectroscopy in agreement with the work of Camps.[12]

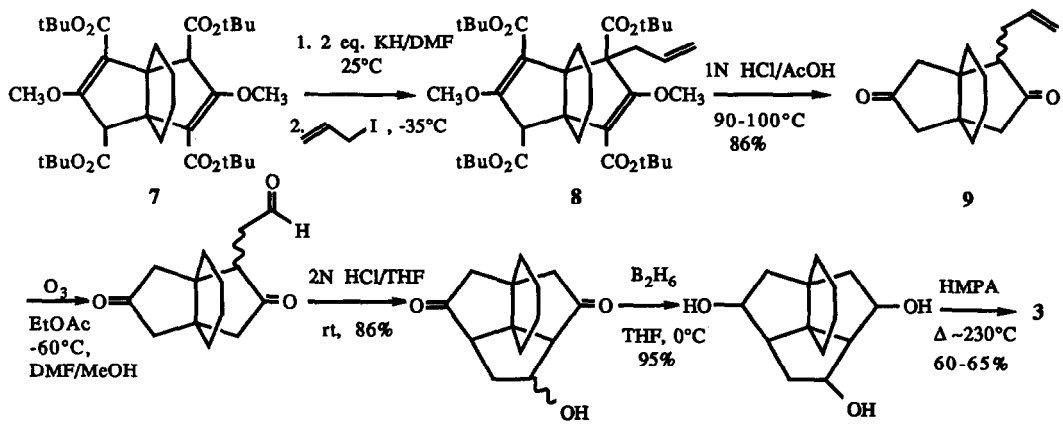
Scheme I



4 **5** **6** **7**

The bisenol ether **7** was stirred at 25°C with 2.2 equivalents of potassium hydride in DMF for one hour, followed by addition of allyl iodide (2.2 eq) at -35°C. Regiospecific monoalkylation was effected in high yield. Hydrolysis and decarboxylation of the

Scheme II



7 **8** **9**

10a (endo) 3
10b (exo) 2

11 **12**

intermediate tetraester **8** gave the desired monoallyl [4.3.3]propellanedione **9** in 86% overall yield from **7**. The monoallyl derivative was isolated as a mixture of *endo* and *exo* stereoisomers (3:2, GC and ^{13}C NMR). Conversion of the allyl group of **9** into the aldehyde function of **10** was carried out by ozonolysis, according to published procedures (>90% yield).[7,13] Aldol cyclization of **10** to **11** was executed under conditions of tautomeric equilibrium (2N HCl/THF) to permit the *exo* stereoisomer **10b** to epimerize to the *endo* diastereomer **10a**.[7] Once the aldol reaction of **10a** had taken place, the newly formed carbon-carbon bond was stable and retroaldolization of **11** to **10** did not occur. Although the aldol reaction was slow (5-6 days), it was highly efficient. When **11** was stirred in borane-THF (1N) solution at 0°C for twenty-four hours, a mixture of stereoisomers represented by **12** was isolated in 95% yield. These triols were not separated but were heated in HMPA at 230-240°C for twenty hours under conditions analogous to those employed for the conversion of other polyols into polyquinenes[7,14] [Note. Care must be taken to employ a cold finger (dry-ice/acetone) condenser in this process to prohibit the escape of volatile polyquinenes]. Careful extraction of the HMPA solution with pentane/water, followed by distillation of the pentane layer through a column packed with glass beads, furnished the propellane triquinacene **3**[15] in 60-65% yield, accompanied by two minor olefinic isomers (GC-ratio 90:4:6). When the mixture of propellane triquinacenes was stirred in the presence of *para* toluene sulfonic acid (CH_2Cl_2/pentane)[14] the minor isomers disappeared and **3** was isolated in pure form (GC retention time 8.2 min). As expected from the C_2 symmetry of **3**, ten signals were observed in its ^{13}C NMR spectrum of this triene and five resonance signals were found in the proton NMR at δ 5.54 (2H, dd, J_1=6.0 Hz, J_2=2.8 Hz), 5.53 (2H, s,), 5.40 (2H, dd, J_1=6.0 Hz, J_2=1.7 Hz), 3.27 (2H, t, J_1=2.8 Hz, J_2=1.7 Hz) and 1.48 (8H, bs), respectively. This triene **3** is much easier to isolate from this process than triquinacene,[6] since it has a much higher boiling point (60-65°C, 10 mmHg).

The synthesis of **3** *via* the Weiss reaction provides a potential route to a variety of centro-substituted triquinacenes and could be extended to other propellane derivatives.[16] Although triquinacenes have occupied a pivotal position in the development of polyquinane chemistry,[3,4] to our knowledge no previous route to these topologically interesting centro-substituted molecules has been reported. Further work in this area is under way and will be reported at a later date.

