CHEMISTRY OF C-HETEROARYLHYDRAZIDOYL HALIDES. SYNTHESIS AND REACTIONS OF N-(p-NITROPHENYL)-C-(2-THIENYL)-FORMOHYDRAZIDOYL HALIDES

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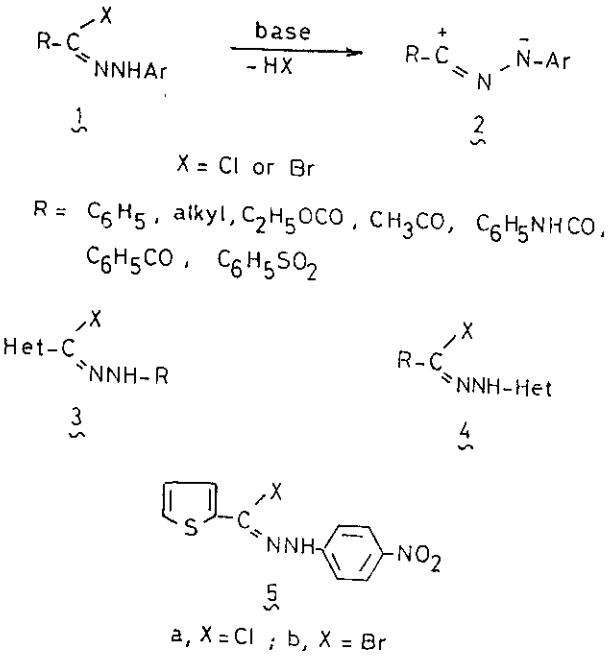
Abstract - Synthesis of C-(2-thienyl)-N-(p-nitrophenyl)formohydrazidoyl chloride 5a and its bromide analog 5b is described. Both 5a and 5b react with oxygen, sulfur and nitrogen nucleophiles in ethanol to give the corresponding substitution products 7-9. The cycloadditions of the nitrilimine 10, generated in situ from 5, to various olefinic dipolarophiles have been carried out. All reactions studied proceed with complete regioselectivity to give the 2-pyrazoline derivatives 11-13 and 16. Moreover, cycloaddition of 10 with enolates of various active methylene compounds afforded the pyrazole derivatives 22 and 27 in high yields. The cycloaddition regioselectivity is discussed in terms of the frontier orbital method.

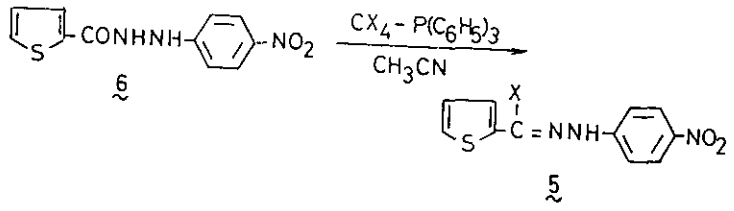
Hydrazidoyl halides 1 represent a unique class of compounds which undergo 1,3-base catalyzed elimination reaction to give nitrilimines 2 (Scheme 1).[2] The latter are versatile synthetic intermediates especially useful for 1,3-dipolar cycloaddition reactions that have been employed in synthesis of numerous heterocycles.[2] Despite the fact that many hydrazidoyl halides with various groups on carbon and nitrogen atoms have been synthesized and their reactions were extensively investigated, there appears to have no study of the chemistry of C-heteroaryl-N-arylformohydrazidoyl halides 3. As part of our ongoing interest in reactions of hydrazidoyl halides with heteroaryl group on the terminal nitrogen 4,[3] we thought it worthwhile to explore the chemistry of C-heteroaryl counterparts 3. In this paper, we report on the synthesis and reactions of two examples of this new class of hydrazidoyl halides, *namely* C-(2-thienyl)-N-(p-nitrophenyl)formohydrazidoyl chloride 5a and its bromide analog

5b (Scheme 1). Our interest in these compounds stems from the fact that many interesting changes in biological behaviour occur when the phenyl rings in biologically active compounds are replaced by thiophene rings.[4] Hydrazidoyl halides 1 proved to be biologically active and their properties depend on the nature of the groups on the carbon and nitrogen atoms. For example, C-alkyl hydrazidoyl halides possess miticidic, insecticidic and herbicidic properties[5], whereas their C-aryl- and C-aroyl-analogues exhibit antiviral and antimicrobial properties.[6,7] C-Acetyl- and C-ethoxycarbonyl-formohydrazidoyl halides were reported to be active against red spiders on beans and apple trees.[8]



