Synthesis of Several New Pyrazolo[5,1-*c*][1,2,4]triazoles, Imidazo[1,2-*b*]-pyrazoles, and Pyrazolo[3,4-*b*]pyrazines. Reaction of Nitrilimines with Amino- and Oxo-substituted Azoles. II

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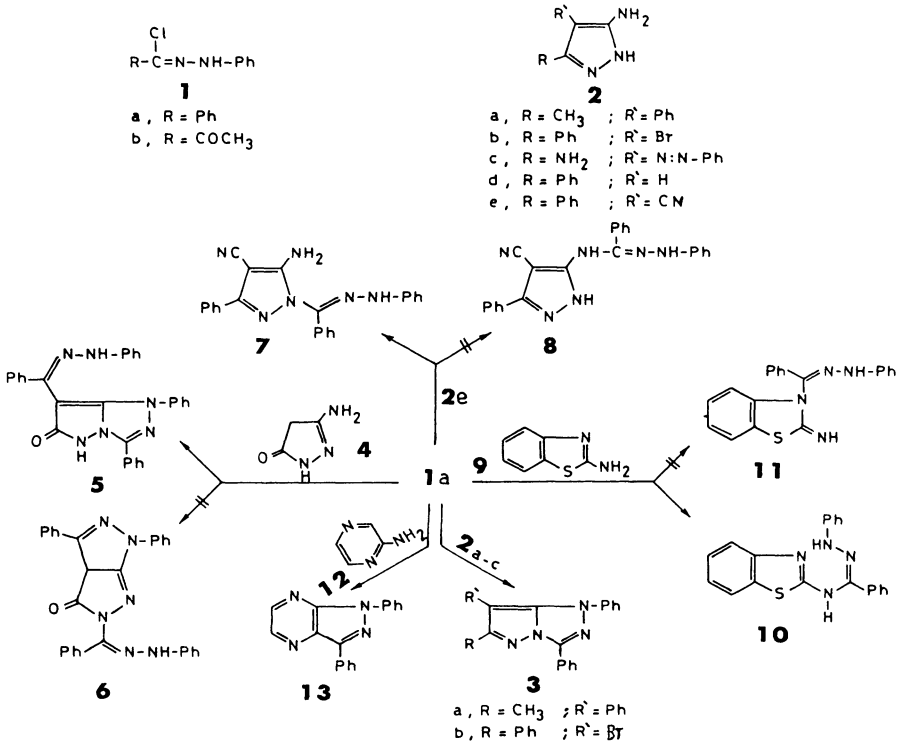
The reactivity of amino and hydroxy azoles toward nitrilimines and hydrazonoyl halides was investigated. Several novel rotes for synthesis of derivatives of known heterocyclic systems are reported.

Nitrilimines, usually synthesised *in situ* by base-catalysed elimination of halogeno acid from hydrazonoyl halides, are reactive intermediates that have found extensive use in heterocyclic syntheses.[1] Recently we reported that these reactive intermediates react readily with amino and oxo diazoles, thus, enabling preparation of a variety of new, otherwise difficult to obtain, fused azole derivatives.[2,3] We have been interested to see if reactions of this type can be utilized to constitute a general route to fused azoles. In the present paper we reported the results of our investigation on the reactivity of *N*-phenylbenzohydrazonoyl chloride (**1a**) and *N*-phenylpyruvohydrazonoyl chloride (**1b**) toward a variety of amino and oxo azoles in order to define the exact behaviour of **1a,b** toward this class of compounds.

