Communications to the Editor

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A New Rearrangement of 3-Diazoaminoisoxazoles[*1]

In the course of our works on isoxazole series, a new rearrangement of 3-diazoaminoisoxazoles (IIa, IIb) to 2-substituted-5-acetonyltetrazoles (IIIa, IIIb) has been encountered.

Diazotization of 3-amino-5-methylisoxazole (I) with sodium nitrite in hydrochloric acid resulted in formation of 1,3-bis(5-methyl-3-isoxazolyl)triazene (IIa), pale yellow crystals, m.p.[*2] 145~146°(from EtOH); UV λ_{max}^{EtOH} mμ (log ε) : 291 (4.25)(*Anal.* Calcd. for $C_8H_9O_2N_5$: C, 46.37; H, 4.38; N, 33.80. Found : C, 46.35; H, 4.61; N, 33.75). The same kind of abnormal diazotization was reported by Quilico1) on 3-aminoisoxazole. Reaction of *p*-nitrobenzenediazonium chloride with equimolar amount of (I) in hydrochloric acid yielded 3-(*p*-nitrophenyldiazoamino)-5-methylisoxazole (IIb) as pale yellow needles, m.p. 169~171°(from Me_2CO); UV λ_{max}^{EtOH} mμ (log ε) : 286 (4.26)(*Anal.* Calcd. for $C_{10}H_9O_3N_5$: C, 48.58; H, 3.65; N, 28.33. Found : C, 48.22; H, 3.71; N, 28.22).

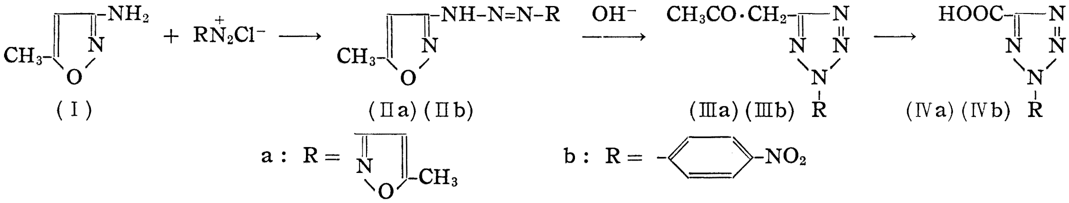

Chart 1.

These diazoaminoisoxazoles (IIa, IIb) were dissolved in warm dilute sodium hydroxide or ammonia to produce the tetrazole derivatives in excellent yield respectively; i. e. 2-(5-methyl-3-isoxazolyl)-5-acetonyltetrazole (IIIa), colorless plates, m.p. 147~149° (decomp.)(from ACOEt); UV λ_{max}^{EtOH} mμ (log ε) : 237 (4.08)(*Anal.* Calcd. for $C_8H_9O_2N_5$: C, 46.37; H, 4.38; N, 33.80. Found : C, 46.64; H, 4.66; N, 33.78) and 2-(*p*-nitrophenyl)-5-acetonyltetrazole (IIIb), colorless plates, m.p. 132~134°(from AcOEt); UV λ_{max}^{EtOH} mμ (log ε) : 285 (4.28)(*Anal.* Calcd. for $C_{10}H_9O_3N_5$: C, 48.58; H, 3.65; N, 28.33. Found : C, 48.76; H, 3.94; N, 28.08). In their infrared spectra, (IIIa) and (IIIb) exhibited a characteristic band due to carbonyl group at 1728 cm^{-1} and 1730 cm^{-1} ($CHCl_3$) respectively and (IIIa) showed isoxazole ring stretching bands2) at 1617 cm^{-1}, 1483 cm^{-1} and 1413 cm^{-1} ($CHCl_3$). On the other hand, these isoxazole ring bands are missing in the spectrum of (IIIb).

On the basis of these studies, 2-substituted-5-acetonyltetrazole structures for (IIIa) and (IIIb) were proposed. To establish these structures, (IIIa, IIIb) were oxidized with potassium permanganate in boiling acetone-water to yield the corresponding 2-substituted 5-tetrazolecarboxylic acid; i. e. 2-(5-methyl-3-isoxazolyl)-5-tetrazolecarboxylic acid (IVa), colorless crystals, m.p. 158°(decomp.)(from H_2O); UV λ_{max}^{EtOH} mμ (log ε) : 236 (4.10)(*Anal.* Calcd. for $C_6H_5O_3N_5$: C, 36.93; H, 2.58; N, 35.89. Found: C, 36.86; H, 2.83; N, 36.06) and 2-(*p*-nitrophenyl)-5-tetrazolecarboxylic acid (IVb), colorless needles, m.p. 172~174°(decomp.)(from H_2O-Me_2CO); UV λ_{max}^{EtOH} mμ (log ε) : 285.5 (4.29)(*Anal.* Calcd. for

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[*1] "Studies on Isoxazole Derivatives. XIII." Part XII. Hideo Kano, Yasuo Makisumi, Kazuko Ogata : This Bulletin, **6**, 105 (1958).

[*2] Melting points were determined on Kofler-Block "Monoscope IV" and are uncorrected.

1) A. Quilico : Gazz. Chim. Ital., **61**, 670 (1931) (C. A., **26**, 2972(1932)).

2) A. R. Katritzky, A. J. Boulton : Spectrochim. Acta, **17**, 238 (1961); *Idem* : Tetrahedron, **12**, 41 (1961).

$C_8H_5O_4N_5$: C, 40.86; H, 2.14; N, 29.78. Found : C, 40.89; H, 2.36; N, 29.40). During this oxidation, liberation of acetic acid could be observed. Definitive proof concerning the structure was obtained by the identity of (IVb) with an authentic sample synthesized by Bladin's[3] procedure in their melting points, infrared and ultraviolet[4] spectra.

The conversion of (IIa, IIb) to (IIIa, IIIb) probably follows a mechanism, in which attack of base on acidic amine attached to 3-position of isoxazole induces cleavage of the N-O bond in the isoxazole ring, with subsequent rearrangement of the cleaved intermediate to tetrazole caused by the shift of conjugated double bonds.

The detailed studies of this investigation will be reported in the near future.

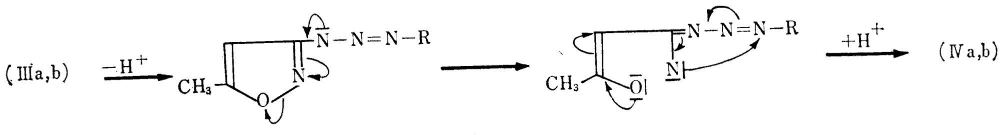

Chart 2.

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Research Laboratory,
Shionogi & Co., Ltd.,
Fukushima-ku, Osaka.

Hideo Kano (加納日出夫)
Eiko Yamazaki (山崎 瑛子)

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[3] J.A. Bladin : Chem. Ber., **25**, 1411 (1892).

[4] R. Huisgen, H.J. Koch : Ann. **591**, 200 (1955).