

THE WITTIG REACTION OF 2-ADAMANTANONE AND 1,3-DIAZA-6-ADAMANTANONE

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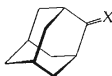
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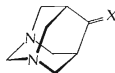
By reaction of triphenylmethylenephosphorane with the tricyclic ketones *Ib* and *IIb* have been obtained spectrographically pure exomethylene derivatives *Ia* and *IIa*, respectively. Contrasting with this, the alternative procedure based on dehydration of the tertiary alcohol *IIIa* in acid medium may afford also the isomerised product *IV* instead of the adamantoid hydrocarbon *Ia*.

In spite of its wide application in the synthetic organic chemistry, the Wittig reaction has up to recently not been applied to the carbonyl group forming part of the adamantanoid skeleton. The lately described¹ first successful reaction of triphenylmethylenephosphorane with 2-adamantone (*Ib*) stimulated us to publish this paper, in which we describe two successfully accomplished preparations of 2-methyleneadamantane (*Ia*) and 6-methylene-1,3-diazaadamantane (*IIa*).

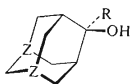
In reproducing the work according to ref.² we found that the dehydration of the 2-hydroxy derivative *IIIa* with phosphoric acid can be complicated by a not unambig-



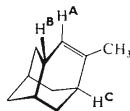
Ia, X = CH₂
Ib, X = O



IIa, X = CH₂
IIb, X = O



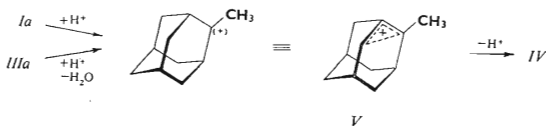
IIIa, Z = CH, R = CH₃
IIIb, Z = N, R = CH₃
IIIc, Z = N, R = H



IV

ous mechanism of water elimination from the molecule. On rapid heating with the dehydrating agent, compound *IIIa* affords the desired hydrocarbon *Ia* as the main product, but on slower heating appears in the reaction mixture the isomeric hydrocarbon *IV* which under suitable conditions becomes the predominant olefinic product.

The comparison of the 60 MHz PMR spectra of the isomers *Ia* and *IV* enabled us to suggest the structure of compound *IV*. For the exomethylene isomer *Ia* are characteristic the singlet due to the olefinic protons in the =CH₂ group at δ 4.57 and the broadened signal at δ 2.55 due to the methine protons in position 1 and 3. For the hydrocarbon *IV* with an endocyclic double bond are typical four signals, the singlet for the olefinic proton H^A at δ 5.16, the broadened multiplets for the methine protons H^B and H^C at δ 2.97 and δ 2.25 and the sharp singlet for the methyl protons at δ 1.22. In addition, both isomers *Ia* and *IV* show in the δ 2.5–1.4 region overlapping multiplets for the remaining methine and methylene protons in the molecule. Also the infrared spectra of compounds *Ia* and *IV* are consistent with their structural differences. The formation of compound *IV* may be explained by a prototropic isomerisation of the non-classical carbonium ion *V* (Scheme 1) which is facilitated by its longer presence in the reaction mixture on slower dehydration.



SCHEME 1

The mentioned complications taking place on dehydration prompted us to carry out the reaction of ketone *Ib* with triphenylmethylenephosphorane³. In the reaction mixture uniquely olefine *Ia* was always present, which could be isolated in 52% yield.

The preparation of the 6-ketone *Iib* by oxidation of the secondary alcohol *IIIc* with chromium trioxide was reported in the preliminary communication⁴. The attempts to oxidise the analogous N,N'-diacetyl-9-hydroxybispidine, described by Stetter and coworkers⁵ together with compound *IIIc*, led only to a mixture of destruction products of the carbon skeleton. In the attempted reaction of the 6-ketone *Iib* with methylmagnesium iodide we did not succeed in isolating the expected tertiary alcohol *IIIb* and could only isolate a complicated mixture of not further identified products. With ketone *Iib* the Wittig reaction could not be effected unless dimethyl sulphoxide was used as solvent. In the modified procedure⁶ in which dimethyl sulphoxide takes part in the formation of the phosphorane, the yield of the desired methylene derivative *Iia* was practically unchanged. Compound *Iia* is unstable and therefore it is better to store it in form of the hydrochloride.

