Short Communications

The Reaction of 2-Phenylbicyclo-[2.2.1]hept-2-ene with Formaldehyde and Methylammonium Chloride in Acetic Acid

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The reaction of 2-phenylbicyclo[2.2.2]hept-2-ene with formaldehyde and dimethylammonium chloride in molar ratio 1:1:1 with acetic acid as solvent has been found to give amino alcohol 1, aldehyde 2, and secondary amines 3 and 4 as the main products. Minor products in this reaction are the unsaturated tertiary amine 5, tricyclic amine 6 and tertiary amines 7 and 8. Products 1, 5 and 6 are normal aminomethylation products of an alkene (cf. Ref. 2), whereas 2, 3 and 4 are anomalous, involving a 1,5- or 1,3-hydrule shift in an intermediate step of the reaction. Amines 7 and 8 are Eschweiler methylation products of 3 and 4.

Hydride shifts in the reaction of an alkene with formaldehyde and a secondary amine have been found for bicyclo[2.2.2]hept-2-ene,\textsuperscript{9} 2,6,6-trimethylbicyclo[3.1.1]hept-2-ene,\textsuperscript{9} 6,6-dimethyl-2-methylenebicyclo[3.1.1]heptane,\textsuperscript{6} 2-methylenebicyclo[2.2.1]heptane\textsuperscript{7} and 2-methylbicyclo[2.2.1]hept-2-ene,\textsuperscript{7} in addition to 2-phenylbicyclo[2.2.1]hept-2-ene. A transannular hydride abstraction leading to an unsaturated amino ketone has been reported for the reaction of cyclodecenone with formaldehyde and monomethylamine.\textsuperscript{8} The investigation described in this paper deals with the reaction of 2-phenylbicyclo[2.2.1]hept-2-ene with formaldehyde and methylammonium chloride in acetic acid. The principal purpose was to find out which route is predominant in this case: the usual one leading to an amino alcohol, an amino alkene or an oxazine (cf. Ref. 2), or the special one associated with hydride shifts and leading to saturated amines.\textsuperscript{4}

To test the two possibilities, 2-phenylbicyclo[2.2.1]hept-2-ene was heated with paraformaldehyde and methylammonium chloride in acetic acid for 10 min. The gas chromatogram of a neutralized sample of the reaction mixture showed one main and several minor components. The main component was identified as oxazine 9 from its $^1$H NMR and mass spectra. The $^{13}$C NMR spectrum of 9, which was run after the actual structure elucidation, is in accordance with the presented formula.

The experiment was then repeated using a longer reaction time. The gas chromatographic analysis of the product mixture after several minutes again showed oxazine 9 to be the main component. After a reaction time of 1 h a second main component was found. The proportion of 9 was decreased and the proportion of the
new main component increased as the heating was continued. After 3 h, the heating was discontinued and the reaction mixture worked up. The new main component and six other basic products were separated by preparative gas chromatography. On the basis of the mass and $^1$H NMR spectral data, the structure 10 was proposed for the main product and the structures 3, 5, 6, 7, 11, and 12 for the minor basic products. To confirm the structure analysis of 10, it was converted into the tertiary amine 5 by Eschweiler-Clarke methylation.

The previously unreported, tricyclic secondary amine 11, was isolated in pure state only for mass spectral analysis. The assignment of the structure 11 was confirmed by converting the compound into the known tricyclic tertiary amine 6 via Eschweiler-Clarke methylation.

The other products isolated, the primary amine 12, secondary amine 3, and tertiary amines 5, 6, and 7, have been described most. The theoretically possible amino alcohol 13 could not be isolated from the reaction mixture. The impurity peaks in the mass spectrum of the primary amine 12 at m/e 231, 213, and 44, which are not present in the mass spectrum of the authentic 12,13 show, however, that 13 could be present in the reaction mixture. The peak m/e 231 could be the molecular ion peak, 213 could be due to loss of water and 44 could represent the CH$_2$NHCH$_3$ group of 13.

