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STEREOSELECTIVE SYNTHESIS OF DIMETHYL TETRACYCLO[5.2.1.0^{2,6}.0^{3,8}]DECANE-7,8-DICARBOXYLATE

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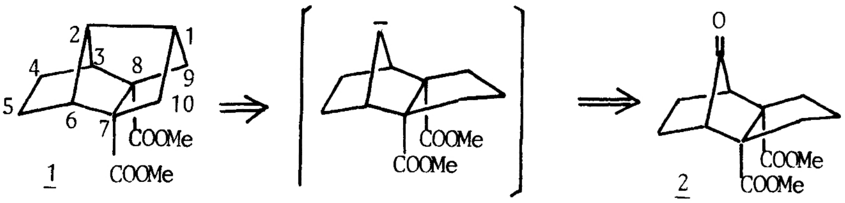
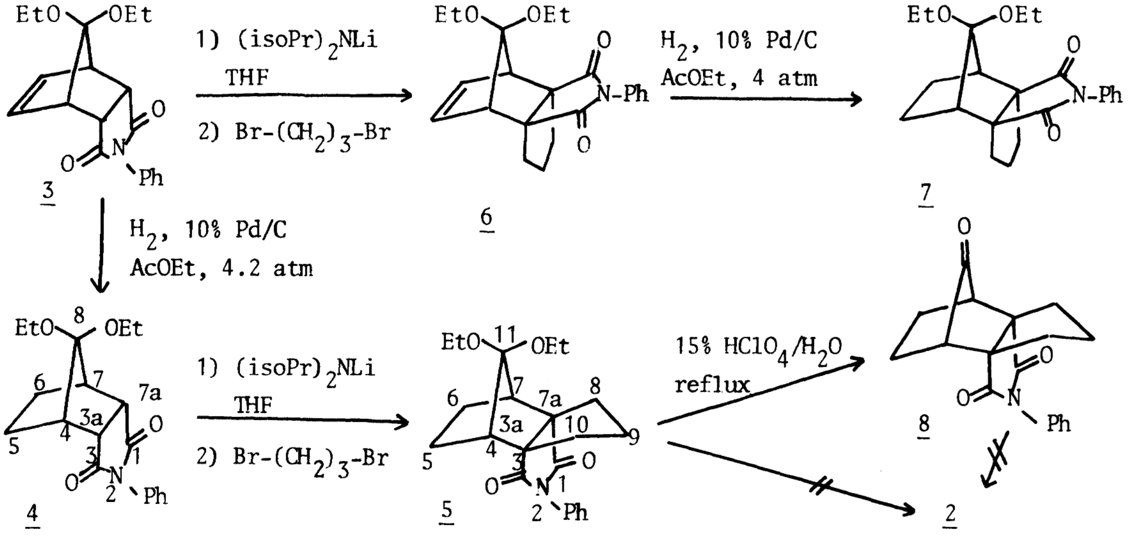
A short synthesis of the titled compound, a possible intermediate to prepare dodecahedrane, whose key-steps are the stereoselective trimethylene-annelation in the C_2 and C_3 positions of dimethyl 7,7-diethoxynorbornane-2,3-dicarboxylate and the high-yield intramolecular C-H insertion of a carbene generated from a 10-oxotricyclo[5.2.1.0^{2,6}]decane derivative, is described.

As part of our interest on polyquinanes[1)] we planned the synthesis of dimethyl tetracyclo[5.2.1.0^{2,6}.0^{3,8}]decane-7,8-dicarboxylate, 1, as a possible intermediate to synthesize dodecahedrane.[2)] Only a few articles dealing with compounds containing the carbocyclic skeleton of 1 have been published until today.[3)] Most of them are related to the photochemistry of several polychlorinated endo-tricyclo[5.2.1.0^{2,6}]decane derivatives. The parent hydrocarbon was synthesized in 1976[3d)] from exo-tricyclo[5.2.1.0^{2,6}]decan-10-one, the bond between C_4 and C_{10} being formed by intramolecular insertion of a carbene generated at C_{10} into a C_4-H bond. Since this type of transformation could be applied, in principle, to prepare diester 1, our new target molecule was dimethyl (1R,2S,6R,7S)-10-oxotricyclo[5.2.1.0^{2,6}]decane-2,6-dicarboxylate, 2, a compound that we have recently synthesized[1b)] through a Diels-Alder reaction between 6,6-dimethylfulvene and cyclopent-1-ene-1,2-dicarboxylic anhydride. However, the lack of stereoselectivity of this reaction led us to develop the stereoselective synthesis herein described.

