Communications to the Editor

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Novel Rearrangement of Pyrazole N-Imines with Acetic Anhydride

2-Amino-1,3-dimethylindazolium mesitylenesulfonate (I) was allowed to react with a large excess of acetic anhydride in the presence of anhydrous sodium acetate to give the unexpected rearrangement products, 3-acetoxymethyl-1-methylindazole (IV), 3-acetylaminomethyl-1-methylindazole (V) and the deaminated product, 1,3-dimethylindazole(II), and the desired product, pyrazolo[2,3-*b*]indazole derivative(III), could not be obtained. Likewise, the same reactions of 2-amino-1,3,5-trimethylpyrazolium mesitylenesulfonate(VII) and 2-amino-1,3,4,5-tetramethylpyrazolium mesitylenesulfonate(VIII) gave the rearrangement products, 5-acetoxymethyl-1,3-dimethylpyrazole(IX) and 5-acetoxymethyl-1,3,4-trimethylpyrazole(X), respectively. This is the first example of a rearrangement reaction of aromatic amine N-imine with acid anhydride. The desired product(III) was obtained by the reaction of 2-amino-1-methylindazolium mesitylenesulfonate(XIV) with acetylacetone in the presence of triethylamine, followed by oxidation with lead tetraacetate.

It is well known that aromatic amine N-oxides react with acid anhydrides to yield rearrangement products.[1] On the other hand, as we previously reported,[2] the reaction of aromatic amine N-imines, isoelectronic with aromatic N-oxides, with acid anhydrides resulted in the formation of N-acylated N-imines or cyclized products and did not give any rearrangement products. This cyclization reaction was successfully utilized for the syntheses of nitrogen-bridged heteroaromatics such as pyrazoloazines[2a,b] and pyrazoloazoles.[2c,d] In the course of an extention of this cyclization method to the syntheses of pyrazoloisoazoles from isoazole N-imines, we have found that a novel rearrangement occurs when pyrazole N-imines are allowed to react with acetic anhydride.

In this paper, we report the first example of a rearrangement reaction of aromatic amine N-imine with acid anhydride. The N-amino compound, 2-amino-1,3-dimethylindazolium mesitylenesulfonate (I), mp 205°, prepared by the reaction of 1,3-dimethylindazole (II) with O-mesitylenesulfonylhydroxylamine, was heated with a large excess of acetic anhydride and anhydrous sodium acetate by refluxing for 12 hours. The expected cyclization product, pyrazolo[2,3-*b*]-indazole derivative (III), was not obtained, but rearrangement products, IV (68.6%) colorless oil, $C_{11}H_{12}O_2N_2$, *m/e*: 204 (M^+), IR ν_{max}^{liq} cm^{-1}: 1744, 1224 (-COO-), NMR ($CDCl_3$) δ: 2.08 (3H, s, $C\underline{H}_3CO$-), 4.04 (3H, s, N-$C\underline{H}_3$), 5.44 (2H, s, -$C\underline{H}_2O$-), 7.15—7.50 (3H, m), 7.60—7.85 (1H, m), V (10.5%), mp 152—153° colorless needles, $C_{11}H_{13}ON_3$, *m/e*: 203 (M^+), IR ν_{max}^{KBr} cm^{-1}: 3295 (NH), 1638 (CO), NMR ($CDCl_3$) δ: 2.03 (3H, s, $C\underline{H}_3CO$-), 3.99 (3H, s, N-$C\underline{H}_3$), 4.75 (2H, d, J=5 Hz, -$C\underline{H}_2NH$), 6.30 (1H, broad s, D_2O exchangeable, N$\underline{H}$), 7.15—7.50 (3H, m), 7.60—7.85 (1H, m), and the deaminated product II (9.1%) were isolated. The compound (IV)[3] was easily hydrolyzed by heating with 18% hydrochloric acid to afford the corresponding alcohol (VI), colorless oil, $C_9H_{10}ON_2$, *m/e*: 162 (M^+), IR ν_{max}^{liq} cm^{-1}: 3320 (OH), NMR ($CDCl_3$) δ: 3.90 (3H, s, N-$C\underline{H}_3$), 5.00 (2H, s, -$C\underline{H}_2OH$), 3.34 (1H, broad s, D_2O exchangeable, -$CH_2O\underline{H}$), 7.15—7.40 (3H, m), 7.65—7.85 (1H, m).

