

SYNTHESIS OF NORADAMANTANE FUNCTIONALIZED AT C-2

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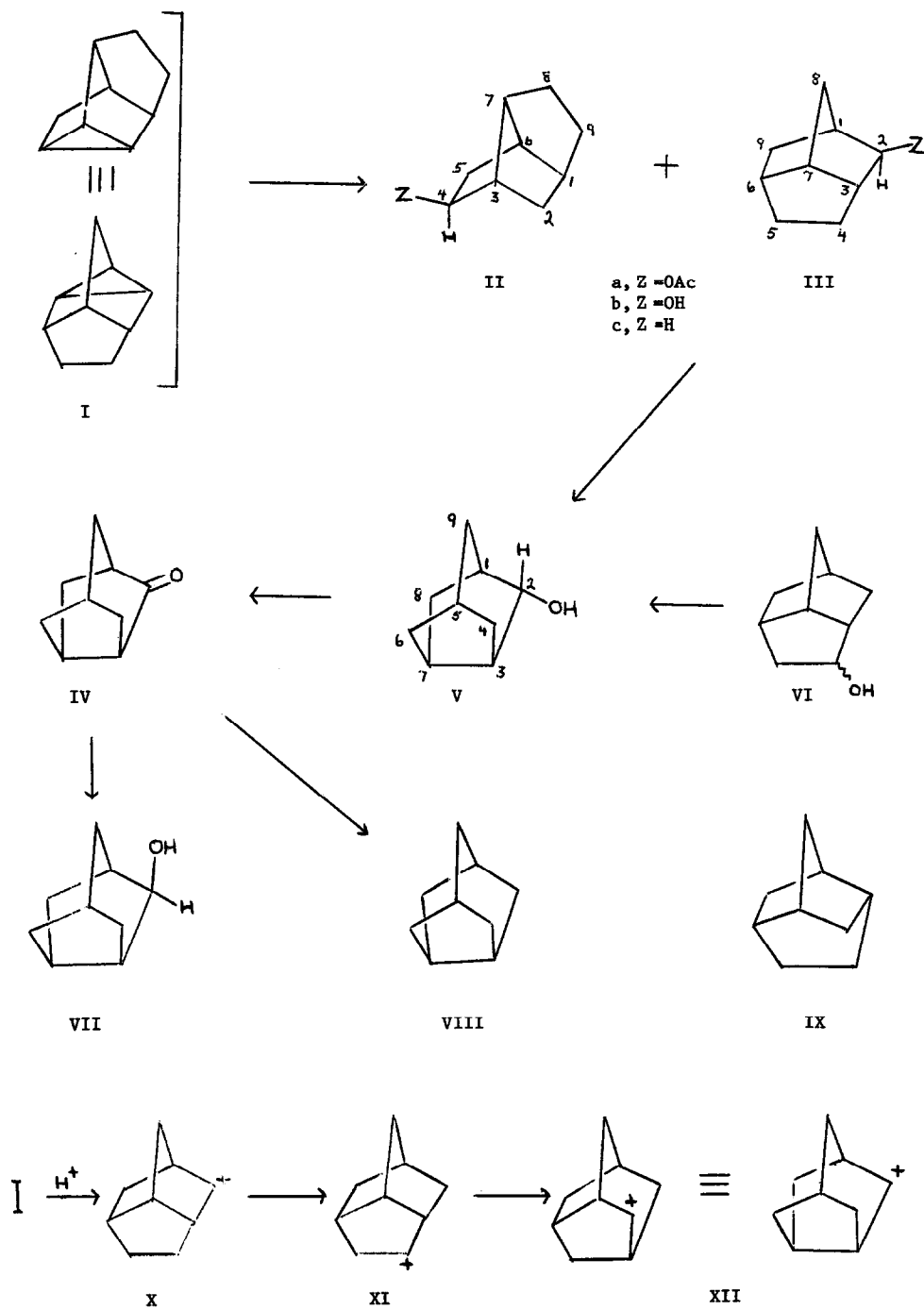
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The tetracyclic hydrocarbon I, trivially known as deltacyclane (1), is readily prepared by a variety of routes (2) and has been shown to be a convenient precursor of the brexane and brendane skeletons (1,2a). For example, acid catalyzed acetolysis of I gives a mixture (initially ca. 1:1) of exo-brexan-4-ol acetate (IIa) and exo-brendan-2-ol acetate (IIIa). The brendyl product is the more stable of the two and predominates almost exclusively if the acetolysis mixture is allowed to equilibrate (1,2a). The possibility of rearranging these skeletons to still more stable ones that retain the functional group led us to explore the opening of deltacyclane under more forcing conditions. These studies have provided a convenient entry to the noradamantane (tricyclo[3.3.1.0^{3,7}]nonane) system functionalized at C-2.

