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A route to pyrazolylazopyrazolo[4,3-*c*]pyrazoles *via* 1,5-dimethyl-3R-pyrazolyl-4-diazonium salts

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1,5-Dimethyl-3R-pyrazolyl-4-diazonium salts (R = H, C≡C–Ph) have been converted into the corresponding 6-(1,5-dimethyl-3R-pyrazol-4-yl)azo-1-methyl-3R-4*H*-pyrazolo[4,3-*c*]pyrazoles 6a,b and it has been shown that the reaction proceeds *via* 1-methyl-5-(1,5-dimethyl-3R-pyrazolyl-4-azo)methyl-3R-pyrazolyl-4-diazonium chlorides 4a,b.

Our studies[1,2] of the thermal cyclization of vicinal alkynylaryl- and heteroaryldiazonium salts have altered current opinion on the use of Richter's reaction as a method of synthesising only 4-hydroxycinnolines.[3] A new understanding of the reaction mechanism has allowed us to establish the role of temperature, the nature of substituents and hydrohalogenic acid and to synthesise not only 4-hydroxy-, but also 4-chloro- and 4-bromo-cinnolines. Moreover, the diazotization of 5-amino-1,3-dimethyl-4-phenylethynylpyrazole and subsequent cyclization have revealed no 4-hydroxypyrazolodiazine.[2]

To clarify the reasons for the 'abnormal' behaviour of pyrazole derivative in Richter's reaction we used isomeric 4-amino-1,5-dimethyl-3-phenylethynylpyrazole **1a**. The electrophilicity of the diazo group and the nucleophilicity of a triple bond depend markedly on their position in the pyrazole ring, and this can affect both the course and ease of cyclization and even the feasibility of the entire reaction scheme.

We have established that an acetylene derivative of a diazonium salt is stable and cannot be cyclized under the usual Richter's reaction conditions to give the corresponding 4-chloro(4-hydroxy)diazine **3a**, heterocyclization of which requires boiling in ethanol in the presence of base (Et_3N). A surprising result of this reaction is the formation of 6-(1,5-dimethyl-3-phenylethynylpyrazol-4-yl)azo-1-methyl-3R-4*H*-pyrazolo[4,3-*c*]pyrazole **6a**. There are two possible ways of preparing product **6a** in sizeable quantities. The first is *via* intermolecular interaction of two molecules of diazonium chloride **2a** with subsequent intramolecular heterocyclization of azo-compound in **6a**. The second is *via* intramolecular cyclization of diazonium salt **2a** with subsequent azo-coupling of the resulting bipyrazole **5a** with initial diazonium salt **2a**. The latter route proved to be correct (although under different conditions), involving cyclization of mesoionic compound 4-diazo-3,5-dimethylpyrazole as an example, *i.e.* in the absence of acetylene substituent.[4]

To isolate possible intermediate (**4a** or **5a**), the reaction mixture was neutralised by $NaHCO_3$ at 5–10 °C after diazotization. The reaction product, according to IR and analytical data, corresponded to 1-methyl-5-(1,5-dimethyl-3-phenylethynylpyrazolyl-4-azo)methyl-3-phenylethynylpyrazolyl-4-diazonium chloride **4a** (yield 93%) which confirm that the reaction follows the former route. Note that diazonium salt **4a** is not cyclized by heating in a boiling water bath for 0.5 h.

This is the first known case in which a diazo group does not add to the vicinal acetylene group but interacts with another substituent under the Richter reaction conditions. To verify that this route is of a more general character, and to exclude the possible appearance of acetylene substituent, we performed similar transformations using 4-amino-1,5-dimethylpyrazole **1b**. As before, under mild conditions a similar intermediate **4b** (86%) was isolated.† Diazonium salts **4a**,**b** can be easily converted into the corresponding condensed pyrazolo[4,3-*c*]pyrazoles **6a** (54%) and **6b** (69%) by boiling in ethanol in the presence of base.‡

All novel compounds were characterised and gave NMR, IR spectroscopic and microanalytical data in accordance with the assigned structures.§

Thus, diazotization of 4-amino-1,5-dimethyl-3R-pyrazoles can give either azodiazonium salts or the corresponding pyrazolo[4,3-*c*]pyrazoles.

