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SYNTHESIS OF PENTACYCLO[4.3.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]NONANE AND SOME 4-SUBSTITUTED DERIVATIVES

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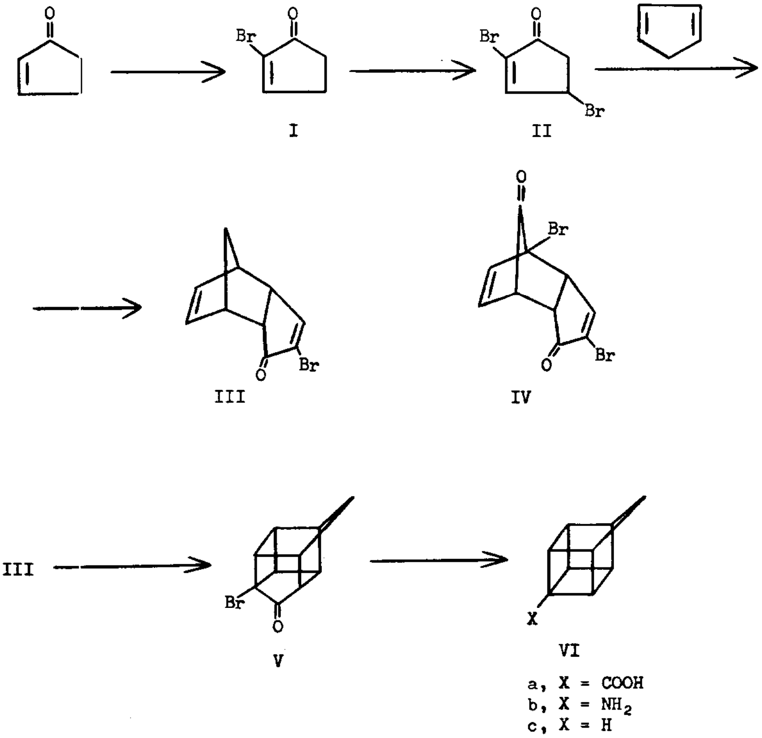
The synthesis of pentacyclo[4.3.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]nonanes containing two or more functional groups has been described by Eaton and Cole (1), and by Scherer, Lunt and Ungefug (2). We wish to report a method for preparing pentacyclo[4.3.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]nonanes containing a single functional group, and to describe the conversion of the 4-carboxylic acid to the parent hydrocarbon.

A key step in this synthesis is a Diels-Alder reaction between cyclopentadiene and 2-bromocyclopentadienone to give adduct III. The adduct was cyclized photochemically and the intermediate pentacyclodecanone (V) was converted to VIa by a Favorskii ring contraction. Cyclopentadienone and α-halocyclopentadienones have been employed previously (3,4,5,6) for the synthesis of polycyclic ring systems. We have used a modified method to prepare 2-bromocyclopentadienone through the novel intermediate, 2-bromo-2-cyclopentenone (I).

The carboxyl group of VIa was eliminated by a modified Hunsdiecker reaction, and the product was dehalogenated to give the hydrocarbon, pentacyclo[4.3.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]nonane (VIc). Alternatively the decarboxylation was accomplished by radical decomposition of the t-butyl perester.



Bromination of 2-cyclopentenone in carbon tetrachloride at 0° followed by dehydrobromination of the unisolated intermediate, 2,3-dibromocyclopentanone, with triethylamine gave a 42% yield of 2-bromo-2-cyclopentenone (I)*, mp 39-39.5°; ultraviolet maximum at 238 mμ (ε 8470);

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* All new compounds gave satisfactory elemental analyses. Ultraviolet spectra were carried out in 95% ethanol. Infrared spectra were taken in Nujol mull unless otherwise indicated. NMR spectra were carried out on a Varian A-60 in $CDCl_3$ solution, unless indicated otherwise, with TMS as internal standard.

infrared absorption at 5.91 (C = O) and 6.32 μ (C = C); and nmr peaks at δ 7.86 (1 H triplet, J = 3 cps), and at δ 2.88 - 2.43 (4 H multiplet). The bathochromic shift of 20 mμ (7) from the ultraviolet maximum of 2-cyclopentenone (218 mμ), the absence of the α vinyl proton peak of cyclopentenone (8) at δ 6.11, and the decrease in multiplicity of the β vinyl proton from a sextet in cyclopentenone to a triplet in the product support the structure of I. Allylic bromination of I with N-bromosuccinimide in boiling carbon tetrachloride (24 hr) gave a good yield of dibromoenone II which was used without purification. An ethereal solution of II was added slowly to a cold (-10°) mixture of cyclopentadiene and triethylamine in ether. The crude reaction product was chromatographed on neutral alumina. The benzene and the initial benzene-chloroform (1:1) eluates gave, after recrystallization from petroleum ether (30-60°), a 29% yield (from I) of 2-bromo-3a,4,7,7a-tetrahydro-4,7-methanoinden-1-one (III), mp 56-57°; ultraviolet maximum at 246 mμ (ε 6000); infrared absorption at 5.88 (C = O) and 6.35 μ (C = C); and nmr peaks at δ 7.56 (1 H doublet, J = 2.8 cps) and at δ 5.92 (2 H symmetrical multiplet). A bathochromic shift of 20 mμ in the ultraviolet spectrum of III from that shown by dicyclopentadien-1-one (226 mμ) and the simplification of the nmr peaks of dicyclopentadien-1-one from a quartet (1 H) at δ 7.47 (J = 2.8 cps) and a multiplet (3 H) at δ 6.15 - 5.74 to a doublet (1 H) and a multiplet (2 H) are consistent with structure III. All further column eluates gave mixtures of III and what we assume to be IV as indicated by the infrared absorption at 5.50 μ (C = O) (5) also present in the crude product. A solution of III in ethyl acetate was irradiated (pyrex filter) under nitrogen for 32 hr with a Hanovia 450 watt medium pressure mercury vapor lamp giving a 79% yield of 5-bromopentacyclo $[5.3.0.0^{2,5}.0^{3,9}.0^{4,8}]$decan-6-one (V), mp 39-40°; infrared absorption