A pentane solution of I was added dropwise to 96% sulfuric acid at -5 to -2°. After a few minutes a hydrolytic work-up produced a good yield (ca. 80%) of noradamantan-2-ol (V); m.p. 221-222° (from pentane-cyclohexane); ν (CCl₄) 3610 (O-H), 1082 (C-O) cm⁻¹. Oxidation with Brown's reagent (3) gave noradamantan-2-one (IV), m.p. 214.5-215° (from pentane); semicarbazone m.p. 209-210°; p-toluenesulfonylhydrazone m.p. 161-162°. The infrared spectrum of the ketone showed the carbonyl band at 1746 cm⁻¹ (CCl₄) typical of a 5 membered ring ketone and showed no absorption at 1400-1420 cm⁻¹ characteristic of an alpha CH₂ group (2a). Reduction of IV with lithium aluminum hydride in ether proceeded with high stereoselectivity and gave, after an alkaline work-up, epi-noradamantan-2-ol (VII), m.p. 246-246.5° (from pentane); ν (CCl₄) 3618 (OH), 1040 (C-O) cm⁻¹. The epi-alcohol was oxidized to the original ketone to confirm that no skeletal change had occurred.

Wolff-Kishner reduction of the semicarbazone of IV gave noradamantane (VIII) directly (m.p. 201-203° sealed immersed capillary). After removal of a slight impurity by preparative gas chromatography, the spectroscopic features were as follows. Nmr (CCl₄): peaks centered



near δ 2.40 (2H) and δ 2.10 (2H) attributed to the two pairs of bridgehead protons, and a main absorption near δ 1.60 (10H); considerable fine structure is associated with each of these three absorptions. Mass spectrum (m/e): 122 (parent ion) and some principal fragment peaks at 93, 81, 80 (base peak), 79, 78, 77, 67, 66, 53, 41, 39. The ir spectrum (CCl_4) is relatively simple with three sharp peaks at 1458, 1316, and 1076 cm^{-1} , accompanied by nearby weak bands.

From the method of preparation and the spectroscopic data of IV, V, VII, and VIII, and the availability from our earlier work (2a) of brendane, brexane and their derived ketones and alcohols for direct comparison, only one structure, IX, remained as an alternative skeleton for our present compounds. Even though IX may be reasonably excluded on the basis of what its nmr spectrum should be, confirmation of the noradamantane system was provided by direct comparison of our hydrocarbon VIII (identical ir and nmr) with a sample prepared independently by two other routes.*

That the OH group is equatorial with respect to its 6-membered ring [i.e. is anti to the C-9 bridging carbon] in noradamantanol (V), and is axial in epi-noradamantanol (VII), is indicated by the nature of the low field α -proton signal in the nmr spectrum of each epimer in CDCl_3 after exchange of the OH proton with D_2O . The axial C-2 proton in V appears as an asymmetric singlet (δ 3.91; $W_{1/2} \sim 3\text{Hz}$) whereas the equatorial C-2 proton in VII appears as an incompletely resolved broad multiplet (δ 4.05; $W_{1/2} \sim 12\text{Hz}$). Molecular models show that the rigid noradamantane structure distorts a chair cyclohexane ring and increases the dihedral angles between the C-2 axial proton and the adjacent bridgehead protons but decreases these dihedral angles for an equatorial C-2 proton. The vicinal couplings should be larger in VII than in V in accord with the assigned structures (4).

A reasonable sequence for acid isomerization of I to the noradamantyl skeleton could involve formation of the brendyl-2 cation (X) followed by a 1,3-hydride shift to produce the brendyl-4 cation (XI), which is related to the noradamantyl cation XII by a Wagner-Meerwein shift. The scheme, which uses classical cationic structures for convenience, implies that

* When we learned that noradamantane was obtained independently by Vogt and Hoover by a rational synthetic route and by Schleyer and Wiskott by an isomerization route, simultaneous publication was mutually agreed upon (see accompanying papers). We are grateful to Dr. Vogt and to Professor Schleyer for informing us of their work. Professor Schleyer kindly provided us with a sample for direct comparison.

breneryl derivatives functionalized at C-2 or at C-4 might serve as precursors of the functionalized noradamantyl system. Indeed, we found that exo-brendan-2-ol (IIIb) was converted to V on treatment with 96% sulfuric acid at 2-5° for 3 hr. Furthermore, when brendan-4-ol (VI; epimeric mixture produced by reduction of brendan-4-one (2a) with lithium aluminum hydride) was heated at 75° in HCOOH-H₂SO₄ followed by saponification of the derived esters and sublimation, we obtained noradamantanol (V) in excellent purity. We are continuing our studies on the interconversions of brexyl, breneryl, and noradamantyl systems and on the solvolyses of their derivatives.

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