EXPERIMENTAL

The temperature data are uncorrected. Melting points were determined in sealed capillaries on a Boetius micro melting point apparatus. Infrared spectra were taken on a Perkin-Elmer 325 spectrophotometer, PMR spectra on a Tesla 477 instrument (60 MHz, internal standard tetramethylsilane), and mass spectra on a LKB spectrometer 9000 (70 eV, direct insertion). Unless otherwise stated, the chromatography was carried out on alumina of activity II, and in thin-layer chromatography the detection was performed with iodine vapours.

Dehydration of the Hydroxy Derivative *IIIa*

A) Substance *IIIa* (1.04 g, m.p. 206–207°C, ref.²) in 85% phosphoric acid (10 ml) was heated at 85°C for one hour, then at 115–120°C for a further hour, and finally within 20 min the temperature was raised to 240°C. The sublimed portion as well as the reaction mixture, after diluting with water, were extracted with altogether 40 ml of ether, the combined extracts were dried over magnesium sulphate and then evaporated. The residue (820 mg) was chromatographed on a column of 50 g of alumina (using pentane as eluent), and the composition of the fractions (each of about 20 ml) was controlled by thin-layer chromatography. Fractions 3–6 afforded 620 mg of a partially crystalline olefinic substance (b.p. 90–92°C/2 Torr, m.p. 68–76°C) which, after removing the oily admixture on a porous plate, was repeatedly sublimed at a bath temperature of 125–130°C/14 Torr to give 297 mg of olefine *IV* melting at 86–88°C. For C₁₁H₁₆ (148.2) calculated: 89.12% C, 10.88% H; found: 88.82% C, 11.05% H. Mass spectrum: [M]⁺ *m/e* 148, which is different from the spectrum of the isomer *Ia*. IR spectrum (CCl₄): 3050 cm⁻¹ ν(=CH₂), 1650 cm⁻¹ ν(C=C), 1375 cm⁻¹ δ(CH₃), 848 cm⁻¹ (γ-trisubstituted C=C-H). From fractions 12–16 (using chloroform as eluent) was isolated the alcohol *IIIa* (220 mg).

B) Compound *IIIa* (1.00 g) in 85% phosphoric acid (10 ml) was heated at 180–240°C for 1 h. In an analogous manner as in the foregoing experiment, by chromatography of the reaction product (470 mg) on 75 g of alumina using light petroleum as eluent was isolated olefine *Ia* (410 mg) which, after being sublimed at 125–130°C/745 Torr had m.p. 136–137°C. Lit.² gives m.p. 135.8–136.5°C.

Wittig Reaction of the 2-Oxo Derivative *Ib*

To a suspension of triphenylmethylphosphonium bromide (5.34 g) in ether (30 ml) a solution of 16 millimol of butyl lithium in 10 ml of ether was added dropwise under nitrogen during 15 min at room temperature. After stirring for 4 h, to the solution was added dropwise substance *Ib* (800 mg) in ether (20 ml), whereupon the mixture was refluxed for 1 h and subsequently heated in an autoclave to 80–85°C (bath temperature) and decomposed with 10 ml of water. After separating the ethereal layer, the aqueous phase was extracted with altogether 30 ml of ether, the combined ethereal extracts were dried over magnesium sulphate and the solvent removed over a column. The residue was treated with light petroleum (10 ml) and the deposited triphenylphosphine oxide was collected by suction and washed with light petroleum (5 ml). After evaporating the filtrate, the residue was chromatographed in pentane on a column of 80 g of alumina. Fractions 20–40 (each fraction of about 10 ml) afforded the hydrocarbon *Ia* (410 mg; 52%), m.p. 136–137°C, whose spectral characteristics were identical with the data obtained for the dehydration product of substance *IIIa* (procedure B). For C₁₁H₁₆ (148.2) calculated: 89.12% C, 10.88% H; found: 88.99% C, 10.99% H. IR spectrum (CCl₄): 3065 cm⁻¹ ν(CH₂), doublet at 1645 and 1660 cm⁻¹ ν(C=C), 880 cm⁻¹ γ(CH₂).