(CH_2Cl_2) at 5.56, 5.60 (sh), 5.63, 5.67, 5.70 μ (C = O);** and nmr peaks at δ 3.68 - 2.72 (6 H multiplet), at δ ~ 2.4 (1 H multiplet) and at δ 1.79 (2 H singlet with half height width of 3 cps, small "wings" at δ 1.58 and δ 2.00). Upon heating V in 30% aqueous potassium hydroxide for 4 hr, a quantitative yield of pentacyclo[$4.3.0.0^{2,5}.0^{3,8}.0^{4,7}$]nonan-4-carboxylic acid (VIa) was obtained, mp 93-95°; infrared absorption at 5.96 μ (acid C = O); and nmr peaks at δ 11.45 (1 H singlet, COOH), at δ 3.72 - 3.05 (7 H multiplet), and at δ 1.72 (2 H singlet). The acid was converted to amine VI b in 56% yield by a Curtius reaction and characterized as the hydrochloride salt, mp 188-190° dec; nmr peaks (D_2O/DCl) at δ 3.68 - 3.17 (7 H multiplet) and at δ 1.73 (2 H singlet).

The acid (VIa) was converted to a mixture of the 4-chloro and 4-bromo compounds in 40% yield by a modified Hunsdiecker reaction (9) using mercuric oxide and bromine in boiling carbon tetrachloride. The halohydrocarbon mixture was dehalogenated with lithium and t-butyl alcohol in tetrahydrofuran giving a 10% yield of pentacyclo[$4.3.0.0^{2,5}.0^{3,8}.0^{4,7}$]nonane (VIc), mp (sealed capillary) 107-108°; nmr peaks at δ 3.40 - 3.00 (8 H unsymmetrical doublet) and at δ 1.69 (2 H singlet). The hydrocarbon was also prepared (in low yield) by decomposition of the t-butyl perester of VIa in p-diisopropylbenzene at 150° but the product was contaminated with ca. 6% p-diisopropylbenzene which was difficult to remove. The hydrocarbon shows a molecular ion peak in the mass spectrum at m/e 118, a more intense peak at m/e 117 and a major peak at m/e 103.

The multiplet (1 H) at δ ~ 2.4 in the nmr spectrum of bromoketone V concerned us since, if it were due to the unique proton 5, α to the ketone, it would be expected to appear downfield from the other methine protons,

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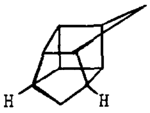
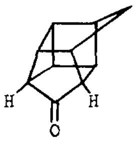
** Eaton and Cole (1,5) also have reported similar carbonyl multiplicity in caged ketones.

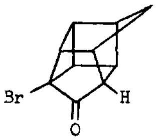
not upfield. An upfield displacement of two methine protons in this cage system has also been reported by Eaton and Cole (5) without comment. Nickon and coworkers (10), as well as Wellman and Bordwell (11) have shown that in some α-haloketones the α-equatorial proton unexpectedly is shielded, but the α-axial proton is still strongly deshielded by the carbonyl. Both protons however are deshielded by the carbonyl in the nonhalogenated ketones. We have been able to show that the multiplet at $\delta \sim 2.4$ in the nmr spectrum of V is most likely due to the α proton. The nmr spectra of compounds VII (12) and VIII (13), prepared for other studies,



VII



VIII



V

were compared with that of V. Hydrocarbon VII shows methine absorption at δ 2.96 - 2.33 (8 H), grossly as a broad unsymmetrical doublet, but ketone VIII, in addition to a similarly shaped broad doublet at δ 3.30 - 2.60 (6H), shows two upfield 1 H multiplets, at $\delta \sim 2.4$ and at $\delta \sim 2.2$. When one α proton of VIII is replaced by a bromine atom (V) the $\delta \sim 2.2$ upfield multiplet disappears. Therefore, we can assign with confidence the $\delta \sim 2.4$ multiplet in the nmr spectrum of V to the remaining α proton. The reason for the upfield shift of these protons is not readily apparent.

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