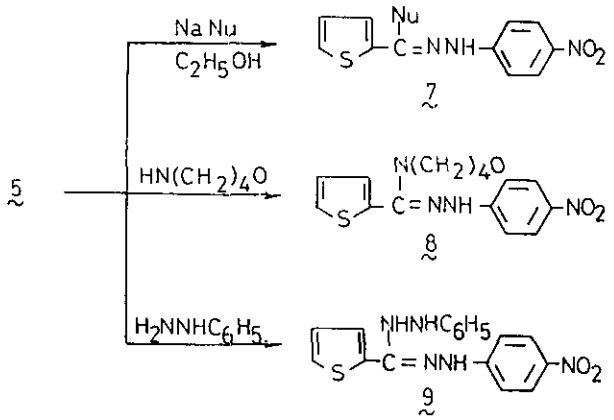
Scheme 1

The method of Wolkoff[9] in transforming 1-benzoyl-2-arylhydrazine into the corresponding hydrazidoyl halide was applied in this study to the preparation of 5. Thus, addition of carbon tetrachloride to a suspension of 1-(p-nitrophenyl)-2-(2-thenoyl)hydrazine 6 and triphenylphosphine in dry acetonitrile afforded the chloride 5a in 80 % yield. When carbon tetrabromide was used in place of carbon tetrachloride the bromide 5b was obtained in 65 % yield (Scheme 2). The structures of 5a and 5b were identified by their spectra, elemental analyses, and their substitution reactions. Thus, treatment of 5a or 5b with various nucleophiles in ethanol results in the displacement of the halogen atom and affords the corresponding substitution products 7a-e (Scheme 3). Morpholinolysis and hydrazinolysis of 5a give 8 and hydrazidine derivative 9, respectively. The structures of the products 7-9 follow their method of preparation and their physical data (see Experimental section).



