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Unusual reactions of enhydrazinopyrazolones and dipyrazolylmethanes with 5-oxopyrazoles

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The reaction of 6-phenyl-1,2,4-triazine-4-oxide **1** with pyrazolones **2a**–**d** gives enhydrazino-derivatives **3a**–**d**. On heating with pyrazolones **2**, products **3** are transformed into the corresponding symmetrical **4** or unsymmetrical derivatives **5** of dipyrazolylmethane. Heating of dipyrazolylmethane derivatives **4** with pyrazolones **2** results in the substitution of some pyrazolone residues for others.

We have previously shown that CH acids react with 3,6-diphenyl-1,2,4-triazin-4-oxide in the presence of bases to form products of substitution at the H-5 atom of the triazine ring.[1] Under similar conditions, 6-phenyl-1,2,4-triazine-4-oxide reacts with CH acids with cleavage of the triazine ring *via* the C(3)–N(4) bond and formation of the corresponding hydrazino derivatives.[2]

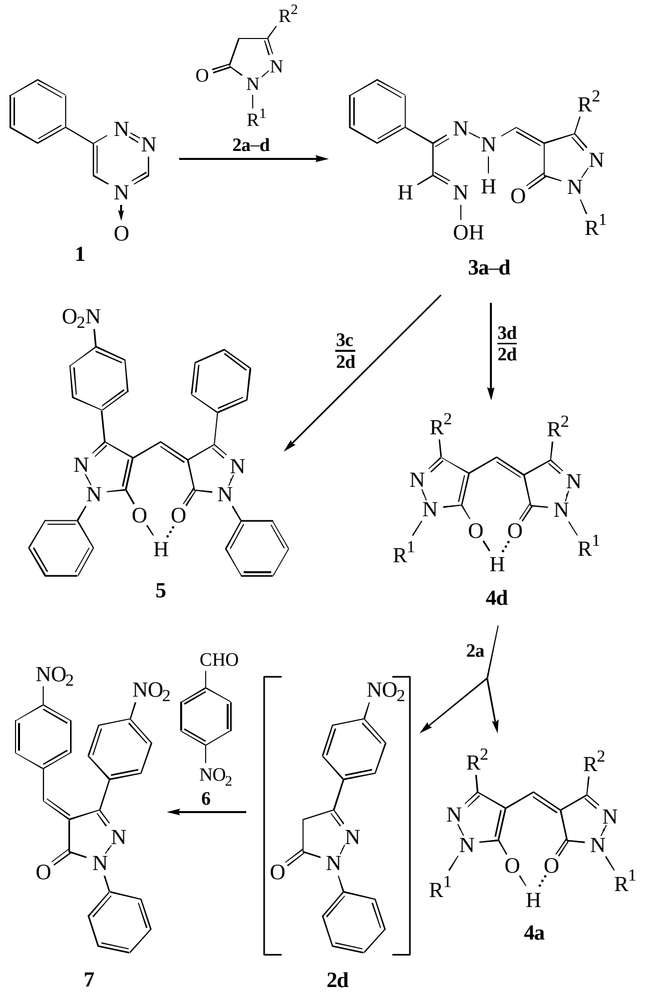
In the present work we have found that 6-phenyl-1,2,4-triazine-4-oxide **1** reacts with pyrazolones **2a**–**d** on heating in butanol in the absence of bases to form hydrazino derivatives **3a**–**d**.[†]

The structure of products **3** was confirmed by ^{1}H NMR spectroscopy. The ^{1}H NMR spectrum of these compounds contains proton signals in accordance with the structure suggested. For example, the aromatic proton signals for compound **3b** are observed in the region of 7.45–7.90 (5H, $\mathrm{CH_{arom}}$) and 8.2–8.4 ppm (4H, $\mathrm{CH_{arom}}$, $\mathrm{R^1}$) (Figure 1). The H-6 enhydrazine group proton is observed at 8.55, and the H-10 phenylglyoxal fragment proton is observed at 8.46 ppm.