Thus, it has been found that **1a** reacts with the aminopyrazole derivatives **2a—c** in the presence of triethylamine to yield the pyrazolo[5,1-*c*][1,2,4]triazole derivatives **3a—c**. The formation of **3a—c** is assumed to proceed *via* 2+3 dipolar cycloaddition mechanism. Similar mechanism was suggested to account for the formation of pyrazolo[5,1-*c*][1,2,4]triazole derivative from the reaction of **1a** with **2d**.[3] The 3-amino-2-pyrazolin-5-one (**4**) reacted with **1a** to yield a product with the molecular formula $C_{29}H_{22}N_6O$ (M^+=470). Two theoretically possible isomeric structure **5** and **6** were considered for the product. Structure **6** was readily ruled out based on IR and ^{1}H-NMR spectrum of the product as well as its chemical behaviour. The IR spectrum revealed absorption at 1690 cm^{-1} for ring CO group. Whereas the ^{1}H-NMR spectrum showed no pyrazole C(4)–H signal at δ_H *ca.* 6.0. Furthermore the reaction product proved to be stable under conditions reported to effect decomposition of *N*-substituted pyrazoles of structure similar to that of **6**.[3] The formation of **5** is assumed to proceed *via* reaction of **4** with two molecules of **1a** and elimination of ammonia.

In contrast to the behaviour of **2a—c**, reaction of aminopyrazole derivative **2e** with **1a** afforded *N*-alkylated product (M^+=378) which may be formulated as **7** or **8**. The isomeric structure **7** was established for the reaction product showed a signal for NH_2 at δ 5.9. Attempts to effect cyclization of this product were unsuccessful. The formation of **7** in this case is assumed to proceed *via* alkylation sequence. Alkylation of aminoazoles with hydrazonoyl halides has been previously observed.[3]



Similar to the behaviour of **2e**, 2-aminobenzthiazole (**9**) reacted with compound **1a** under the same experimental condition to yield an alkylated product, although structures **10** and **11** seemed possible, structure **11** was readily ruled out based on IR spectrum which revealed the absence of absorption at 1670—1630 cm^{-1} for exocyclic C=N.

2-Aminopyrazine (**12**) reacted with **1a** to yield the pyrazolo[3,4-*b*]pyrazine derivative **13**. The structure of **13** was established based on analytical and spectral data. The formation of **13** in this reaction represents the first observed 2+3 cycloaddition of nitrilimine to diazine derivative.

Whereas compound **1b** reacted with **2a** to yield the imidazo[1,2-*b*]pyrazole derivative **14** (M^+=315), it reacted with compounds **2b, c, e** to yield only the acyclic *N*-alkylated products **15a—c**. The formation of **14** may be assumed to proceed either *via* the stepwise sequence