a, X = Cl b, X = Br

Scheme 2



a, Nu = CN c, Nu = SC_6H_5 e, Nu = N_3

b, Nu = OC_6H_5 d, Nu = $SO_2C_6H_5$

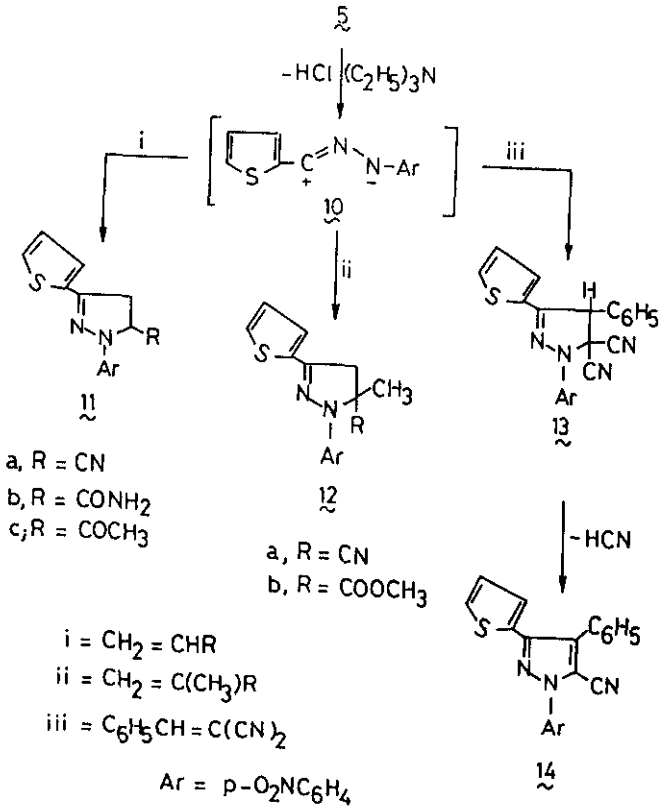
Scheme 3

N-(p-Nitrophenyl)-C-(2-thienyl)nitrilimine 10, generated in situ from the halide 5a or 5b and triethylamine in dry chloroform, reacts with ethylenic dipolarophiles such as acrylonitrile, acrylamide and methyl vinyl ketone to afford exclusively 5-substituted 3-(2-thienyl)-1-(p-nitrophenyl)-2-pyrazolines 11a-c respectively in good yield (Scheme 4). The assigned 5-R substituted 2-pyrazoline structures 11a-c were supported by analytical and spectral data (ir and ^{1}H nmr) . In ^{1}H nmr spectra, the cycloadducts 11b and 11c exhibit ABX patterns, whereas the adduct 11a shows an A_2X pattern due to the resonances of the 4-CH_2 and 5-CHR protons. The chemical shifts of the methine and methylene hydrogens of 11a-c compare favourably with the chemical shifts of the corresponding protons in 5-R substituted 1-aryl-3-phenyl-2-pyrazolines.[10] Such similarity, while confirming the assigned structures , it indicates that both substituents, phenyl and 2-thienyl at C-3, would have similar effects on the chemical shifts of the methylene protons at C-4 of substituted 2-pyrazoline derivatives. Also, the structure of 11a was further confirmed by the absence of the nitrile absorption in its infrared spectrum, as it is the case in aliphatic nitriles activated by a nitrogen or an

oxygen atom in the α-position.[11]

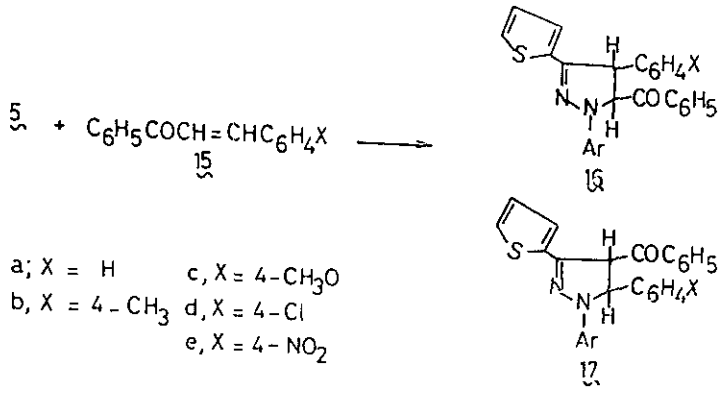
The reflux of 5a or 5b with 2-methylacrylonitrile and methyl 2-methylacrylate in chloroform in the presence of triethylamine yields the 2-pyrazoline derivatives 12a and 12b respectively. TLC and nmr analyses of the reaction mixture in each case revealed the absence of the other possible regioisomer (Scheme 4). The structures of 12a,b were established on the basis of analytical data and spectral properties (see Experimental section).

The reaction of 5a with benzalmalononitrile in chloroform in the presence of triethylamine produced 1-(p-nitrophenyl)-3-(2-thienyl)-4-phenyl-5-cyanopyrazole 14 as the exclusive product (Scheme 4). This product undoubtedly results from the elimination of hydrogen cyanide from the cycloadduct 13. The structure of 14 was established by elemental analysis, ^{1}H nmr and ir spectra. The regiochemistry of 14 was confirmed by comparison of its spectra with those of the pertinent regioisomer, 1-(p-nitrophenyl)-3-(2-thienyl)-4-cyano-5-phenylpyrazole 22f. The latter was prepared by the reaction of 5a with the sodium salt of phenacyl cyanide 18f in ethanol at room temperature (Scheme 6).



