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FIRST EXAMPLE OF THE TRANSFORMATION OF AZINIUM RINGS TO FORM HYDROGENATED CYCLIC KETONES

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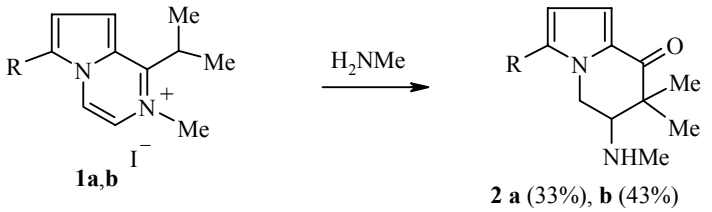
Azacycles capable of isomerization recyclization have certain structural features, including the presence of a methylene group on the six-membered aromatic ring in the α-position to the nitrogen atom. Aromatic carbocycles and heterocycles are the products of such rearrangements [1]. In studying the nucleophilic rearrangement of hetarenes containing a methine group in that position, we unexpectedly observed formation of hydrogenated cyclic ketones.

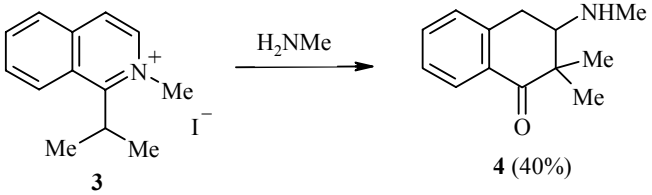
Quaternary 1-isopropylpyrrolo[1,2-*a*]pyrazinium salts **1a,b**, when heated up to 140°C with an alcoholic solution of methylamine, are rearranged to form 5,6,7,8-tetrahydroindolizin-8-ones **2a,b** containing a methylamino group in the 6 position of the indolizine ring.



1a,**b** **2 a** (33%), **b** (43%)

1, **2 a** R = H, **b** R = Me

This rearrangement is a general one, and is also realized in the case of isoquinolinium salts with an isopropyl substituent in the 1 position. Thus 1-isopropylisoquinolinium iodomethylate (**3**) under analogous conditions is converted to 2,2-dimethyl-3-methylamino-α-tetralone (**4**).



3 **4** (40%)

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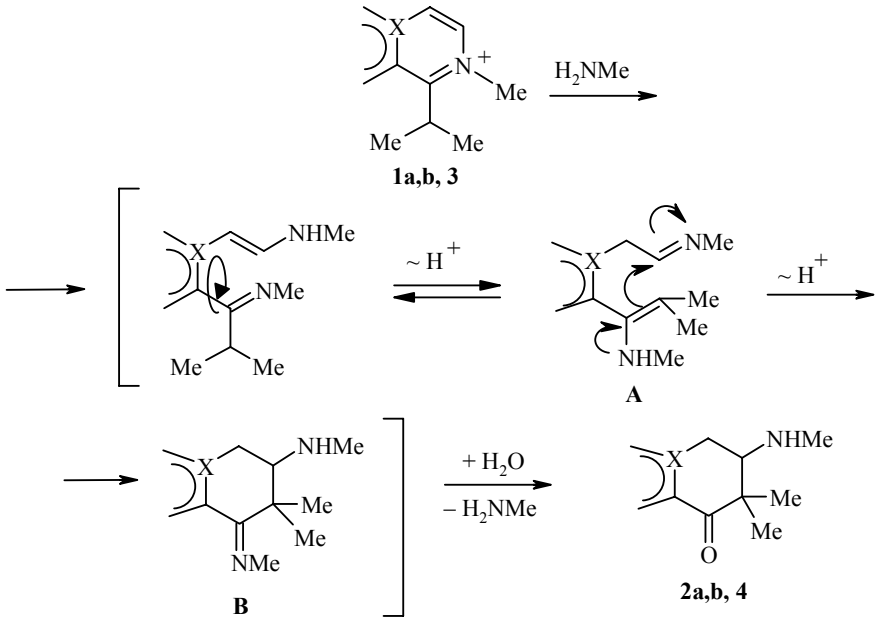
Such a ring transformation obviously goes through several steps. Attack of the nucleophile at the carbon atom α to the quaternary nitrogen atom leads to opening of the heterocyclic ring and formation of intermediate **A**. As a result of attack by the β-position of the enamine moiety on the imine carbon atom of this intermediate, the cyclic imine **B** is formed which then is hydrolyzed to form the hydrogenated cyclic ketone. Since the α-methine group contains only one hydrogen atom, aromatization is not possible and recyclization ends in formation of the hydrogenated compound.