1) *a*) E. Ochiai, "Aromatic Amine Oxides," Elsevier Publishing Co., Amsterdam, 1967, p. 290; *b*) A.R. Katritzky and J.M. Lagowski, "Chemistry of the Heterocyclic N-Oxides," Academic Press, London and New York, 1971, p. 353.

2) *a*) M. Hirobe, Y. Minamoto, and T. Okamoto, Abstracts of Papers, the 90th Annual Meeting of Pharmaceutical Society of Japan, Sapporo, August, 1970, p. II-47; *b*) K. Kasuga, M. Hirobe, and T. Okamoto, *Chem. Pharm. Bull.* (Tokyo), **22**, 1814 (1974); *c*) H. Koga, M. Hirobe, and T. Okamoto, *Chem. Pharm. Bull.* (Tokyo), **22**, 482 (1974); *d*) H. Koga, M. Hirobe and T. Okamoto, Abstracts of Papers, The 94th Annual Meeting of Pharmaceutical Society of Japan, Sendai, April, 1974, p. II-141.

3) M.A. Kazanbieva, B.A. Tertov, and F.T. Pozharskii, *Khim. Geterotsikl. Soedin., Akad. Nauk Latv. SSR*, **1965**, 125 [*Chem. Abstr.*, **63**, 4272 (1965)].

Likewise, the same reaction of VII (mp 175°) or VIII (mp 214°), obtained by the reaction of 1,3,5-trimethyl- or 1,3,4,5-tetramethylpyrazole with O-mesitylenesulfonylhydroxylamine, gave the rearrangement product (IX) (65.5%) or (X) (76.9%). The products (IX and X) were also easily hydrolyzed to the corresponding alcohols XI (66.7%) and XII (71.4%) respectively, when heated with 18% hydrochloric acid. The structure of XI was confirmed by comparison with the alcohol, obtained by the reduction of 1,3-dimethyl-5-ethoxycarbonylpyrazole (XIII)[4] with lithium aluminum hydride. Therefore, the structure of IX was established to be 5-acetoxymethyl-1,3-dimethylpyrazole. The structure of X and XII was assumed to be 5-acetoxymethyl-1,3,4-trimethylpyrazole and its corresponding alcohol by comparing their spectral properties[5] with those of IX and XI.

The cleavage reaction of nitrogen bond of pyrazole N-imine derivative was also found in the reaction of 2-amino-1-methylindazolium mesitylenesulfonate (XIV) with dimethyl acetylenedicarboxylate (DAC). The quaternary salt (XIV), mp 198° (decomp.), which was obtained by treating 1-methylindazole with O-mesitylenesulfonylhydroxylamine, was allowed to react with DAC in the presence of potassium carbonate in N,N-dimethylformamide (DMF) to give 2-aminofumaric acid dimethylester (XV) in 27% yield. The structure of XV was confirmed by comparison of its IR and NMR spectra with those of an authentic sample.[6] On the other hand, the reaction of XIV with acetylacetone in the presence of triethylamine in DMF at room temperature for a long while, afforded a cyclized product XVI (mp 72—75°),