1,3-Diaza-6-adamantanone (*Iib*)

A mixture of the dihydrochloride of compound *IIIc* (500 mg; ref.⁵), chromium trioxide (532 mg), and glacial acetic acid (18 ml) was stirred for 2 h at a bath temperature of 90–95°C. After cooling, the excess oxidising agent was removed by bubbling through sulphur dioxide, and the solvent was evaporated *in vacuo* at a temperature not exceeding 40°C. The oily residue was alkalisied with ammonia to pH 11–12, extracted with chloroform (100 ml) and the organic extract, after drying over magnesium sulphate, freed from solvent by distillation through a column. The residue was sublimed at 170°C/15 Torr and the sublimate (170 mg) in chloroform solution subjected to chromatography on a column of 80 g of alumina. Fractions 6–28 (each of about 15 ml) which contained as the only product a substance having an R_F value of 0.17 (thin-layer chromatography, eluent chloroform) were evaporated through a column and the residue was sublimed at 70–80°C/1 Torr to give ketone *Iib* (160 mg; 48%), m.p. 92–93°C. For $C_8H_{12}N_2O$ (152.2) calculated: 63.13% C, 7.95% H, 18.41% N; found: 63.20% C, 7.99% H, 18.30% N. PMR spectrum ($CDCl_3$): singlet at δ 4.25 (—N—CH₂—N—), AB-quartet at δ 3.51 (N—CH₂—C), singlet at δ 2.53 (C—CH—CO). IR spectrum ($CHCl_3$): 1719 cm^{-1} $\nu(C=O)$. Mass spectrum: $[M]^+$ m/e 152.

Wittig Reaction of the 6-Oxo Derivative *Iib*

A) To an ethereal solution of triphenylmethylenephosphorane (prepared from 5.34 g of triphenylmethylphosphonium bromide and 16 mmol of butyl lithium in 40 ml of ether) was added with stirring, under nitrogen, during 10 minutes ketone *Iib* (766 mg) in 10 ml of dimethyl sulphoxide, dried by distillation over calcium hydride. The reaction mixture was heated under reflux for 16 h (bath temperature 65–70°C), the deposited precipitate was then filtered off with suction, the filtrate acidified with dilute hydrochloric acid and evaporated to dryness. The residue was made alkaline by addition of 6 ml of concentrated ammonia and extracted successively with 80 ml of ether and 80 ml of chloroform. The combined organic extracts were dried over magnesium sulphate and freed from solvents by distillation through a column. The oily residue was chromatographed on a column of 300 g of alumina of activity III–IV (column height 42 cm, eluent 1% ethanol in chloroform), and the collected 50 ml-fractions were analysed by thin-layer chromatography. Fractions 6–15 contained a mixture of substances *Iia* and *Iib* and had to be chromatographed anew. Fractions 16–24 containing exclusively the 6-methylene derivative *Iia* were acidified with ethanolic hydrogen chloride solution. Evaporation *in vacuo* followed by crystallising the residue from ethanol provided the dihydrochloride of compound *Iia* (425 mg; 38%), m.p. 234–236°C. For $C_9H_{16}Cl_2N_2$ (223.2) calculated: 48.44% C, 7.23% H, 31.78% Cl, 12.55% N; found: 48.54% C, 7.15% H, 31.39% Cl, 12.47% N. The free base *Iia* liberated by treating the dihydrochloride (350 mg) with 40% aqueous sodium hydroxide (3 ml) was taken up in chloroform (20 ml). After drying over potassium carbonate, the extract was evaporated through a column and the residue sublimed at 130–135°C/14 Torr to give the methylene derivative *Iia* (110 mg) which, after repeated sublimation, had m.p. 129–131°C. Substance *Iia* is strongly basic, hygroscopic, and volatile already at room temperature, and on sublimation part of it always undergoes decomposition. For $C_9H_{14}N_2$ (150.2) calculated: 71.93% C, 9.39% H, 18.65% N; found: 71.65% C, 9.42% H, 18.60% N. Mass spectrum: $[M]^+$ m/e 150. IR spectrum (CCl_4): 3065 cm^{-1} $\nu(=CH_2)$, doublet at 1646 and 1660 cm^{-1} $\nu(C=C)$, 880 cm^{-1} $\nu(C=CH_2)$.

B) A mixture of sodium hydride (250 mg) and dimethyl sulphoxide (5 ml) was stirred under nitrogen for 1 h at 70°C, then was added during 20 min triphenylmethylphosphonium bromide (3.45 g) in dimethyl sulphoxide (10 ml), and finally the browned solution was treated dropwise with substance *Iib* (456 mg) in dimethyl sulphoxide (10 ml). The reaction mixture was heated

at 65–70°C for 16 h and, after cooling, decomposed with 10 ml of 10% hydrochloric acid. In an analogous manner as under A) was isolated the hydrochloride *Ila* (205mg; 31%), m.p. 234 to 236°C.

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