The signals in the ^{13}C NMR spectrum of compound **3b** were assigned based on the data for the model enhydrazines described previously.[2]

When hydrazino derivative **3d** was heated with pyrazolone **2d**, the corresponding symmetrical derivative of dipyrazolylmethane **4d** was isolated.[‡] Previously, we obtained a similar derivative of dipyrazolylmethane **4a** by the reaction of 5-methyl-6-phenyl-1,2,4-triazin-4-oxide with pyrazolone **2a** in the presence of triethylamine. It has been established by X-ray diffraction that a molecule of **4a** is symmetrical relative to the axis passing through the C(1) and H bonding atoms. The central H-bonded eight-membered ring is characterized by a coplanar arrangement of non-hydrogen atoms. The hydrogen atom is located in the middle of the distance between the oxygen atoms of the pyrazole fragments.[2]

We obtained the unsymmetrical derivative of dipyrazoline **5**[§] by heating enhydrazine **3c** with pyrazolone **2d**. The weight of compound **5** determined by mass spectrometry corresponds to that calculated for the structure suggested. Evidently, the formation of product **5** is caused by substitution of the hydrazine residue of the molecule of compound **3c**.



a $\mathrm{R^1 = Ph, R^2 = Me}$
b $\mathrm{R^1} = p\text{-}\mathrm{NO_2C_6H_4}, \mathrm{R^2 = Me}$
c $\mathrm{R^1 = R^2 = Ph}$
d $\mathrm{R^1 = Ph}, \mathrm{R^2} = p\text{-}\mathrm{NO_2C_6H_4}$

Scheme 1

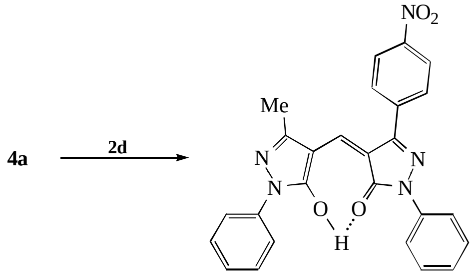
It is of interest that the dipyrazolylmethane derivative **4a** is formed in 50–55% yield when another symmetrical derivative **4d** is heated with pyrazolone **2a**.[¶] The *p*-nitrophenylidene derivative of pyrazolone **7** was obtained after separation of **4a**

[†] *Preparation of enhydrazines* **3a**–**d**. 6-Phenyl-1,2,4-oxide **1** (0.5 mmol) was heated with the corresponding pyrazolone **2** (0.05 mmol) in boiling butanol (3 ml) for 2 h. The reaction mixture was cooled, and product **3** was filtered off and recrystallized from aqueous dimethylformamide. Compound **3a**, mp 103–104 °C, was obtained in 8–10% yield; **3b**, mp 215–216 °C, 25–30% yield; **3c**, mp 126–127 °C, 30–35% yield; mp 122–123 °C, 45–50% yield.

For **3b**: ^{1}H NMR ([^{2}H$_6$]DMSO) δ: 2.28 (s, 3H, Me), 7.45–7.50 (m, 3H, H-14,15,16), 7.80–7.85 (m, 2H, H-13,17), 8.25–8.35 (m, 4H, H-19,20,22,23), 8.46 (s, 1H, H-10), 8.55 (s, 1H, H-6), 12.8 and 13.8 (br. s, 1H, OH and NH). ^{13}C NMR ([^{2}H$_6$]DMSO) δ: 12.62 (Me), 101.26 (C-4), 116.72 (C-18,23), 124.92 (C-20,22), 126.86 (C-13,17), 128.62 (C-14,16), 130.03 (C-15), 135.11 (C-18), 142.32 (C-3), 143.82 (C-9), 143.92 (C-10), 149.58 (C-6), 151.24 (C-21), 164.37 (C-5).

[‡] *Preparation of compound* **4d**. Enhydrazine **3d** (0.045 g, 0.1 mmol) was heated in boiling butanol (3 ml) with 1-*p*-nitrophenyl-3-methyl-5-oxopyrazole **2d** (0.1 mmol) for 5 h. The reaction mixture was cooled to room temperature, and the precipitate that formed was filtered off and recrystallized from dimethylformamide. Product **4d** with mp 279–280 °C was obtained in 9% yield (0.005 g). MS, *m*/*z*: 572 (M$^+$, calc. for $\mathrm{C_{31}H_{20}N_6O_6}$: 572).

[§] *Preparation of compound* **5**. Compound **3c** (0.082 g, 0.2 mmol) was refluxed in butanol (5 ml) with pyrazolone **2d** (0.056 g, 0.2 mmol) for 5 h. The reaction mixture was cooled, and the precipitate that formed was filtered off. Product **5** with mp 222–223 °C was obtained in 8% yield (0.008 g). MS, *m*/*z*: 527 (M$^+$, calc. for $\mathrm{C_{31}H_{21}N_5O_4}$: 527).