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References and Notes

1. This paper is dedicated to Professor David Ginsburg on the occasion of his retirement.
2. E. Carceller, M. L. Garcia, A. Moyano, M. A. Pericas and F. Serratosa, Tetrahedron, 42, 1831 (1986).
3. L. A. Paquette, R. I. Teransky, D. W. Balogh and G. Kentgen J. Am. Chem. Soc., 105, 5446 (1983). W. D. Fessner, G. Sedelmeier, P. R. Spurr, G. Rihs and H. Prinzbach J. Am. Chem. Soc., 109, 4626 (1987).
4. R. B. Woodward, T. Fukunaga and R. C. Kelly J. Am. Chem. Soc., 86, 3162 (1964); D. M. Müller, Chem. Weekblad., 59, 334 (1963); I. T. Jacobson, Acta. Chem. Scand., 21, 2235 (1967).
5. W. P. Roberts and G. Shoham, Tetrahedron Lett., 22, 4895 (1981); E. D. Stevens, J. D. Kramer and L. A. Paquette, J. Org. Chem., 41, 2266 (1976); P. Deslongchamps and P. Soucy, Tetrahedron, 37, 4385 (1981).
6. S. H. Bertz, G. Lannoye and J. M. Cook Tetrahedron Lett., 26, 4695 (1985). For other syntheses of **2** see reference 4 and also C. Mercier, P. Soucy, W. Rosen and P. Deslongchamps Syn. Comm., 3, 161 (1973); M. J. Wyvratt and L. A. Paquette, Tetrahedron Lett., 2433 (1974); A. De Meijere, D. Kaufman and O. Schallner, Angew. Chem., Int. Ed. 10, 417 (1971); A. De Meijere Tetrahedron Lett., 1845 (1974); E. Carceller, M. L. Garcia, A. Moyano and F. Serratosa J. Chem. Soc. Chem. Commun., 825 (1984).
7. G. Kubiak, K. Sambasivarao and J. M. Cook J. Org. Chem., submitted.
8. M. Venkatachalam, M. N. Deshpande, M. Jawdosiuk, G. Kubiak, S. Wehrli, U. Weiss and J. M. Cook, Tetrahedron, 42, 1597 (1986).
9. P. Gund and T. M. Gund, J. Am. Chem. Soc., 103, 4458 (1981).
10. U. Weiss and J. M. Edwards Tetrahedron Lett., 4885 (1968). R. W. Weber and J. M. Cook Can. J. Chem., 56, 189 (1978).
11. D. Ginsburg, Acc. Chem. Res., 2, 121 (1969); Ibid, 5, 249 (1972); W. D. Stohrer and R. Hoffman, J. Am. Chem. Soc., 94, 779 (1972); J. V. Silverton, G. W. A. Milne, P. Eaton, K. Nyi and G. H. Temme III J. Am. Chem. Soc., 96, 7429 (1974); K. B. Wiberg and F. H. Walker J. Am. Chem. Soc., 104, 5239 (1982).
12. P. Camps Tetrahedron Lett., 4067 (1974).
13. G. L. Lannoye, PhD Thesis, University of Wisconsin-Milwaukee, Milwaukee, WI, 1987.
14. M. N. Deshpande, M. Jawdosiuk, G. Kubiak, M. Venkatachalam, U. Weiss and J. M. Cook J. Am. Chem. Soc., 107, 4786 (1985).
15. **6**: mp 196-198°C, ^{13}C NMR (62 MHz, $CDCl_3$) δ 171.34, 169.89, 169.34, 112.91, 81.94, 57.95, 53.01, 31.19, 28.51, 28.16, 21.17; **7**: mp 124-125°C, ^{13}C NMR (62 MHz, $CDCl_3$) δ 170.24, 164.55, 163.74, 117.48, 81.85, 79.97, 57.23, 56.41, 54.38, 31.22, 28.38, 27.98, 21.16; **8**: mp 195-196°C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.92 (1H, m), 4.97 (2H, t), 3.84 (3H, s), 3.77 (3H, s), 3.68 (2H, s), 1.47-1.73 (4H, m); **3**: bp 60-65°C (10 mm/Hg); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.38, 132.13, 131.31, 64.76, 63.92, 59.08, 30.08, 27.69, 17.18, 16.10. High resolution mass spectrum Calcd. for $C_{14}H_{16}$: 184.1252; Found: 184.1275.
16. S. Yang and J. M. Cook J. Org. Chem., 41, 1903 (1976)

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