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STEREOCHEMISTRY OF THE Π-ROUTE TO 2,4-DISUBSTITUTED ADAMANTANES (1)

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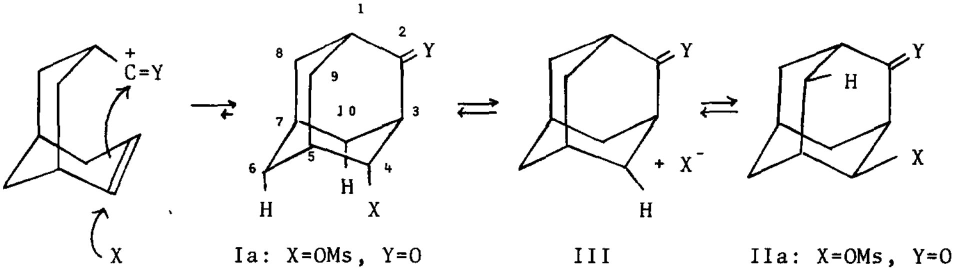
Recently, the π-route to 2-substituted (2) and 2,4-disubstituted adamantanes (3-5) has drawn much attention because of its synthetic utility. However, a dichotomy in the stereochemistry of a 4-substituent introduced by the π-route to 2,4-disubstituted adamantanes remains seemingly unsolved. We wish to report in this communication a reasonable interpretation on the stereochemistry of the π-route to 2,4-disubstituted adamantanes.

When the Schmidt reaction of adamantanone was carried out in methanesulfonic acid by using a prolonged reaction time and a higher temperature, a mixture of 4e- (Ia) and 4a-methylsulfonoxyadamantan-2-one (IIa) was obtained instead of pure Ia under the milder conditions (3). Heating of pure Ia in methanesulfonic acid yielded also an equilibrium mixture of Ia and IIa, indicating a facile equilibriation between the isomers under the reaction conditions. Reinvestigation of the study reported by McKervey et al. (5) revealed that treatment of 4-oxohomoadamantan-5-one with 50% sulfuric acid afforded a 1:6 mixture of 4e- (Ib) and 4a-hydroxyadamantan-2-one (IIb) in 71.5% yield. Furthermore, pure IIb was converted to a mixture of Ib and IIb on treatment with 50% sulfuric acid.

The cyclization process of the π-route to 2,4-disubstituted adamantanes could now be interpreted as depicted in Scheme: an acylium cation cyclizes under the stereoelectronic control to afford initially a 4e-isomer which is unstable under the acidic conditions and is converted to an equilibrium mixture of 4e- and 4a-isomers <u>via</u> a cationic intermediate III.

The equilibrium constants for Ia $\rightleftarrows$ IIa were measured by the nmr analysis,



Ia: X=OMs, Y=O
Ib: X=OH, Y=O

III

IIa: X=OMs, Y=O
IIb: X=OH, Y=O

Scheme

from which the thermodynamic parameters were calculated as summarized in Table. Obviously, IIa is thermodynamically more stable than Ia. This could be explained by the difference of 1,3-ax-ax nonbonded interaction related to the mesylate group between Ia and IIa; in Ia, two such interactions exist between 4e-OMs and 6a-H, and 4e-OMs and 10a-H, while in IIa, only one between 4a-OMs and 9a-H. The obtained -ΔG value is somewhat larger than an half of A value reported for monosubstituted cyclohexanes (6), which might be due to some ring deformation in Ia and IIa (cf. the nmr data in ref. 3).

Table

Temp. (^{o}C)	K(IIa/Ia)	-ΔG (Kcal/mol)	ΔH (Kcal/mol)	ΔS (e.u.)
76.5	5.83	1.23		
65.5	6.01	1.21		
47.5	6.24	1.17		
25.0		1.13 (extrapolated value)	0.54	-1.97

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