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The Resolution of Endo-bicyclo[3.3.1]non-6-en-3-carboxylic acid and its Conversion to Optically Active Adamantanones

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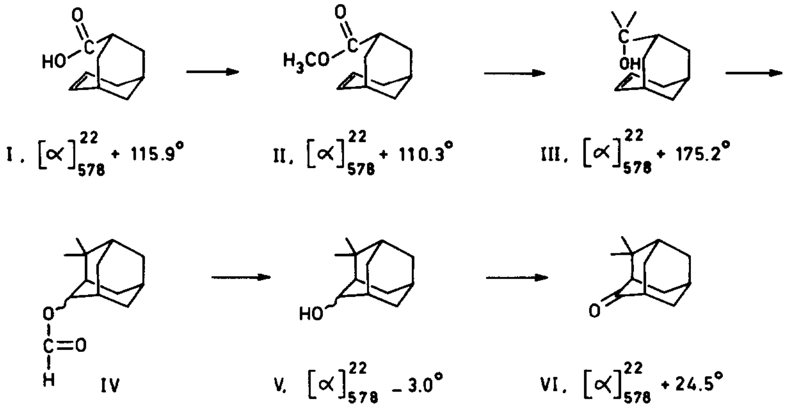
We needed chiral adamantanones in order to explore their usefulness as starting materials in the synthesis of stable optically active 1,2-dioxetanes.[1] The latter compounds are suitable models to study the circular polarisation of chemiluminescence.[2]

No facile route to optically active substituted adamantanones is available.[3a-c] We will describe here, that the π-route cyclisation[4a-c,5] of certain endo-bicyclo[3-3-1]non-6-en-3-yl derivatives provides such a pathway. We wish to report the resolution of the endo-bicyclo[3.3.1]non-6-en-3-carboxylic acid (I)[4a,b,6] and its successful conversion to:

i) (1S) 4,4-dimethyl-adamantan-2-one (VI) (see scheme 1);
ii) the (1R) (4S) 4^e-chloro-adamantan-2-one (VII) and (1R) (4R) 4^a-chloro-adamantan-2-one (VIII);
iii) (1S) 4,4-dideutero-adamantan-2-one (IX).

The absolute configurations of the acid (+) I and of the ketones VI, VII, VIII and IX were established. Determination of the optical purities of the starting acid (+) I and the (+) (1S) 4,4-dimethyl-adamantan-2-one (VI) showed complete retention of enantiomeric excess.

Scheme 1



I. $[\alpha]^{22}_{578}$ + 115.9°

II. $[\alpha]^{22}_{578}$ + 110.3°

III. $[\alpha]^{22}_{578}$ + 175.2°

IV

V. $[\alpha]^{22}_{578}$ - 3.0°

VI. $[\alpha]^{22}_{578}$ + 24.5°

Resolution of the endo-bicyclo[3.3.1]non-6-en-3-carboxylic acid, I, was achieved using (+) dehydroabiethylamine. The diastereomeric salts could be separated by fractional crystallisation from 96% ethanol. Decomposition of the salt, $[\alpha]^{22}_{578}$ + 71.0°,[7] gave optically active acid (+) I, $[\alpha]^{22}_{578}$ + 115.9°.[7]

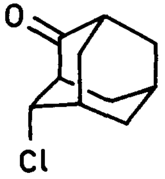
Analytical separation by high pressure liquid chromatography of the mixture of diastereomeric amides, prepared using the acylchloride of acid (+) I and (-)α-phenylethylamine, showed that the enantiomeric excess of (+) I, $[\alpha]^{22}_{578}$ + 115.9°. was 77 ± 3%.

