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SYNTHESIS OF A NORCUBANE DERIVATIVE

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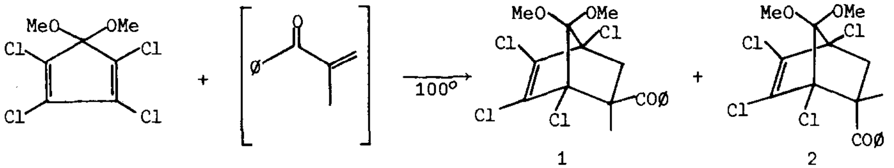
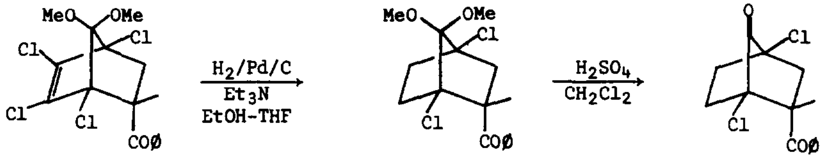
The recent synthesis by Harless and Monti[1] of tricyclo[3.1.1.0^{3,6}]heptane-6-carboxylic acid prompts us to report our synthesis of another representative of this novel ring system ("norcubane"):

Diels-Alder reaction of tetrachlorocyclopentadiene dimethyl ketal[2] with a 25% excess of methacrylophenone, generated in situ from α-methyl-β-dimethylaminopropiophenone hydrochloride[3] plus one equivalent of aqueous sodium acetate produced[4] a 1:2 mixture of exo-5-benzoyl-1,2,3,4-tetrachloro-7,7-dimethoxy-5-methylbicyclo[2.2.1]heptene-2 (1), mp 138-140½°, and its endo epimer, mp 93½-95° (2). These were separable by crystallization from ethanol. They are differentiated by their pmr spectra (Table I). The C-methyl of 1 is shifted upfield by its proximity to the C-C double bond, and the methoxyls of 1 are more separate, owing to the proximity of one to the carbonyl group. Moreover, the carbonyl frequency of 1 is higher, owing to steric interaction with the syn methoxyl, which inhibits conjugation between phenyl and carbonyl. Hydrogenation of 2 over Pd/C in the presence of triethylamine[5] produced endo-2-benzoyl-1,4-dichloro-7,7-dimethoxy-2-methylbicyclo[2.2.1]heptane (3). Hydrolysis[5] of 3 produced endo-2-benzoyl-1,4-dichloro-2-methylbicyclo[2.2.1]heptan-7-one (4), mp 105-8°. Both 3 and 4 could be photoisomerized to alcohols (5 and 6), but the epimer of 3, mp 135½-7°, which could be obtained by hydrogenation of

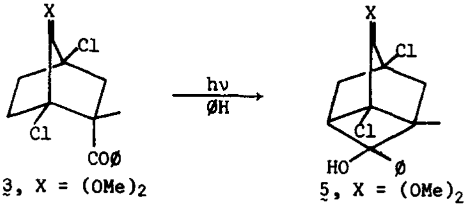


1 2



2 3 4

1, was inert to irradiation; these results further establish the stereochemistry of 1 and 2.