The starting product for this synthesis, 3, can be easily obtained from 5,5-diethoxycyclopentadiene and N-phenylmaleimide.[4)] This compound was hydrogenated



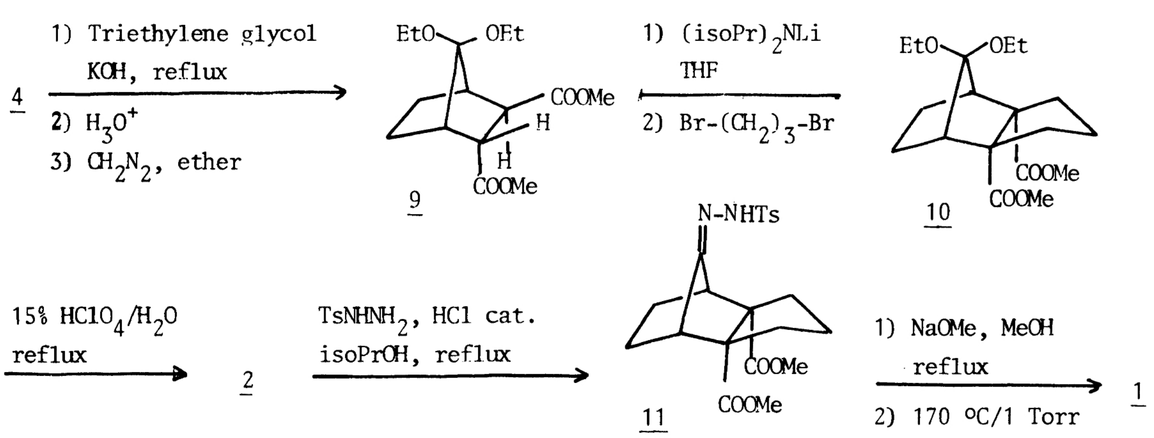
(H_2, 4.2 atm, 10% Pd/C, ethyl acetate, room temperature, 82 h) to give the new compound (3aR,4S,7R,7aS)-8,8-diethoxy-2-phenyl-3a,5,6,7a-tetrahydro-1H,3H-4,7-methanoisoindol-1,3-dione, 4,5) mp 149-152 °C(methanol), in 97.3% yield. Compound 4 was converted into the corresponding dianion and reacted with 1,3-dibromopropane under similar reaction conditions to those used by Garratt4) to convert 3 into 6. Crystallization of the crude reaction mixture from hexane gave a compound that was characterized as (3aR,4S,7R,7aS)-11,11-diethoxy-5,6-dihydro-2-phenyl-1H,3H-4,7-methano-3a,7a-propanoisoindol-1,3-dione, 5,5) mp 132-134 °C(hexane), in 40.2% yield. Hydrogenation (H_2, 4 atm, 10% Pd/C, ethyl acetate, room temperature, 26 h) of a sample of compound 6, prepared as described,4) gave (3aR,4R,7S,7aS)-11,11-diethoxy-5,6-dihydro-2-phenyl-1H,3H-4,7-methano-3a,7a-propanoisoindol-1,3-dione, 7,5) mp 136-138 °C(methanol), in 98% yield. The configuration of compounds 5 and 7 was tentatively assigned on the basis of their ^{1}H NMR spectra and clearly established through the analysis of their ^{13}C NMR spectra. The chemical shift for the $C_{5(6)}$ and $C_{8(10)}$ atoms of compound 7 are 21.1 and 32.0 ppm respectively, relative to internal TMS, while those of compound 5 are 23.6 and 34.3 ppm. The shielding of these carbon atoms in compound 7 as compared with 5 can be easily explained, since in compound 7 there exists a steric interaction (γ-effect) between the methylenes at the 5-10 and 6-8 positions.6) The assignment of the configuration to compounds 5 and 7



confirms the configuration assigned by Garratt4) to compound 6 based on the chemical shift for the bridgehead and olefinic protons.