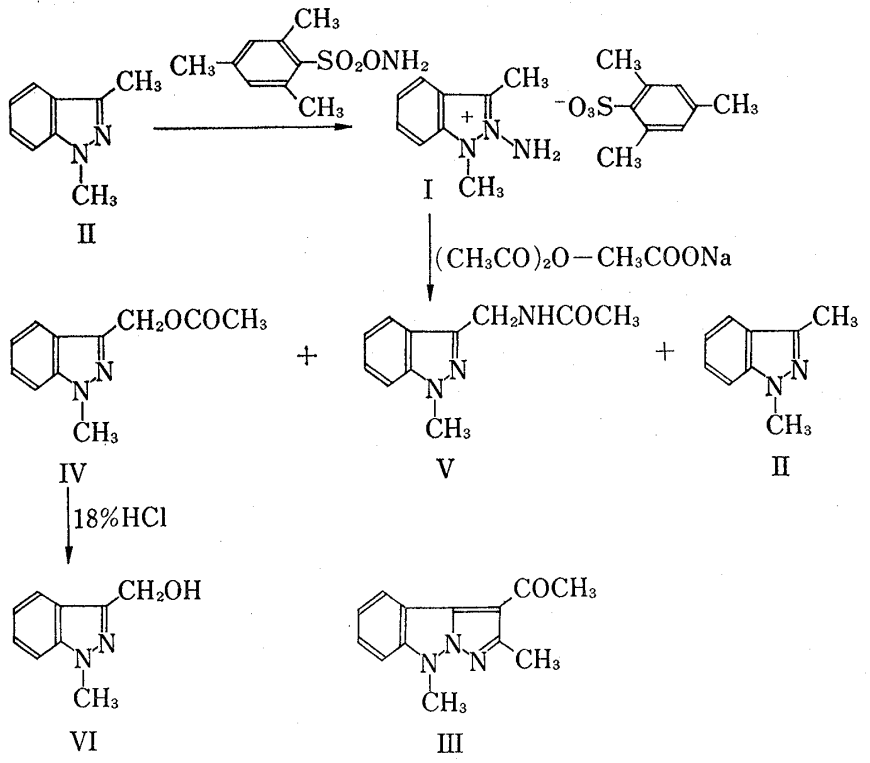
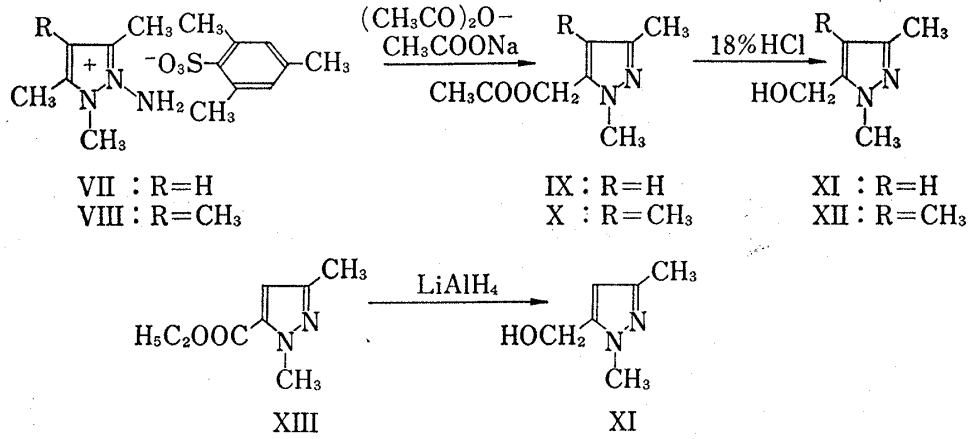


Chart 1

4) J. Elguero, R. Jacquier, G. Tarrago, and H.C.N. Tien Duc, *Bull. Soc. Chim. France*, **1966**, 293.