Examination of the above results shows that the principal route in the reaction of 2-phenylbicyclo[2.2.1]hept-2-ene with formaldehyde and monomethylammonium chloride in acetic acid is the usual one, leading mainly to an oxazine 9 and an unreacted amine 10. If the reaction is controlled kinetically, the faster forming 9 can be isolated as the main product; but by allowing the reaction to approach equilibrium, a proportion of it is rendered most. The proportion of these main products, the side product 11 formed in a similar way, and the methylation products 5 and 6, is about 90%. The proportion of primary amine 12 formed via a hydride shift and its methylation products 3 and 7 is only about 10%. Hence the route involving hydride shifts is only a side reaction in the aminomethylation of 2-phenylbicyclo[2.2.1]hept-2-ene with formaldehyde and methylammonium chloride. Because methyleamine could have been methylated as well under the reaction conditions used, (cf. Ref. 9) it cannot be stated conclusively that all of the secondary amine 3 and the tertiary amine 7 were formed from the primary amine 12 via methylation. Dimethylamine produced by the methylation of methyleamine would react with 2-phenylbicyclo[2.2.1]hept-2-ene and formaldehyde to form 3, as was pointed out earlier.14 The products 5 and 6 might also form, in addition to the ways presented above, from 2-phenylbicyclo[2.2.1]hept-2-ene, formaldehyde and any dimethylamine formed from methylamine.

Experimental. The mass and $^1$H NMR spectra were recorded and the gas chromatographic analyses and separations performed as described earlier.15 The $^1$C NMR spectrum of oxazine 9 was run on a Jeol FX-100 instrument.

Reaction of 2-phenylbicyclo[2.2.1]hept-2-ene with formaldehyde and methylammonium chloride. 2-Phenylbicyclo[2.2.1]hept-2-ene (20.4 g, 0.12 mol), paraformaldehyde (3.8 g, equivalent to 0.12 mol of formaldehyde) and methylammonium chloride (6.5 g, 0.10 mol) were heated in 40 ml of acetic acid for 10 min. After cooling to room temperature, the reaction mixture was poured into 400 ml of water. The unreacted starting materials and the neutral products were separated from the basic products by extraction, as described earlier.16 The neutral products, yield 12.4 g, were not examined more closely. Distillation of the basic fraction (12.4 g) twice gave as the main component (90% o) oxazine 9 (C$_7$H$_8$N$_2$O, $^1$H NMR; $^1$C NMR; 43.34), yield 7.40 g (48%), b.p. 125–127 °C/20 Pa. MS (70 eV; m/e [% rel. int.]): 243 (33, M), 171 (34), 170 (34), 142 (85), 105 (58), 77 (44), 73 (41), 58 (75), 44 (100, [CH$_3$NHCH$_3$]), 42 (47).

$^1$H NMR (60 MHz, CDCl$_3$): $^1$ 7.33 (5 H, broad s, Ph protons), 3.81 and 3.58 (2 H, AB-system of O—CH$_3$—N protons, $^J$ 7 Hz), 2.68–2.17 (5 H, m), 2.05 (3 H, s, NCH$_3$), 1.65–0.95 (6 H, broad signal).

$^1$C NMR (25.06 MHz, CDCl$_3$): 141.1, 127.9, 127.8 and 127.0 (Ph carbons), 84.6 (benzylidene carbon), 81.2 (O—CH$_3$—N), 53.7 (CH$_2$N), 49.8 (CH), 44.1 (CH), 42.9 (CH), 41.5 (CH$_2$N), 37.0 (CH$_3$), 30.6 (CH$_2$), 22.4 (CH$_3$).

The experiment was repeated as above, but with a heating time of 3 h. Distillation of the amine fraction (11.2 g) gave 7.5 g of mixture, boiling range 135–160 °C/60 Pa. The products were separated by preparative gas chromatography. The main component (60%) was N-methyl-3-phenylbicyclo[2.2.1]hept-2-ene-2-methamine (10) (C$_{15}$H$_{17}$N, mol. wt. 213.31).