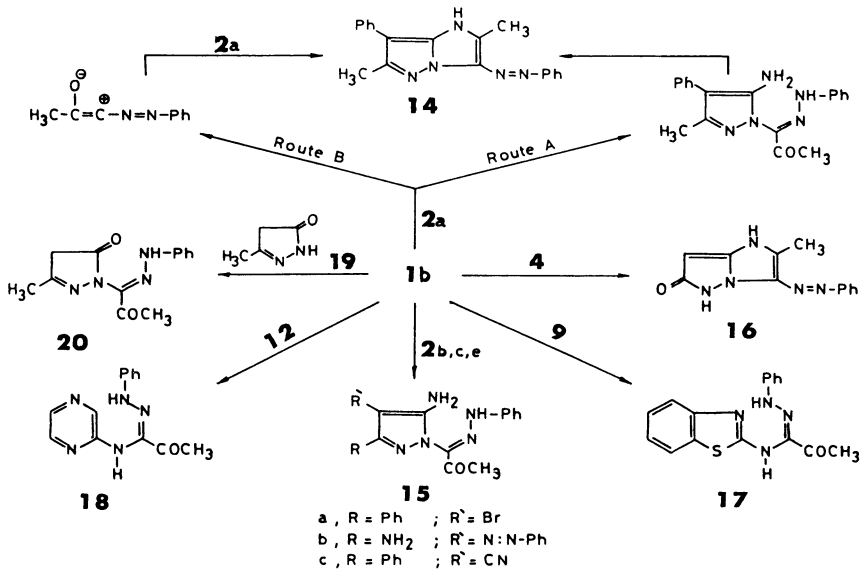


TABLE 1. LIST OF PRODUCTS OF REACTION OF THE HYDRAZONOYL CHLORIDES **1a, b** WITH AMINO- AND OXO-SUBSTITUTED AZOLES

Compound (Colour)	Crystallization solvent	Mp θ_m/°C	Yield %	Mol formula (Mol weight)	Found Calcd (%) C	H	N
3 (Yellow)	EtOH	208	74	$C_{23}H_{18}N_4$ (350)	79.2 (78.9	5.2 5.1	16.2 16.0)
3 (Yellow)	EtOH	214—216	28	$C_{22}H_{15}N_4Br$ (415)	63.3 (63.6	3.6 3.6	13.3 13.5)
3 (Yellow)	MeCOMe	236—238	85	$C_{22}H_{17}N_7$ (379)	69.8 (69.7	4.4 4.5	25.7 25.9)
5 (Buff)	MeCONMe2	246—248	24	$C_{29}H_{22}N_6O$ (470)	73.6 (74.0	4.8 4.7	17.7 17.9)
7 (Yellow)	EtOH	188	80	$C_{23}H_{18}N_6$ (378)	73.1 (73.0	4.6 4.8	22.4 22.2)
10 (Colourless)	MeCOMe	170	88	$C_{20}H_{16}N_4S$ (344)	69.6 (69.8	4.9 4.7	16.1 16.3)
13 (Colourless)	EtOH	250—252	35	$C_{17}H_{12}N_4$ (272)	75.0 (75.0	4.8 4.4	20.5 20.6)
14 (Orange)	MeCOMe	176—178	90	$C_{19}H_{17}N_5$ (315)	72.1 (72.4	5.2 5.4	22.4 22.2)
15 (Yellow)	MeCOMe	>300	90	$C_{18}H_{16}N_5OBr$ (398)	54.2 (54.3	4.4 4.0	17.8 17.6)
15 (Yellow)	MeCOMe	228—229	92	$C_{18}H_{18}N_8O$ (362)	59.8 (59.7	5.1 5.0	30.6 30.9)
15 (Yellow)	MeCOMe	242—244	88	$C_{19}H_{16}N_6O$ (344)	66.0 (66.3	5.0 4.7	24.6 24.4)
16 (Violet)	MeCONMe2	>300	82	$C_{12}H_{11}N_5O$ (241)	59.5 (59.8	4.6 4.6	29.2 29.0)
17 (Yellow)	MeCOMe	238—239	60	$C_{16}H_{14}N_4OS$ (310)	61.7 (61.9	4.7 4.5	18.2 18.1)
18 (Yellow)	MeCOMe	158—159	40	$C_{13}H_{13}N_5O$ (255)	61.0 (61.2	5.2 5.1	27.2 27.5)
20 (Brown)	MeCOMe	159	52	$C_{13}H_{14}N_4O_2$ (258)	60.5 (60.5	5.2 5.4	21.5 21.7)