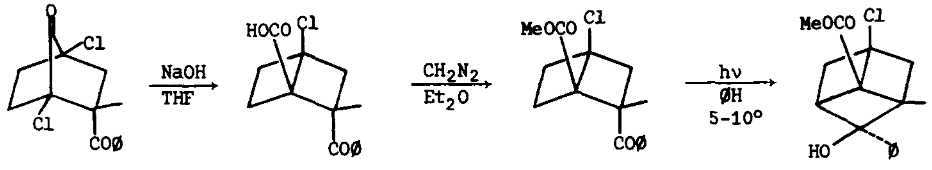
3, X = $(OMe)_2$
4, X = O

5, X = $(OMe)_2$
6, X = O

Table I. Spectroscopic Data

Compound	O-Me (δ)	C-Me (δ)	CH & CH$_2$ (δ)	Phenyl (δ)	ir (cm^{-1})
1	3.40, 3.51	1.43	2.19,3,07(2H,J=11)	7.20-7.80(5H,m)	1695
2	3.47, 3.53	1.82	2.47,2.83(2H,J=11)	7.21(3H,m),7.55(2H,m)	1684
3	3.42 (2Me)	1.67	1.7-2.4(5H,m),3.05(1H)	7.23(3H,m),7.67(2H,m)	1684
4	---	1.52	1.9-2.8(5H,m),3.27(1H,J=12)	7.33(3H,m),7.78(2H,m)	1678,1812
5	3.52 (2Me)	1.35	1.6-2.8(6H,m)	7.18(5H,s)	3600(broad)
6	---	1.42	1.8-3.0(5H,m)	7.18(5H,s)	3600,1790
7	---	1.67	2.3-3.2(6H,m)	7.55(3H,m),7.82(2H,m)	3000(vbroad) 1692(broad)
8	3.73	1.60	2.3-3.2(6H,m)	7.31(3H,m),7.82(2H,m)	1727,1669
9	3.65	1.40	2.1-3.0(6H,m)	7.17(5H,s)	3500(broad) 1724

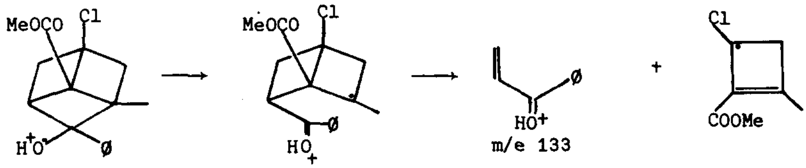
Ring contraction of 4 with NaOH in dry THF[5] at 0° produced endo-2-benzoyl-4-chloro-2-methylbicyclo[2.2.0]hexane-1-carboxylic acid (7), mp 134-7°, in 70% yield, along with a ring-opened product, as judged by its nmr integral and especially by a 3.43 δ peak due to CHCl. This latter acid was readily separable, since its sodium salt was only slightly soluble in aqueous solutions. Irradiation of 7 produced only olefinic material, which polymerized on standing. Therefore



4 7 8 9

conversion of 7 to its methyl ester (8) was effected with diazomethane. Crude preparations of this ester showed an additional peak at 1.77 δ, which we ascribe to the 1-chloro-4-carboxylic acid isomer. A similar upfield shift of methyl adjacent to carbomethoxy is observed in methyl *cis*-2-methyl-cyclobutanecarboxylate.[6] It is on the basis of this comparison that the structural assignment of 7 was made.

Irradiation of 8 (0.1% in benzene, 450W Hanovia lamp with Pyrex filter, cooling with ice-water), followed by chromatography on silica gel, produced a good yield of methyl 5-chloro-2-hydroxy-1-methyl-2-phenyltricyclo[3.1.1.$0^{3,6}$]heptane-6-carboxylate (9). The pmr and ir spectra are consistent with this structure and inconsistent with any monocyclic or bicyclic isomer. The mass spectrum showed m/e: 292 & 294 (M^+), 197 (8), 160 (8), 153 (12), 147 (7), 133 (6), 106 (9), 105 (100), 91 (10), 77 (46). Especially notable is the m/e 133 peak, which is absent in the precursors of 9. We attribute this to the fragmentation



These data do not exclude the tricyclo[3.2.0.$0^{3,6}$]heptan-2-ol isomer,[7] but photochemical cyclopentanol formation seems to require weakened δ C-H bonds.[8] Furthermore, cyclobutanol formation is quite common,[7,9,10] and molecular models suggest that the transition state[8] for abstraction of the γ hydrogen in 8 is, as usual, less strained than that for the δ hydrogen. Assignment of the stereochemistry at C_2 is based on analogy to the observations of Lewis *et al.*,[9] but definitive proof must await an X-ray diffraction study of a crystalline derivative. Thus we have prepared another example of the tricyclo[3.1.1.$0^{3,6}$]heptane ("norcubane") ring system. This differs from the carboxylic acid of Harless and Monti[1] in having additional functionality. Furthermore, it arises by a different and shorter route, one that features not only a Favorskii rearrangement to a bicyclo[2.2.0]hexane but also a photochemical formation of the third four-membered ring.

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