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The Reaction of 7-Methylenebicyclo[3.3.1]nonan-3-one and Bicyclo[3.3.1]nonane-3,7-dione with Several Nucleophiles[1]

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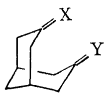
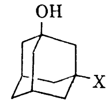
In connection with the current interest in bicyclo[3.3.1]nonane system,[2–4] we had occasion to examine the behavior of some nucleophiles towards 7-methylenebicyclo[3.3.1]nonan-3-one (Ia) as well as bicyclo[3.3.1]nonane-3,7-dione (Ib), reactions of which led to some novel products.

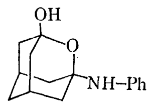
In the following reactions, transannular cyclization took place giving *adamantane* derivatives. In the reaction of Ia with aniline, Schiff's base (Ic) was not formed, but 3-phenylaminoadamantan-1-ol (IIa) was obtained as the sole isolable product in a 90% yield.



I



II



III

a: X=O; Y=CH_2
b: X=Y=O
c: X=Ph-N; Y=CH_2
d: X=Y=Ph-N
e: X=O; Y=Ph-N

a: X=Ph-NH
b: X=Ph-NMe
c: X=Ph-O
d: X=Ph-S

By the similar treatment of Ia with *N*-methylaniline, 3-*N*-methylphenylaminoadamantan-1-ol (IIb) was obtained in a 56% yield. The Eschweiler-Clarke methylation[5] of IIa afforded IIb; thus, a structural correlation between IIa and IIb was established. *N*,*N*-Dimethylaniline did not react with Ia under the reaction conditions. With phenol, Ia afforded 3-phenyloxyadamantan-1-ol (IIb) in a 38% yield, with thiophenol 3-phenylthioadamantan-1-ol (IId) in a 53% yield. The structures of these compounds were all supported by the spectral data. The transannular reaction described herein did not take place without molecular sieves. Stetter has pointed out that Ia cyclizes under acid

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[1] Part of this work was presented at the 24th Annual Meeting of the Chemical Society of Japan, Osaka, April, 1971.

[2] For pertinent references, see G. Buchanan, "Topics in Carbocyclic Chemistry," D. Lloyd, ed., Vol. 1, Logos Press, London, p. 236; H. Kato, *J. Synth. Org. Chem. Japan*, **28**, 682 (1970).

[3] a) H. Stetter, J. Gartner, and P. Tacke, *Chem. Ber.*, **98**, 3888 (1965), b) H. Stetter and J. Gartner, *Chem. Ber.*, **99**, 925 (1966), c) H. Stetter, J. Gartner, and P. Tacke, *Chem. Ber.*, **99**, 1435 (1969), d) A. R. Gagneux and R. Meier, *Tetrahedron Lett.*, **1969**, 1365, e) K. Kimoto and M. Kawanisi, *Chem. Ind.* (London) **1971**, 1174.

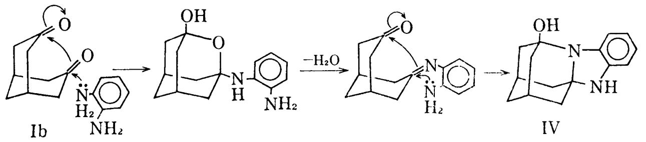
[4] a) T. Mori, K. Kimoto, M. Kawanisi, and H. Nozaki, *Tetrahedron Lett.*, **1969**, 3653, b) A. G. Yurchenko, A. T. Voroschenko, and F. N. Stepanov, *Zh. Org. Khim.*, **6**, 189, (1970). T. Mori, K. H. Yang, K. Kimoto, and H. Nozaki, *Tetrahedron Lett.*, **1970**, 2419.