An important competing process is nucleophilic dealkylation of the starting salts **1a,b, 3** to form the corresponding bases, the yield of which can be as high as 20%.

The ^{1}H NMR spectra were recorded on a Varian VXR-400 spectrometer (400 MHz) in $CDCl_3$ at 28°C, internal standard TMS. The mass spectra were recorded on a Kratos MS-90 with electron impact ionization energy 70 eV. The IR spectra were obtained on a UR-20 spectrometer in CCl_4. The course of the reaction and the purity of the compounds were monitored using TLC on Alufol plates in the systems benzene, benzene–ethyl acetate 1:1, visualization in iodine vapors and with an alcoholic ninhydrin solution.

General Procedure for Obtaining Compounds 2a,b, 4. A mixture of the quaternary salt **1a,b, 3** (1 mmol) and a 40% alcoholic solution of methylamine (4-5 ml) was heated for 8 h up to 140°C in a sealed glass ampul. Then the mixture was evaporated under vacuum and the reaction products were isolated using column chromatography on neutral aluminum oxide (standard Brockmann activity I) in benzene.

7,7-Dimethyl-6-methylamino-5,6,7,8-tetrahydroindolizinone (2a). IR spectrum, ν, cm^{-1}: 3340 (NH), 1653 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.98 (1H, dd, J_{12} = 4.1, J_{13} = 1.5, H-1); 6.81 (1H, dd, J_{32} = 2.2, J_{31} = 1.5, H-3); 6.26 (1H, dd, J_{21} = 4.1, J_{23} = 2.2, H-2); 4.32 (1H, dd, J_{5a5b} = 12.9, J_{5a6} = 3.8, H_a-5); 4.05 (1H, dd, J_{5b5a} = 12.9, J_{5b6} = 6.9, H_b-5); 2.96 (1H, dd, J_{65b} = 6.9, J_{5a6} = 3.8, H-6); 2.51 (3H, s, NH$\underline{CH_3}$); 1.31 (3H, s, 7-CH_3); 1.21 (3H, s, 7-CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 192 $[M]^+$ (18), 149 (27), 107 (53), 94 (33), 98 (100), 57 (48), 42 (57).

3,7,7-Trimethyl-6-methylamino-5,6,7,8-tetrahydroindolizinone (2b). IR spectrum, ν, cm^{-1}: 3350 (NH), 1675 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.95 (1H, d, J_{12} = 3.7, H-1); 6.04 (1H, d, J_{21} = 3.7, H-2); 4.12 (1H, dd, J_{5a5b} = 13.1, J_{5a6} = 3.8, H_a-5); 3.80 (1H, dd, J_{5b5a} = 13.1, J_{5b6} = 6.8, H_b-5); 2.93 (1H, dd, J_{65b} = 6.8,

J_{65a} = 3.8, H-6); 2.51 (3H, s, NH$\underline{CH_3}$); 2.28 (3H, s, CH_3(3)); 1.29 (3H, s, 7-CH_3); 1.18 (3H, s, 7-CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 206 $[M]^+$ (42), 121 (33), 108 (53), 98 (100), 93 (49), 80 (42), 58 (57), 42 (49), 40 (36).

2,2-Dimethyl-3-methylamino-α-tetralone (4). IR spectrum, ν, cm^{-1}: 3370 (NH), 1680 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.02 (1H, dd, J_{98} = 7.8, J_{97} = 1.2, H-9), 7.46 (1H, td, J_{76} = J_{78} = 7.8, J_{79} = 1.2, H-7); 7.30 (1H, t, J_{87} = J_{89} = 7.8, H-8); 7.23 (1H, d, J_{67} = 7.8, H-6); 3.24 (1H, dd, J_{4a4b} = 16.8, J_{4a3} = 3.7, H_a-4); 2.90 (1H, dd, J_{4b4a} = 16.8, J_{4b3} = 7.2, H_b-4); 2.85 (1H, dd, J_{34b} = 7.2, J_{34a} = 3.7, H-3); 2.47 (3H, s, NH$\underline{CH_3}$); 1.28 (3H, s, 2-CH_3); 1.17 (3H, s, 2-CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 203 $[M]^+$ (55), 160 (100), 145 (32), 118 (33), 91 (27), 70 (31), 59 (41), 39 (43).

REFERENCES

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