5) IX: colorless oil, $C_8H_{12}O_2N_2$, *m/e* 168 (M^+), IR ν_{max}^{liq} cm^{-1}: 1746, 1228 (-COO-), NMR ($CDCl_3$) δ: 2.07 (3H, s, $C\underline{H}_3CO$), 2.21 (3H, s, 3-$C\underline{H}_3$), 3.81 (3H, s, $NC\underline{H}_3$), 5.03 (2H, s, -$C\underline{H}_2O$-), 6.05 (1H, s, 4-H). X: colorless oil, $C_9H_{14}O_2N_2$, *m/e* 182(M^+), IR ν_{max}^{liq} cm^{-1}: 1745, 1228 (-COO-), NMR ($CDCl_3$) δ: 2.04 (3H, s, $C\underline{H}_3CO$), 2.14 (3H, s, 3-CH_3), 3.77 (3H, s, $NC\underline{H}_3$), 5.02 (2H, s, -$C\underline{H}_2O$-), 1.97 (3H, s, 4-$C\underline{H}_3$). XI: colorless oil, $C_6H_{10}ON_2$, *m/e* 126 (M^+), IR ν_{max}^{liq} cm^{-1}: 3250 (OH), NMR ($CDCl_3$) δ: 2.16 (3H, s, 3-$C\underline{H}_3$), 3.75 (3H, s, $NC\underline{H}_3$), 4.53 (2H, s, -$C\underline{H}_2OH$), 5.90 (1H, s, 4-H), 3.30 (1H, broad s, D_2O exchangeable, O$\underline{H}$), XII: mp 106°, $C_7H_{12}ON_2$, *m/e* 140 (M^+), IR ν_{max}^{KBr} cm^{-1}: 3210 (OH), NMR ($CDCl_3$) δ: 2.11 (3H, s, 3-$C\underline{H}_3$), 3.67 (3H, s, $NC\underline{H}_3$), 4.48 (2H, s, -$C\underline{H}_2OH$), 1.90 (3H, s, 4-CH_3), 3.20 (1H, broad s, D_2O exchangeable, OH).

6) R. Huisgen, K. Herbig, A. Siegel, and H.Huber, *Chem. Ber.*, **99**, 2526 (1966).



VII : R=H
VIII : R=CH3

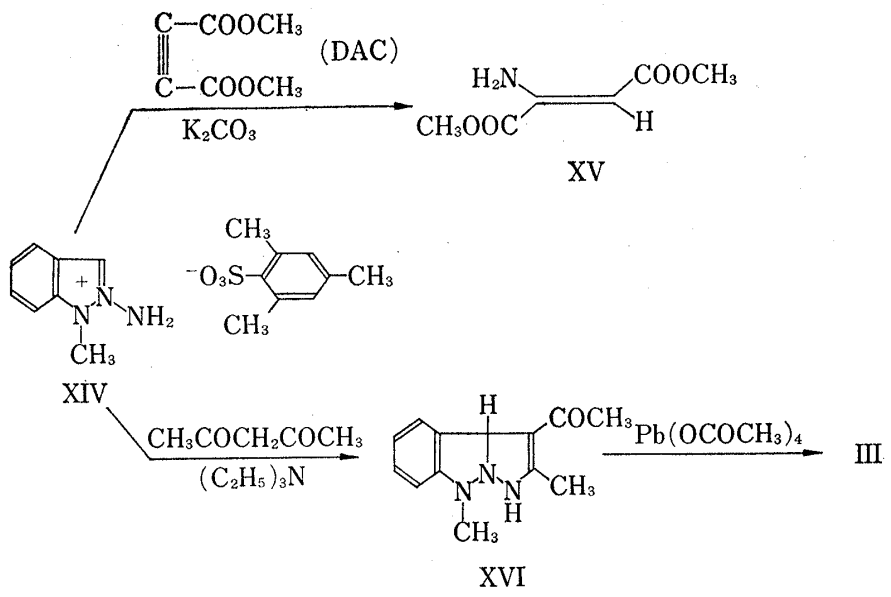
IX : R=H
X : R=CH3

XI : R=H
XII : R=CH3

XIII

XI

Chart 2



XV

XIV

XVI

III

Chart 3

in 30.1% yield, which was oxidized with lead tetraacetate to give the desired product (III) in 13.3% yield, mp 127—128°, IR ν_{max}^{KBr} cm^{-1}: 1620 (CO), NMR ($CDCl_3$) δ: 2.56, 2.72 (3H, each, s, $C\underline{H}_3$), 3.82 (3H, s, $NC\underline{H}_3$), 7.20—7.90 (4H, m), $C_{13}H_{13}ON_3$, *m/e* 227 (M^+).

Such a rearrangement reaction of aromatic amine N-imines would serve to elucidate the mechanism of the rearrangement of aromatic amine N-oxides with acid anhydride which has not exactly been clarified to date.[1a,b] Details of the mechanism of these reactions will be reported in connection with that of the reaction in N-oxides.

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