

THE REACTION OF CARBONYL-STABILIZED SULFUR YLIDES WITH
NITRILE IMINES; A FACILE PREPARATION OF PYRAZOLES

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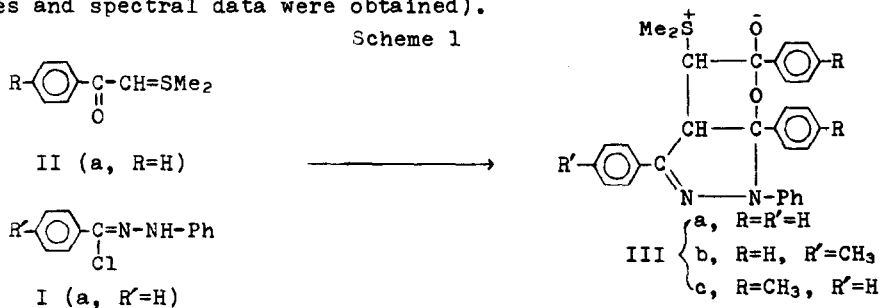
(Received in Japan 23 December 1968; received in UK for publication 22 January 1969)

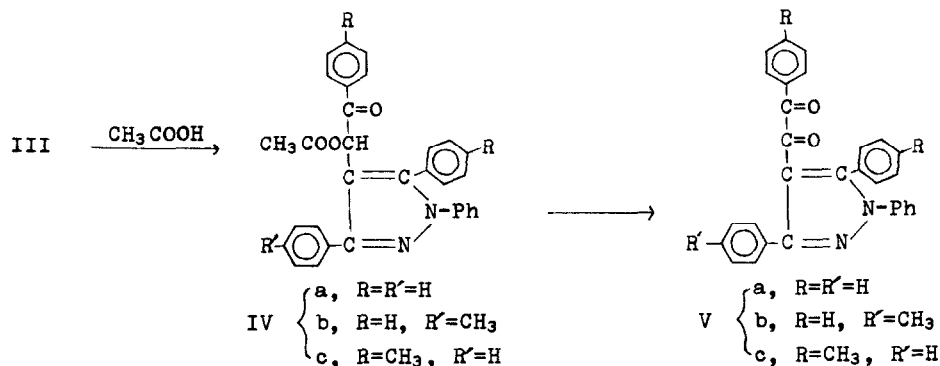
Recent publications concerned with resonance-stabilized sulfonium ylides have covered their preparation, but relatively few of their chemical reactions have been described.

1,3-Dipoles are useful starting materials for the synthesis of heterocycles. In a recent note¹⁾, the result of the reaction between nitrile imine and dimethyloxosulfonium methylide was reported. The latter ylide was shown to cause consecutive transfer of two methylene groups to the former, giving rise to a pyrazoline. The reaction of phosphorus ylides with nitrile oxides gave interesting products²⁾.

We investigated the reaction of carbonyl-stabilized sulfur ylides with nitrile imines by mixing a cold benzene solution of sulfur ylides with N-(α -chlorobenzylidene)-N'-phenylhydrazine, a precursor of nitrile imine. The sulfur ylides acted as bases to generate the nitrile imine and the sulfonium chloride precipitated quantitatively.

The results are summarized in Scheme 1 and Table 1 (satisfactory elemental analyses and spectral data were obtained).



Table 1 Melting point ($^{\circ}\text{C}$) of the products

	a	b	c
III(dec.)	158-159	157-159	147-148
IV	137-139	152-153	170-172
V	155-157	123-124	155-157

The reaction between Ia and IIa is described as the representative.

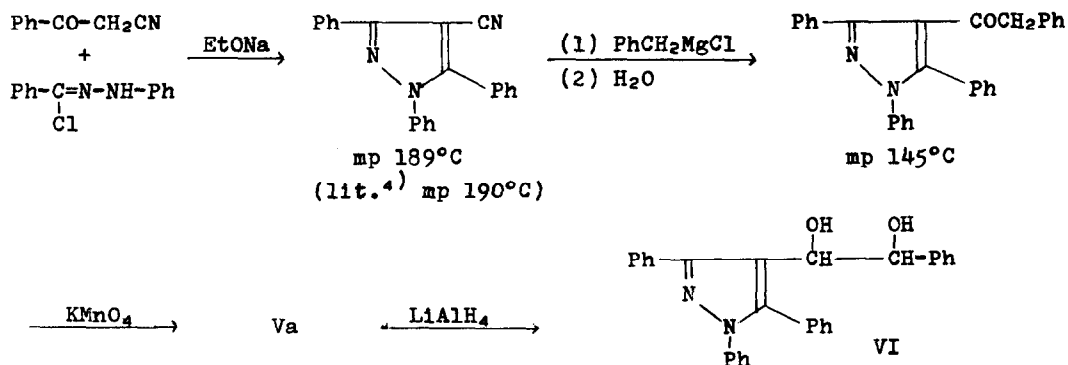
The precipitate from the reaction mixture was washed with warm water to leave a pale pink almost pure product (IIIa). Recrystallization of the product from ethylenedichloride gave an analytical sample; IR (nujol), no C=O, N-H and OH stretching; anal., $\text{C}_{21}\text{H}_{28}\text{N}_2\text{O}_2\text{S}$; 95% yield based on Ia. Definitely clear NMR spectra of IIIa were not available as solubility of IIIa in common solvents was very small and IIIa was not stable at high temperatures.