TABLE 2. SPECTROSCOPIC DATA OF PRODUCTS LISTED IN Table 1

Compound	IR $\tilde{\nu}$/cm^{-1} (selected bands)	^{1}H-NMR δ
3	1640 (C=N)	2.2(3H, s, CH_3); 6.8—8.3 (15H, m, 3 phenyl protons)
3	1610 (C=N)	7.2—8.6(15H, m, 3 phenyl protons)
3	3400, 3200 (NH_2); 1625 (δNH_2); 1610 (C=N)	7.2—8.5(15H, m, 3 phenyl protons); 8.8 (2h, s, NH_2)
5	3250 (NH); 1690 (CO); 1630 (C=N)	7.2—7.8 (20H, m, 4 phenyl protons); 8.2 (1H, s, NH); 11.2 (1H, s, NH)
7	3500, 3300, 3200 (NH and NH_2); 2220 (CN); 1620 (C=N)	6.0 (2H, s, NH_2); 6.8—7.4 (15H, m, 3 phenyl protons); 10.2 (1H, s, NH)
10	3500—3300 (NH); 1610 (C=N)	7.1—7.7 (14H, m, 2 phenyl protons and C_6H_4); 8.2 (1H, s, NH); 8.4 (1H, s, NH)
13	1620 (C=N)	7.2—7.7 (10H, m, 2 phenyl protons); 8.0—8.3 (2H, m, pyrazine H-3 and H-4)
14	3500—3350 (NH); 1620 (C=N)	2.5 (3H, s, CH_3); 2.7 (3H, s, CH_3), 6.8—7.4 (10H, m, 2 phenyl protons); 12.1 (1H, br, s, NH)
15	3450, 3300, 3200 (NH and NH_2);	2.5 (3H, s, CH_3); 5.6 (2H, s, NH_2), 7.0—7.8 (10H, m, 2 phenyl protons); 10.7 (1H, br, s, NH)
15	3450—3300 (NH and NH_2); 1660 (CO); 1620 (C=N)	2.45 (3H, s, CH_3); 5.8 (2H, br, s, NH_2); 6.8—7.5 (12H, m, 2 phenyl protons and NH_2), 10.7 (1H, s, NH)
15	3500—3150 (NH and NH_2); 2220 (CN); 1660 (CO); 1620 (C=N)	2.5 (3H, s, CH_3); 6.8 (2H, s, NH_2); 7.0—7.8 (10H, m, 2 phenyl protons); 10.7 (1H, s, NH)
16	3500 (NH); 3100—2500 (chelated NH); 1700 (CO); 1610 (C=N)	Insoluble in commonly used NMR solvents
17	3500, 3200 (NH); 1705, 1680 (CO); 1620 (C=N)	
18	3500—3200 (NH); 1690 (CO);1610 (C=N)	
20	3500—2500 (chelated NH); 1680—1650 (acetyl and ring CO); 1610 (C=N)	

(route A) or dipolar addition mechanism (route B). We believed that **14** is formed mainly *via* a cycloaddition mechanism as acyclic intermediate for the reaction of **1b** and **2a** could not be traced. Moreover compounds **15a—c** were found resistant to cyclization under the reaction conditions or even more drastic conditions.

Reactivity of **1b** toward **4**, **9** and **12** was also investigated. Only in the case of **4** the cyclic product **16** was obtained (M^+=241). With other aminoazoles only the alkylated products **17** and **18** were obtained. Similarly **1b** reacted with 3-methyl-2-pyrazolin-5-one (**19**) to yield the acyclic *N*-alkylated product **20**.

It may thus concluded that nitrilimines would react with aminoazoles either *via* a 2+3 dipolar cycloaddition or by alkylation sequence. The exact course of the reaction seems to depend on the nature of the aminoazole and the nitrilimine. Fused azoles can only be readily obtained from a cycloadditions, trials to cyclise products of alkylation has failed in our hands.

Experimental

All melting points are uncorrected. IR spectra were recorded (KBr) on a Pye Unicam SP-1000 spectrophotometer. ^{1}H-NMR spectra were obtained in an EM-390 spectrometer at 90 MHz with DMSO-d_6 as solvent and TMS as internal reference. Analytical data were obtained from the Analytical Data Unit at Cairo University.

Reaction of the Hydrazonoyl Chlorides ***1a, b*** *with Amino and/or Oxo-substituted Azoles. General Procedure*: A suspension of compound **1a** or **1b** (20 mmol) and the appropriate amino or oxo-substituted azoles (20 mmol) in ethanol (30 ml) was refluxed with triethylamine (20 mmol) for 3 h and then evaporated to dryness under reduced pressure. The residue was washed with petroleum ether, triturated with ethanol, and the resulting solid product was filtered off and crystallized from the appropriate solvent (Table 1). Analytical and spectroscopic data are given in Table 1 and 2.

References

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