Cyclisation of (+)-2(endo-bicyclo[3.3.1]non-6-en-3-yl)propan-2-ol, (+)(III), $[\alpha]^{22}_{578}$+ 175.2°[7] in hot formic acid, yielded after hydrolysis of the initial product IV, a mixture of epimeric alcohols V, $[\alpha]^{22}_{578}$ - 3.0°.[7] Oxidation of the alcohol mixture with chromic acid gave 4,4-dimethyladamantan-2-one, VI, $[\alpha]^{22}_{578}$ + 24.5°.[7] The enantiomeric excess was found to be 77 ± 3% and was determined using ^{13}CMR spectroscopy on the mixture of diastereomeric ketals,[8] obtained from reaction of the ketone (+) VI with (-)-2,3-butanediol.[9] Stereochemical integrity is evidently maintained during these reactions. In contrast, when the acid (+) I was stirred in methanesulphonic acid at 90° for one hour the isolated mixture of 4-methylsulphonyloxy-adamantan-2-ones[4a] showed no optical activity. The most likely explanation for this loss of optical activity is that in methanesulphonic acid the double bond is protonated rapidly, followed by the formation of the

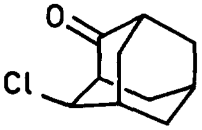
4-oxahomoadamantan-5-one.[4a] The latter symmetrical intermediate then reacts further to the thermodynamically more stable products. This explanation is in accord with the data reported by Mc Kervey for the reaction of the acid I and the lactone under these conditions.[4a]

The absolute configuration of (+) VI could be assigned as 1S on the basis of the positive sign of the cotton effect for the $n\pi^*$ transition ($\Delta\varepsilon_{max}$ 0.61 at 303 nm) and the data Snatzke[11a-b] reported for the epimeric 4-methyl-adamantan-2-ones. Knowledge of the absolute configuration of (+) ketone VI as 1S leads to the assignment of the absolute configuration of the starting acid (+) I as 3R.

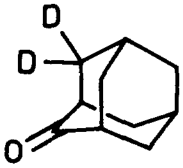
The availability of (+) acid I allows ready entry into a variety of optically active derivatives. For example we have also succeeded in the synthesis of the epimeric optically active 4-chloro-adamantan-2-ones VII and VIII by treatment of the acylchloride of (+) I with borontrifluoride etherate in dimethoxyethane.[4b]



VII



VIII



IX

The equatorial 4-chloro-adamantan-2-one VII showed a negative sign of the cotton effect at 296.5 nm, whereas the axial ketone VIII had a positive sign at 294 nm in the circular dichroism spectrum.

Knowing the absolute configuration of the acid (+) I as (3R) the absolute configuration of these epimeric chloro-ketones[10] and thus the signs of their cotton effects for the $n\pi^*$ transitions are readily correllated. Our data are in accord with Snatzke's results,[11a-b] giving the absolute configuration of VII as (1R) (4S) and of VIII as (1R) (4R).

The synthesis of optically active (1R) 4,4-dideutero-adamantan-2-one (IX) using an analoguous route,[5] has been completed and will be reported on shortly in detail.

References:

1) H. Numan and H. Wynberg, J. Am. Chem. Soc., 99, 603 (1977).
2) H. Numan and H. Wynberg, submitted for publication.
3) a. G. Snatzke and D. Marquarding, Chem. Ber., 100, 1710 (1967);
   b. G. Snatzke and G. Eckhardt, Chem. Ber., 101, 2010 (1968);
   c. W.S. Briggs, M. Suchy and C. Djerassi, Tetrahedron Letters, 1968, 1097.
4) a. D. Faulkner and M.A. Mc Kervey, J. Chem. Soc. (C), 1971, 3906;
   b. M.A. Mc Kervey, D. Faulkner and H. Hamill, Tetrahedron Letters, 1970, 1971;
   c. F. Blancey, D. Faulkner, M.A. Mc Kervey, J. Chem. Soc., Perkin I, 2697 (1972).
5) D.J. Raber, G.J. Kane and P. von R. Schleyer, Tetrahedron Letters, 1971, 1671.
6) A.C. Udding, H. Wynberg and J. Strating, Tetrahedron Letters, 1968, 5719.
7) All rotations were measured in 96% ethanol with $c = 1.0\ \mathrm{g}/_{100\ \mathrm{ml}}$. Yields as published in ref. 4.
8) H. Hiemstra and H. Wynberg, to be published.
9) J. Casanova Jr and E.J. Corey, Chem. and Ind., 1664 (1961).
10) Note that the absolute configurations of ketones VI, VII, VIII and IX depend on the reaction sequence.
11) a. G. Snatzke and G. Eckhardt, Tetrahedron, 24, 4543 (1968);
    b. G. Snatzke, B. Ehrig and H. Klein, Tetrahedron, 25, 5601 (1969).