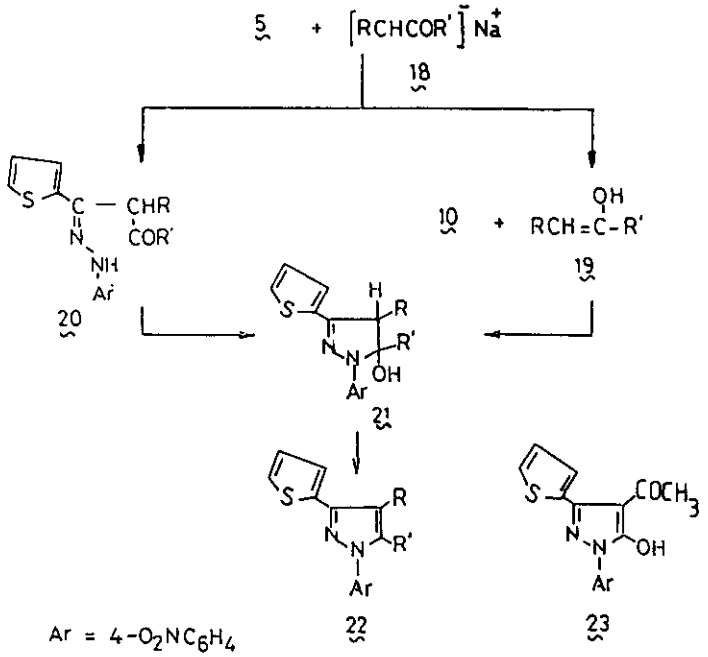
Scheme 4

Next the cycloaddition of 10 to α,β-unsaturated ketones 15a-e was investigated. Thus, treatment of 5a with 15 in refluxing benzene or chloroform in the presence of triethylamine afforded in each case, only one product identified as 1-(p-nitrophenyl)-3-(2-thienyl)-4-aryl-5-aroyl-2-pyrazoline 16 (Scheme 5). In no case the other regioisomer 17 was detected. The structures of the cycloadducts 16a-e were assigned on the basis of their spectral properties and elemental analyses (see Experimental). The regiochemical assignment is based on the chemical shifts of the 4-CHAr and 5-CHCOAr protons. For example, each cycloadduct exhibits two doublets near δ 4.6 and 5.6 ppm with J value of 6 Hz. These chemical shifts are similar to those reported for the resonances of 4-CHAr and 5-CHCOAr protons of the throughly studied 1,3,4-triaryl-5-benzoyl-2-pyrazolines.[12]



Scheme 5

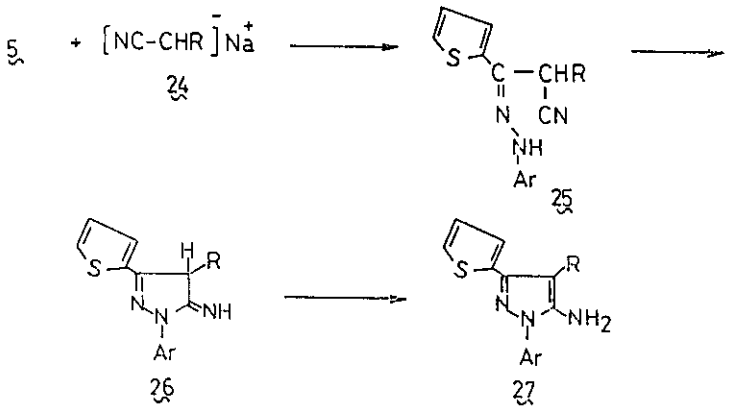
Next the reactions of 5 with active methylene compounds were examined. Treatment of 5a with acetylacetone in ethanol in the presence of sodium ethoxide at room temperature gives 1-(p-nitrophenyl)-3-(2-thienyl)-4-acetyl-5-methylpyrazole 22a in good yield (Scheme 6). Similarly, other active methylene compounds 18b-f reacted with 5a under similar conditions and yield the corresponding pyrazole derivatives 22b-f, respectively (Scheme 6). In no case, the acyclic hydrazone 20 was detected. This finding together with the fact that no 5-hydroxypyrazole derivative 23 was formed from 5a and ethyl acetoacetate indicate that the pyrazole derivatives 22a-f are probably formed by a concerted cycloaddition of 10 to the enol tautomers 19a-f of the active methylene compounds used (Scheme 6). Treatment of 5a with malononitrile, ethyl cyanoacetate and cyanoacetanilide in ethanol in the presence of sodium ethoxide afforded the 5-aminopyrazole derivatives 27a-c, respectively (Scheme 7). The structures of the latter products were based on their elemental and spectral analyses. The formation of 27 can be reasonably explained by the stepwise path involving electrophilic substitution to give the acyclic hydrazone 25. Cyclization of the latter followed by tautomerization lead to 27. The alternative direct formation of 27 by concerted cycloaddition of 10 to the ketimine tautomers of the active hydrogen nitriles used cannot be still ruled out.