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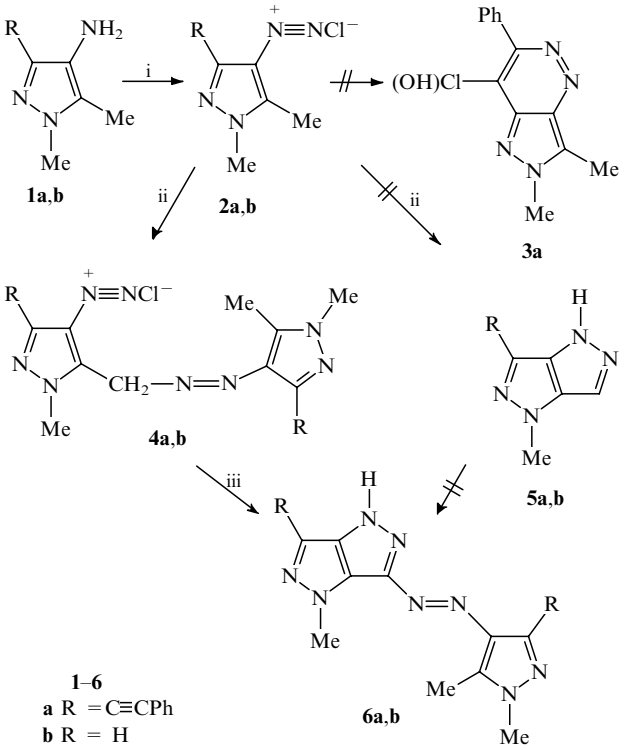

Scheme 1 *Reagents and conditions*: i, $NaNO_2$/HCl; ii, $NaHCO_3$; iii, Et_3N/EtOH.

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† In a typical experiment, 5 mmol of **1a**,**b** was added to 10 ml of cooled hydrochloric acid, then 4 ml of 15% (by weight) of aqueous $NaNO_2$ was added dropwise with stirring at −10 °C. The solution was neutralized with $NaHCO_3$ and stirred at room temperature for 14 h. The resulting solid was filtered and recrystallized from EtOH to give diazonium salt **4a**,**b** (mp could not be determined owing to the thermocyclization of **4a**,**b** to **6a**,**b**).

‡ 2.5 mmol of diazonium salt **4a**,**b** and 10 ml Et_3N in 100 ml EtOH were boiled until the salt dissolved, after which the mixture was concentrated, diluted with 30 ml of ether and the precipitate was filtered and chromatographed on an Al_2O_3 (neutral) column with $CHCl_3$ as the eluent. After evaporation of the solvent from the eluate the remaining solid was crystallized from C_6H_6–$CHCl_3$ to give 6-azopyrazolo[4,3-*c*]pyrazole **6a** (mp 246–247 °C), **6b** (mp 265–266 °C).

§ Examples of IR and ^{1}H NMR spectra are given below. **4a**: IR ν/cm^{-1} (0.25% KBr) 2230 (C ≡ C), 2340 (N$^+$ ≡ N). **6a** IR (0.25% KBr) 2230 (C ≡ C), 3400 (NH). ^{1}H NMR (δ, $CDCl_3$) 2.66 (c, 3H, 5-CH_3), 3.88 (c, 3H, N–CH_3), 4.45 (c, 3H, N–CH_3), 7.38 (m, 6H, Ph), 7.55 (m, 4H, Ph). **4b**: IR (0.25% KBr) 2300 (N$^+$ ≡ N). **6b** IR (0.25% KBr) 3400 (NH). ^{1}H NMR (δ, $CDCl_3$) 2.60 (c, 3H, 5-CH_3), 3.85 (c, 3H, N–CH_3), 4.26 (c, 3H, N–CH_3), 7.39 (c, 1H, 3-H), 7.94 (c, 1H, 3-H).

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