IIIa is soluble in acetic acid developing red color which fades away within a day at room temperature. A product (IVa, quantitative yield) was isolated from this colorless solution and dimethyl sulfide (as mercuric chloride complex, 70% yield) was also obtained from the volatile portion of the solution. These reactions were traced by NMR in perdeuteroacetic acid. NMR spectrum of the red solution showed, COOH at τ -1.22 (singlet, 2H), ArH at τ 2.2-2.9 (multiplet, 20H), SCH₃ at τ 6.91 and τ 7.12 (two 3H singlets). Two singlets at τ 6.91 and τ 7.12 disappeared gradually and new singlet at τ 7.97 (CH₃SCH₃) appeared. The rate of appearance of the new singlet was first order (k is about $5 \times 10^{-5}\text{sec}^{-1}$ at 24°C).

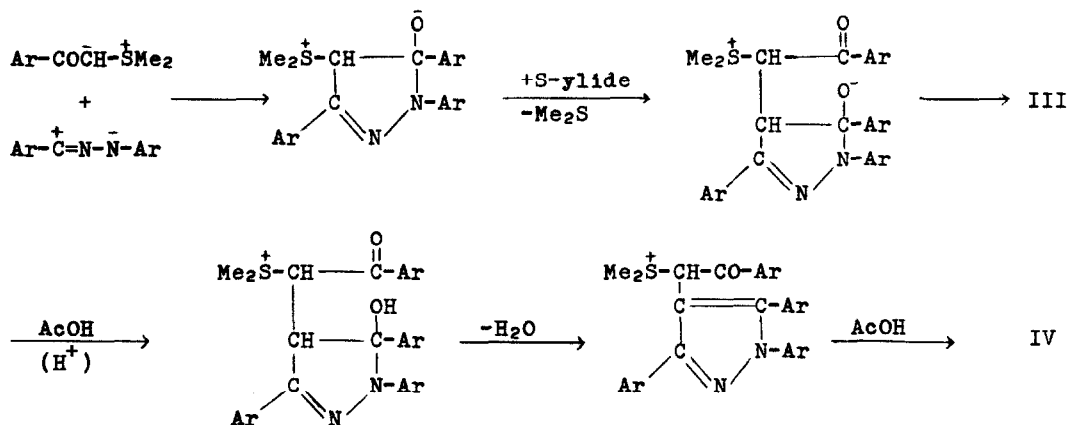
Recrystallization of IVa from ethanol gave an analytical sample; IR (nujol), $\nu_{C=O}$ 1740, 1705 cm^{-1} ; NMR(CDCl_3), ArH at τ 2.2-3.0 (multiplet, 20H), $-\text{CH}$ at τ 3.05 (singlet, 1H), COCH_3 at τ 7.71 (singlet, 3H); anal., $\text{C}_{31}\text{H}_{24}\text{N}_2\text{O}_3$ (MW, calcd.: 472.5, found: 456). Hydrolysis of IVa in ethanolic potassium hydroxide solution gave a pale yellow product (Va, 90% yield); IR (nujol), $\nu_{C=O}$ 1685, 1650 cm^{-1} ; NMR(CDCl_3), ArH at τ 2.10-2.90 (multiplet); anal., $\text{C}_{29}\text{H}_{20}\text{N}_2\text{O}_2$. Va is stable in concentrated sulfuric acid and to permanganate oxidation, hydrogen peroxide oxidation in acetic acid (the reaction conditions of oxidation of benzils³). Lithium aluminum hydride reduction of Va gave a glycol (VI); mp 157°C; NMR(CDCl_3), ArH at τ 1.45-2.2, 2.4-2.9 (multiplet, 20H), $-\text{CH}$ at τ 5.23 and τ 5.45 (two doublets, 2H, $J_{\text{H-H}} = 8$ cps), OH at τ 8.11 (singlet, 2H); anal., $\text{C}_{29}\text{H}_{24}\text{N}_2\text{O}_2$.

The structure of Va was shown to be benzoyl [1,3,5-triphenylpyrazolyl-(4)] ketone by its failure to depress the melting point of an authentic specimen prepared as described in Scheme 2.

Scheme 2

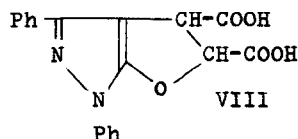
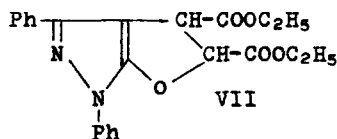


The structural assignment of IV seems reasonable from the results mentioned above and facile oxidation of benzoin⁵). The structure of III is not yet substantiated, but some tentative conclusions about the mechanism of these reactions can be drawn as described below.



These mechanisms suggest the resemblance to the reaction of the sodium derivatives of active methylene compounds with α -halohydrazone, an economical and practical method of pyrazole synthesis⁶⁾ (see Scheme 2).

The reaction of ethyl (dimethylsulfuranylidene)acetate with Ia gave VII (mp 120-122°C) and hydrolysis of VII gave a dibasic acid (VIII, mp 210°C), while the reaction of carbethoxymethylene triphenylphosphorane with Ia gave 1 : 1 reaction product⁷⁾.



Further studies of these reactions are in progress and more complete details will be reported later.

References

- 1). G.Gaudiano, A.Umani-Ronchi, P.Bravo, M.Acampora, Tetrahedron Letters, 107 (1967).
- 2). H.J.Bestmann, R.Kunstmann, Angew. Chem., 78, 1059 (1966)
- 3). J.E.Leffler, J. Org. Chem., 16, 1785 (1951)
- 4). R.Fusco, R.Justoni, Gazz. Chim. Ital., 67, 3 (1937).
- 5). H.Klinger, Ber., 19, 1868 (1886).
- 6). T.L.Jacobs, "Heterocyclic Compounds", R.C.Elderfield, Ed., Chapman and Hall LTD., New York, Vol. 5, p87 (1957).
- 7). Hayashi, Oda, unpublished result.