[5] M. L. Moore, *Org. React.*, **5**, 301 (1949).

catalysis,[3d] and in the present case the molecular sieves probably act as an acidic catalyst.[6]

In the reaction of Ib with aniline, an *oxaadamantane* derivative, 3-phenylamino-2-oxaadamantan-1-ol (III), was formed as a labile product in a 28% yield. The structure of III was supported by its spectral data. The prolonged heating of Ib under the same conditions produced another product (Id) at the expense of III; this was confirmed by following the progress of the reaction by means of glc. We also observed that III was converted into Id by the reaction with aniline in the presence of molecular sieves. These observations suggest that III, a metastable hemiacetal, is dehydrated by the action of molecular sieves into an intermediate such as Ie, which subsequently condenses with aniline to give Id.

In the similar reaction of Ib with *o*-phenylenediamine, an intriguing cyclization took place to give IV, an *azaadamantane* derivative, in an 81% yield as a considerably unstable compound. The structure of IV could be assigned on the basis of the physical data. The NMR spectra, however, were not reproducible because of the instability of IV in solution. The formation of IV can be tentatively explained by the following scheme:



Experimental

All the melting points are uncorrected. The microanalyses were performed by Mrs. Kiyoko Fujimoto. The IR spectra were obtained on a Shimadzu IR-27 spectrophotometer. The mass spectra were taken using a Hitachi RMS-4 mass spectrometer. The NMR spectra were obtained on a JEOL C-60-H spectrometer in a $CDCl_3$ solution, with TMS as the internal standard.

Reagents. 7-Methylenebicyclo[3.3.1]nonan-3-one (Ia)[3d] and bicyclo[3.3.1]nonan-3,7-dione (Ib)[4b] were prepared according to the reported methods. The aniline, *N*-methylaniline, phenol, thiophenol, and *o*-phenylenediamine were of commercial reagent grade. The molecular sieves was of Type 3A.

Preparation IIa. A mixture of Ia (0.9 g), aniline (0.69 g), and molecular sieves (2 g) in benzene (20 ml) was refluxed for 26 hr, and then the molecular sieves were removed by filtration. The evaporation of the solvent yielded 1.69 g of a brown oil which gradually solidified. Recrystallization from benzene gave 1.43 g (90%) of pure IIa; mp 115—118°C. Found: C, 78.87; H, 8.64; N, 5.92%. Calcd for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76%. IR (KBr): 3300, 3280, 2920, 1600, 1495, 1320, 1125, 1050, 910, 770, 740, 695 cm^{-1}. NMR: δ 1.33—1.93 (m, 12H), 2.27 (br. s, 2H), 2.73 (s, 2H), 6.67—7.33 (m, 5H). MS: *m/e* 243 (M^+), 93 (M^+—150: 100%).

Preparation of IIb. A mixture of Ia (0.9 g) *N*-methylaniline (0.65 g), and molecular sieves (2 g) in benzene (20 ml) was treated similarly; a subsequent work-up as described above gave a white solid (0.86 g; 56%). Recrystallization from petroleum ether (bp 40—60°C) yielded pure IIb; mp 114.5—116.5°C. Found: C, 79.08; H, 8.85; N, 5.45%. Calcd for $C_{17}H_{23}NO$: C, 79.33; H, 9.01; N, 5.44%. IR (KBr): 3240, 2920, 1595, 1490, 1445, 1305, 1260, 1100, 1010, 940, 800, 770, 695 cm^{-1}. NMR: δ 1.35—1.70 (m, 12H), 2.25 (br. s, 3H), 2.76 (s, 3H), 7.27 (s, 5H). MS: *m/e* 257 (M^+), 107 (M^+—150; 100%).

Methylation of IIa. A mixture of IIa (12 mg), formaldehyde (37%; 2 ml), and formic acid (99%; 1.5 ml) was heated under reflux for 24 hr. The base liberated by the addition of potassium hydroxide was extracted with ether and chloroform. The extracts were combined and dried (Na_2SO_4). Evaporation left a white solid, the sublimation of which gave pure IIb (58 mg; 88%); mp 115—117°C.

