Tetrahedron Letters No. 25, pp. 2339-2342, 1971. Pergamon Press. Printed in Great Britain.

THE SYNTHESIS OF ADAMANTANE-2,2-DICARBOXYLIC ACID AND DERIVATIVES

S. Reiffers, J. Strating and Hans Wynberg
Department of Organic Chemistry, The University,
Zernikelaan, Groningen, The Netherlands

(Received in UK 12 May 1971; accepted in UK for publication 20 May 1971)

In spite of many attempts[1,2] the preparation of adamantane-2,2-dicarboxylic acid and/or its derivatives has failed thus far.

Our interest in the spiroadamantanes[3] and their precursors prompted us to persevere in attempts to prepare I and we wish now to report our first results in this field.

The most successful method discussed below amounts to a new technique for the preparation of malonic acids from monocarboxylic acids. It is based on observations of the behaviour of α-anions of carboxylic acids[4,5,6] towards electrophilic agents. Although in the paper concerning the alkylations[5] of α-anions carbon dioxide is also mentioned as a possible reagent, no communication on this subject has appeared.

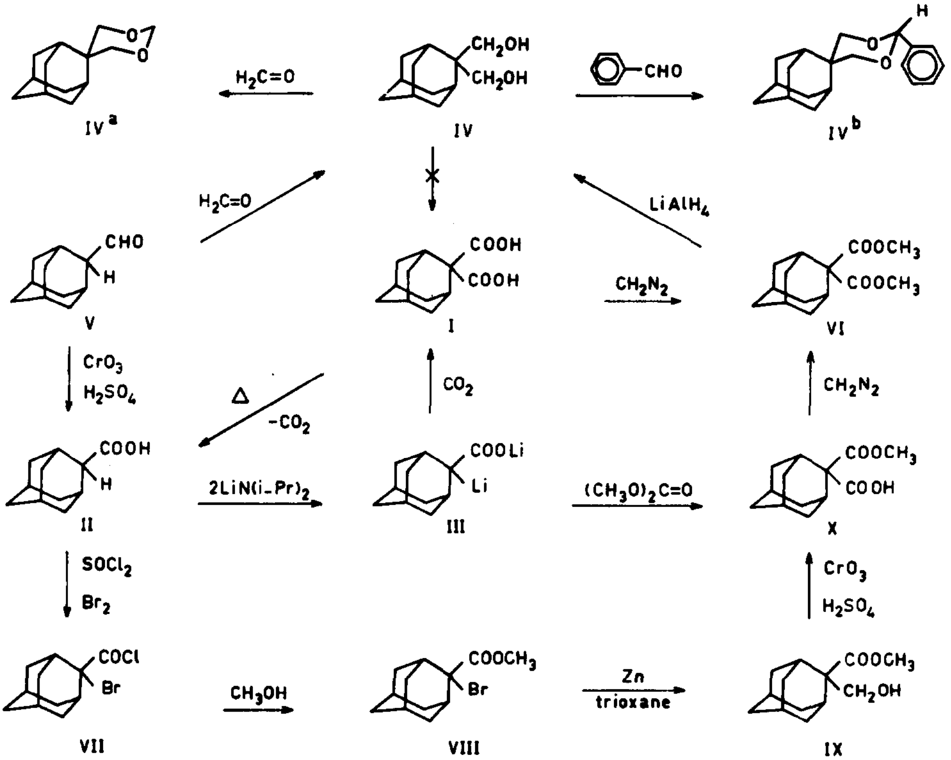
When adamantane-2-carboxylic acid (II) was addded at -5° to a tetrahydrofuran-hexane solution containing 2 equivalents of lithium diisopropylamine, the dilithium salt III was evidently formed, since treatment of the resulting reaction mixture with gaseous CO_2 and subsequent careful acidification furnished a mixture of acids from which adamantane-2,2-dicarboxylic acid (I) with a m.p. 199-201° (dec.) could be isolated in a yield of 30%. The acid was characterized by elemental analysis[7], the IR spectrum, its PMR spectrum, the mass spectrum, as well as its conversion to adamantane-2-carboxylic acid (m.p. and m.m.p. 140-142°) by decarboxylation.

IR spectrum (KBr): 2400-3500 cm^{-1} (s, broad, COOH), 1695-1730 cm^{-1} (s, broad, $\geq$C=O) and 1175 cm^{-1} (s).

PMR spectrum (CD_3COCD_3): τ = 7.2-7.5 (m, 2H, β protons), τ = 0.4-1.0 (m, 2H, COO$\underline{H}$) and τ = 7.8-8.5 (m, 12H, remaining adamantyl protons).

Mass spectrum: M^+ = 224 (parent peak, 0.5%), $[M-H_2O]^+$ = 206 (10%) and $[M-CO_2]^+$ = 180 (base peak)

Although the spectral data shown above as well as the facile decarboxylation to adamantane-2-carboxylic acid (II) make the structure assignment of I as adamantane-2,2-dicarboxylic acid virtually certain, complete confirmation was obtained as follows (see scheme):



1. The 2,2-di(hydroxymethyl)adamantane (IV) obtained by reaction[8] of adamantane-2-carbaldehyde (V) and formaldehyde (aqueous, 40%) in alcoholic potassium hydroxide solution in a yield of 10% proved to be identical with the diol prepared by $LiAlH_4$ reduction of VI, the dimethyl ester of I. The analytically pure compound IV m.p. 163.5-165° showed the following spectral data.