Once established the configuration of compound 5, we tried its conversion into oxodiester 2. (3aR,4S,7R,7aS)-5,6-dihydro-2-phenyl-1H,3H-4,7-methano-3a,7a-propanoisoindol-1,3,11-trione, 8,5) mp 118-119 °C(benzene/hexane) was easily obtained in 95.4% yield by refluxing 5 with 15% aqueous $HClO_4$ for 12 h. However, all attempts to hydrolyze the dicarboximide function of 8 by refluxing this compound with NaOH or KOH in dioxane, DMSO, ethylene glycol, or diethylene glycol were fruitless. Moreover, we were not able to hydrolyze the dicarboximide function of 5 under similar reaction conditions. Reaction of 5 with 100% phosphoric acid at 180 °C for 12 h gave 8 as the only identifiable product. Since these results may be attributable to steric hindrance, we heated compound 4 with KOH in triethylene glycol under reflux for 1.5 h, and obtained an acidic compound that after esterification with ethereal diazomethane gave dimethyl (1RS,2RS,3RS,4SR)-7,7-diethoxynorbornane-2,3-dicarboxylate, 9,5) probably slightly contaminated with the *meso*-stereoisomers (GLC and ^1H and ^{13}C NMR), in 60.3% yield.

In view of these facts and the reports of Garratt7) and Girard8) over the dialkylation and annelation of dianions derived from dimethyl cycloalkane-1,2-dicarboxylates, we allowed to react compound 9 with 1,3-dibromopropane under similar reaction conditions to those used for compounds 3 and 4. After column chromatography, a mixture of starting compound and dimethyl (1R,2S,6R,7S)-10,10-diethoxytricyclo[5.2.1.0^{2,6}]decane-2,6-dicarboxylate, 10, was obtained. Pure 10,5) bp 200-210 °C /0.2 Torr, was isolated in 29.2% yield by careful distillation in a rotary microdistillation apparatus. Heating this compound with 15% aqueous $HClO_4$ under reflux for 5 h, oxodiester 2 was obtained in 82.8% yield, identical (mp, mixed mp, GLC, IR, and ^1H NMR) to the product previously described,1b) showing that annelation of



the dianion derived from diester 9 takes place, as expected, by its *exo*-face. Reaction of oxodiester 2 with tosylhydrazide under HCl catalysis (2-propanol, reflux temperature, 28 h) gave the corresponding tosylhydrazone, 11,5) mp 170-172 °C (2-propanol) in 75.1% yield. Tosylhydrazone 11 was converted into the corresponding sodium salt by reaction with sodium methoxide in refluxing methanol for 2 h. The dried sodium salt was pyrolyzed at 170 °C/1 Torr to give an oily distillate almost consisting of a single product (97% relative area by GLC, 89% yield) that was characterized as diester 1,5) mp 62-63 °C(2-propanol) through its elemental analysis and spectroscopic data (IR, ^{1}H and ^{13}C NMR). In particular, the ^{13}C NMR spectrum showed only eight signals with the expected multiplicity and intensity, according to the symmetry of 1.

Thus, a stereoselective synthesis of compound 1 from the known and easily accessible dicarboximide 3 has been developed. Work is in progress to transform compound 1 into more elaborated possible dodecahedrane precursors.

References

1) a) P. Camps and M. Figueredo, Can. J. Chem., in press; b) P. Camps, J. Castañé, M. Feliz, and M. Figueredo, Tetrahedron, in press.

2) Dodecahedrane has been recently synthesized: R. J. Ternansky, D. W. Balogh, and L. A. Paquette, J. Am. Chem. Soc., 104, 4503(1982).

3) S. Gäb, H. Parlar, and F. Korte, Tetrahedron, 30, 1145(1974); b) F. I. Onuska and M. E. Comba, Biomed. Mass Spectromet., 2, 176(1975); c) E. S. Lahaniatis, H. Parlar, S. Gäb, and F. Korte, Synthesis, 1976, 47; d) J. R. Neff and J. E. Nordlander, J. Org. Chem., 41, 2590(1976); e) H. Parlar, H. Mansour, and S. Gäb, Tetrahedron Lett., 1978, 1597; f) D. Bosse and A. de Meijere, Chem. Ber., 111, 2223(1978); g) J. R. Knox, C. L. Raston, and A. H. White, Aust. J. Chem., 32, 553(1979).

4) P. J. Garratt and F. Hollowood, J. Org. Chem., 47, 68(1982).

5) All the new compounds described in this communication show elemental analyses and spectroscopic data (IR, ^{1}H and ^{13}C NMR) in accord with expectations.

6) For a more detailed discussion in related compounds see Ref. 1b.

7) K. G. Bilyard, P. J. Garratt, and R. Zahler, Synthesis, 1980, 389.

8) C. Girard and R. Bloch, Tetrahedron Lett., 23, 3683(1982)

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