Reaction Ia with Phenol and Thiophenol. The similar reaction of Ia with phenol and with thiophenol afforded IIc (38%) and IId (53%) respectively. Analytical samples were obtained by preparative glc. The physical data of IIc and IId are as follows.

IIc; IR (KBr): 3370, 2950, 1595, 1495, 1115, 1030, 1010, 995, 675 cm^{-1}. NMR: δ 1.27—2.50 (m, 15H), 6.83—7.43 (m, 5H). MS: *m/e* 244 (M^+), 94 (M^+—150; 100%). mp 94—96°C. Found: C, 77.54; H, 8.27%. Calcd for $C_{16}H_{20}O_2$: C, 77.65; H, 8.25%. IId; IR (KBr): 3300, 2920, 1470, 1350, 1100, 1090, 975, 935, 750, 690 cm^{-1}. NMR: δ 1.43—1.90 (m, 12H), 2.03 (s, 1H), 2.23 (br. s, 2H), 7.40 (br. s, 5H). MS: *m/e* 260 (M^+), 151 (M^+—109; 100%). mp 131—133°C. Found: C, 73.67; H, 7.53%. Calcd for $C_{16}H_{20}OS$: C, 73.80; H, 7.74%.

Preparation of III. A mixture of Ib (618 mg), aniline (1.6 g), and molecular sieves (10 g) in benzene (15 ml) was refluxed for 6 hr. The usual work-up yielded a brown oil which solidified afterward. Recrystallizations from benzene gave a white solid (280 mg; 28%). This compound is exceedingly unstable and did not give satisfactory analysis. Mp 81.5—82.5°C. IR (KBr): 3300, 3260, 1605, 1500, 1340, 1190, 1155, 970, 930, 885, 745, 695, 680 cm^{-1}. NMR: δ 1.96—2.95 (m, 12H), 3.44 (s, 2H), 6.55—7.42 (m, 5H). MS: *m/e* 227 (M^+—18), 152 (M^+—93), 95 (M^+—150). The reaction of III and aniline in the presence of molecular sieves in benzene was effected similarly; the formation of Id described below was confirmed by glc.

Preparation of Id. A mixture of Ib (2 g), aniline (3.7 g), and molecular sieves (50 g) in benzene (30 ml) was refluxed for 28 hr. The usual work-up gave a brown oil, which immediately solidified. The solid was washed with ether and recrystallized from benzene, thus yielding pure Id (2 g; 51%); mp 190—191°C. Found: C, 83.28; H, 7.52; N, 9.11%. Calcd for $C_{21}H_{22}N_2$: C, 83.40; H, 7.33; N, 9.26%. IR (KBr): 3060, 2950, 1660, 1595, 1490, 1245, 1185, 1070, 905, 830, 785, 705 cm^{-1}. NMR: δ 1.80—2.85 (m, 14H), 6.70—7.45 (m, 10H). MS: *m/e* 302 (M^+), 170 (M^+ 132), 77 (M^+—225; 100%).

Preparation of IV. A mixture of Ib (110 mg), *o*-phenylenediamine (80 mg), and molecular sieves (2 g) in benzene (3 ml) was refluxed for 2 hr; the catalysts were then removed by filtration while the solution was hot. On cooling, colorless needles were obtained; these were collected by filtration and washed with chilled benzene. The azaadamantane derivative (IV) (141 mg; 81%) was obtained after drying *in vacuo*; mp 191—193.5°C (in nitrogen-sealed tube). Found: C, 74.67; H, 7.73; N, 11.46%. Calcd for $C_{15}H_{18}N_2O$: C, 74.35; H, 7.49; N, 11.56%. IR (KBr): 3390, 3290, 2930, 1594, 1489, 1295, 1145, 1085, 730 cm^{-1}. MS: *m/e* 242 (M^+), 132 (M^+—110; 100%).

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[6] For catalysis by molecular sieves in enamine formation, see K. Taguchi and F. H. Westheimer, *J. Org. Chem.*, **36**, 1570 (1971).