IR spectrum (KBr): 3100-3500 cm^{-1} (s, broad, OH), 1005 cm^{-1}, 1025 cm^{-1} and 1035 cm^{-1} (s, C-O).

PMR spectrum ($CDCl_3$): τ = 6.06 (s, 4H, $-C\underline{H}_2OH$), τ = 6.66 (s, 2H, O-$\underline{H}$) and τ = 7.7-8.7 (m, 14H, adamantyl protons).

Mass spectrum: M^+ = 196 (parent peak, 0.5%), $[M-H_2O]^+$ = 178 (4%), $[M-CH_2OH]^+$ = 165 (70%) and $[M-CH_4O_2]^+$ = 148 (base peak).

The diol was further characterized by its conversion to the spirocyclic compounds IV^a (with formaldehyde) and IV^b (with benzaldehyde).

The reverse proof viz. the conversion of IV to I by oxidation (CrO_3, $KMnO_4$) was not successful.

2. The 2-bromo-adamantane-2-carboxylic acid chloride[9] (VII) was easily transformed into methyl 2-bromo-adamantane-2-carboxylate (VIII, m.p. 36.37.5°; yield 90%).

IR spectrum (neat): 1740 cm^{-1} (s, C=O), 1220 cm^{-1} and 1255 cm^{-1} (s).

PMR spectrum ($CDCl_3$): τ = 6.18 (s, 3H, $OC\underline{H}_3$), τ = 7.3-7.8 (m, 4H, two β and two γ protons), τ = 8.0-8.4 (m, 10H, remaining adamantyl protons).

When this α-bromo ester VIII was made to undergo a Reformatzky reaction under forcing conditions, that is with trioxane in a benzene-toluene solvent system a complex mixture was obtained from which no methyl 2-hydroxymethyl-adamantane-2-carboxylate (IX) could be isolated. However, by oxidation of the reaction mixture with Jones reagent[10] the monomethylester of adamantane-2,2-dicarboxylic acid (X) m.p. 153-156° (decarboxylation) could be obtained in a yield of 5%.

The same compound X could be isolated (in a yield of 17%) as a result of the reaction of the lithium salt III with dimethylcarbonate.*

IR spectrum (KBr): 2400-3400 cm^{-1} (m, broad, COOH), 1740 cm^{-1} (s, $C=O_{ester}$), 1700 cm^{-1} (s, $C=O_{acid}$) and 1205 cm^{-1} (s).

PMR spectrum ($CDCl_3$): τ = 6.26 (s, 3H, $-OC\underline{H}_3$), τ = 7.2-7.4 (m, 2H, β protons), τ = 7.9-8.5 (m, 12H, remaining adamantyl protons) and τ = -0.4 to -0.2 (m, 1H, $COO\underline{H}$).

Mass spectrum: M^+ = 238 (parent peak, 1%), $[M-H_2O]^+$ = 220 (10%), $[M-CH_2O]^+$ = 208 (12%) and $[M-CO_2]^+$ = 194 (base peak).

---

[*] More recently we have converted methyl adamantane-2-carboxylate to its α-lithium salt and transformed directly with gaseous CO_2 into the monomethyl ester of adamantane-2,2-dicarboxylic acid (X) in a yield of 88%.

The dimethyl ester VI obtained in nearly quantitative yield by reaction of X with diazomethane had a m.p. 99-100° and proved to be identical with the dimethyl ester (VI) of I, the reaction product of the latter with diazomethane.

Having established the structure of adamantane-2,2-dicarboxylic acid, a new starting material is available for the preparation of a variety of spiroadamantanes.

REFERENCES

1. J. Kuhnhauss and J. Teubel, *J. Prakt. Chem.* **273**, 87 (1954).
2. E.E. Royals and D.G. Turpin, *J. Am. Chem. Soc.* **76**, 5452 (1954).
3. H. Wynberg, S. Reiffers and J. Strating, *Rec. Trav. Chim.* **89**, 982 (1970).
4. P.L. Creger, *J. Am. Chem. Soc.* **89**, 2500 (1967).
5. P.E. Pfeffer and L.S. Silbert, *J. Org. Chem.* **35**, 262 (1970).
6. P.E. Pfeffer and L.S. Silbert, *Tetrahedron Letters*, **1970**, 699.
7. All new compounds gave satisfactory elemental analyses.
8. A. Franke, *Monatshefte*, **34**, 1904 (1913); T.A. Geissmann, *Org. Reactions II*, 100 (1944).
9. J. Strating, J. Scharp and H. Wynberg, *Rec. Trav. Chim.* **89**, 23 (1970).
10. K. Bowden, I.M. Heilbron, E.R.H. Jones and B.C.L. Weedon, *J. Chem. Soc.* **1946**, 43.