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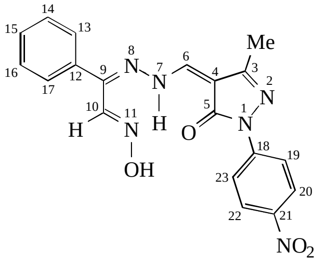
Scheme 2

and treatment of the mother liquor of the reaction mixture with *p*-nitrobenzaldehyde **6**. This indicates that the residue of pyrazolone **2a** is displaced in the unchanged form from the molecule of **4d** (Scheme 1).

It is noteworthy that under similar conditions, derivative **4a** reacts with a two-fold excess of pyrazolone **2d** to form only a minor quantity of unsymmerical derivative **8** (Scheme 2).[††]

The observed *trans*-substitutions of the pyrazole residues in the derivatives of dipyrazolylmethane **4** evidently occur through the stages of formation of intermediate adducts: tripyrazolylmethane derivatives of type **A**, which are cleaved to form new dipyrazolylmethanes **4** and to displace pyrazolones **2**. The stages of addition of pyrazolones to the double bond are similar to the Michael reactions. However, unlike the latter, the reactions observed occur in the absence of base catalysis (Scheme 3).



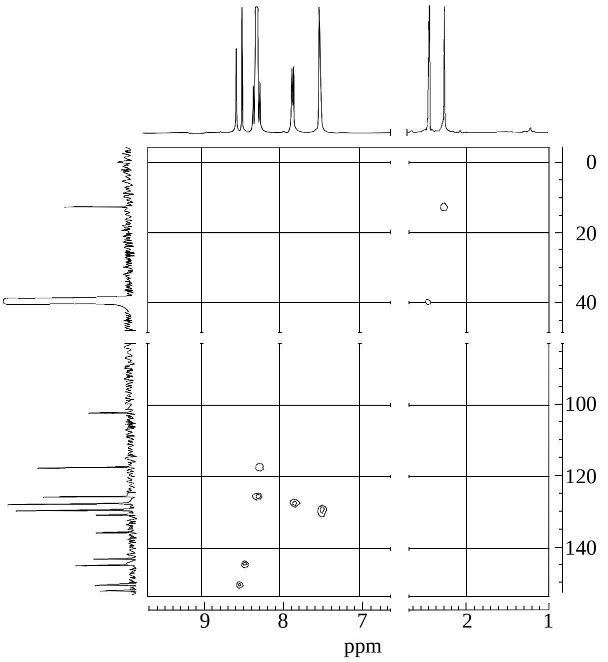
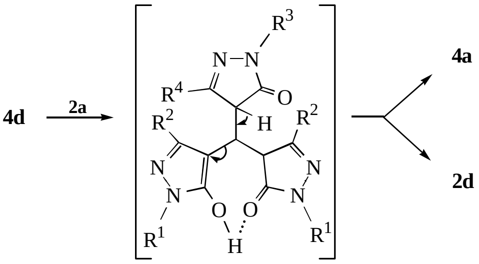


Figure 1 CH-correlation for **3b**.



A

Scheme 3

By and large, the transformations observed can be considered as a component of the multi-stage transformations of 1,2,4-triazine-4-oxide derivatives with CH acids, which is of interest for understanding their possible mechanisms.

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¶ *Reaction of compound* **4d** *with pyrazolone* **2a**. Compound **4d** (0.12 g, 0.2 mmol) was refluxed with pyrazolone **2a** (0.075 g, 0.4 mmol) in butanol (3 ml) for 6 h. The reaction mixture was cooled, and the precipitate of **4a** that formed was filtered off to obtain 0.04 g (53%). *p*-Nitrobenzaldehyde (0.075 g, 0.5 mmol) was added to the mother liquor of the reaction mixture, and the mixture was heated at the boiling temperature for 5 min. The reaction mixture was cooled to room temperature, and the precipitate of **7** that formed was filtered off to obtain compound **7** with mp 252–253 °C in 28% yield (0.05 g). MS, *m*/*z*: 414 (M^+, calc. for $C_{22}H_{14}N_4O_5$: 414).

[††] *Reaction of compound* **4a** *with pyrazolone* **2d**. Compound **4a** (0.094 g, 0.26 mmol) was boiled in butanol (3 ml) with pyrazolone **2d** (0.147 g, 0.52 mmol) for 7 h. The reaction mixture was cooled, and the precipitate of **8** that formed was filtered off to obtain compound **8** in 11% yield (0.014 g), mp 245–247 °C. MS, *m*/*z*: 465 (M^+, calc. for $C_{26}H_{19}N_5O_4$: 465). The mother liquor of the reaction mixture was diluted with water (1:1), and the precipitate of the starting compound **4a** was filtered off to obtain 0.034 g (36.4%).