MS [IP 70 eV; m/e [% rel. int.]): 213 (100, M), 198 (10, M—CH$_3$), 184 (96), 172 (61), 155 (17), 141 (17), 115 (24), 108 (24), 70 (44), 44 (49).

$^1$H NMR (60 MHz, CDCl$_3$): $^1$ 7.23 (5 H, s, Ph protons), 3.34 (2 H, s, CH$_2$N), 3.11 (2 H, broad s, bridgehead protons), 2.40 (3 H, s, CH$_3$N), 2.32–1.08 (6 H, complex signal), 0.89 (1 H, s, NH). Eschweiler-Clarke methylation of 10 gave the known tertiary amine 5.

Oxazine 9 comprised about 16% of the fraction; the other compounds separated and identified were: N-Methyl-endo-3-phenylbicyclo[2.2.1]heptane-exo-2-methamine (3, 8%), whose mass and $^1$H NMR spectra are identical with those of an authentic sample.15 N-Methyl-1-phenylbicyclo[2.2.1.0$_2^2$]heptane-7-methamine (II, 7%, C$_{15}$H$_{17}$N, mol. wt. 213.31).

MS [IP 70 eV; m/e [% rel. int.]): 213 (16, M), 198 (1, M—CH$_3$), 170 (7), 142 (8) 128 (4), 115 (4), 91 (6), 77 (3), 70 (5), 44 (100, [CH$_3$NHCH$_3$]).

The Eschweiler-Clarke methylation of 11 gave the tertiary amine 6 described below.

\[ N,N-Dimethyl-3-phenylbicyclo[2.2.1]hept-2-ene-2-methanamine (5, 3\%, C_{16}H_{21}N, \text{mol. wt. 227.33}), \] which has been described earlier.\(^1\)

MS [IP 70 eV; m/e (% rel. int.)]: 227 (75, M), 212 (28, [M - CH₃]), 198 (40), 186 (39), 155 (35), 115 (23), 91 (27), 84 (72), 67 (29), 58 (100).

\( ^1H \text{ NMR (60 MHz, CCl₄)}: \delta 7.24 (5 \text{ H, s, Ph protons}) \), 3.13 (2 \text{ H, broad s, bridgehead protons}), 2.98 (2 \text{ H, s, CH₃}), 2.20 (6 \text{ H, s, N(CH₃)₂}).

\[ N,N-Dimethyl-1-phenyltricyclo[2.2.1.0²⁶]heptane-7-methanamine (6, 3\%, C_{16}H_{21}N, \text{mol. wt. 227.33}), \] whose structure was confirmed earlier.\(^1\)

MS [IP 70 eV; m/e (% rel. int.)]: 227 (8, M), 115 (3), 91 (2), 84 (1), 77 (1), 58 (100, [(CH₃)₂NCH₃]).

\[ N,N-Dimethyl-endo-3-phenylbicyclo[2.2.1]-heptane-exo-2-methanamine (7, 2\%), \] whose \( ^1H \) NMR spectrum is identical with that reported in the literature.\(^1\)

\[ endo-3-Phenylbicyclo[2.2.1]heptane-endo-3-methanamine (12, 1\%), \] whose mass spectrum has the same peaks as that of an authentic sample.\(^1\)

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Preparation of gem-Dibromocyclopropyl Aldehydes and Acids from Conjugated Dienes

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The gem-dibromocyclopropyl unit is an alene synthetin,\(^1\) and we were interested in compounds where it is connected to a carbonyl function, particularly an aldehyde group. No useful method for the preparation of aldehydes of the general structure 1 has been described. The addition of dihalocarbenes to \( \alpha,\beta \)-unsaturated aldehydes is not a feasible reaction, but addition to the corresponding acetals takes place albeit in poor yields.\(^2\) Subsequent hydrolysis of the acetals afforded the aldehydes and the parent compound, 2,2-dibromocyclo-

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