Ar = 4-$O_2NC_6H_4$

	a	b	c	d	e	f
R	CH_3CO	C_6H_5CO	$C_6H_5SO_2$	C_2H_5OCO	C_6H_5NHCO	CN
R′	CH_3	C_6H_5	C_6H_5	CH_3	CH_3	C_6H_5

Scheme 6



Ar = 4-$O_2NC_6H_4$

	a	b	c
R =	$COOC_2H_5$	$CONHC_6H_5$	CN

Scheme 7

The results reported here clearly show that the hydrazidoyl halide 5 is highly reactive and reacts with nucleophiles with displacement of the halogen atom, and with bases to form nitrilimine 10, that readily undergoes thermal cycloadditions to various dipolarophiles. The latter reactions give access to 3-(2-thienyl) substituted 2-pyrazoline and pyrazole derivatives. All of the cycloaddition reactions of 10 investigated show complete regioselectivity. The regiochemical results observed for 10 are identical with those reported for diphenylnitrilimine (DPNI) with the studied dipolarophiles.[10,12,13] This similarity indicates that the frontier orbitals of 10 compare favourably with those of DPNI. Therefore, by analogy to DPNI, it is not unreasonable to conclude that the cycloadditions of 10 to electron-deficient olefins such as those outlined in Schemes 4 and 5, are controlled by HOMO (dipole)-LUMO (dipolarophile) interaction. On the other hand, the reactions of 10 with electron-rich olefins such as the enolate anions of β-keto esters and β-diketones are LUMO (dipole)-HOMO (dipolarophile) controlled. Since both HOMO and LUMO of electron-deficient alkenes are polarized away from the electron-withdrawing substituent[14], the exclusive formation of the cycloadducts 11-14 and 16 indicates that the larger HOMO coefficient is located on the carbon atom of 10. The change of the regiochemistry on going from electron-deficient olefins to electron-rich enolates indicates also that the carbon coefficient is larger than that of the nitrogen atom in the LUMO of 10. Recently, it was shown that the coefficient of the carbinol carbon is smaller than that of the benzoyl substituted carbon in the HOMO of the enol tautomer of dibenzoylmethane. The LUMO coefficients are opposite in magnitude, but the difference in coefficients is smaller.[15] Therefore, LUMO (10)-HOMO (enol) controlled formation of the pyrazoles 22a-f would be anticipated on the basis that the carbon coefficient in the LUMO of 10 is larger than that of the nitrogen atom.

EXPERIMENTAL

All melting points were determined on Bockmonoscop hot stage apparatus and are uncorrected. Infrared spectra (KBr) were run on a Perkin Elmer 257 spectrophotometer. ^{1}H Nmr spectra were obtained on a Varian T60-A spectrometer using tetramethylsilane as an internal reference. Microanalyses were performed at Microanalytical Laboratory, University of Cairo, Giza, Egypt.

Preparation of N-(p-nitrophenyl)-C-(2-thienyl)formohydrazidoyl halides (5a,b) - Carbon tetrachloride (2 ml, 20 mmole) was added to a stirred suspension of 1-(p-nitrophenyl)-2-(2-thenoyl)hydrazine 6 (5.3 g, 20 mmole) and triphenylphosphine (6.6 g, 25 mmole) in dry acetonitrile (40 ml). The mixture was stirred for 8 h. During this period, the hydrazide 6 dissolved and a yellow solid precipitated. This was collected and crystallized from acetic acid to give 5a in 80 % yield; mp 212°C; δ($CDCl_3$) 8.4 (s, 1H, NH), 6.93 (d, J = 9Hz, 2H), 7.0-7.6 (m, 3H), 8.15 (d, J = 9Hz, 2H) ppm.; $\bar{\nu}$(KBr) 3280 (NH), 1595 (C=N) cm^{-1}. Anal. Calcd for $C_{11}H_8ClN_3O_2S$: C, 46.89; H, 2.86; N, 14.91; S, 11.38. Found: C, 46.65; H, 2.75; N, 14.60; S, 11.21.

Repitition of the above procedure using carbon tetrabromide (6.64 g, 20 mmole) in place of carbon tetrachloride, the bromide 5b was obtained in 65 % yield; mp 217°C (acetic acid); δ($CDCl_3$) 8.5 (s, 1H), 6.9 (d, J = 9Hz, 2H), 7.0-7.7 (m, 3H), 8.2 (d, J = 9Hz, 2H) ppm; $\bar{\nu}$ (KBr) 3260 (NH), 1590 (C=N) cm^{-1}. Anal. Calcd for $C_{11}H_8BrN_3O_2S$: C, 40.49; H, 2.47; N, 12.88; S, 9.38. Found: C, 40.26; H, 2.33; N, 12.71; S, 9.20.

Reaction of 5 with dipolarophiles. General Method - To a solution of the hydrazidoyl chloride 5a or its bromide analog 5b (5 mmole) and the appropriate dipolarophile (5 mmole) in chloroform (30 ml) was added triethylamine (0.7 ml, 5 mmole) at room temperature. The mixture was refluxed for 12-18 h and then cooled. The mixture was extracted with water and the organic layer was collected, dried (anhydrous sodium sulfate), then filtered. The solvent was evaporated and the residue left was triturated with little methanol where it solidified. The solid was collected and crystallization from acetic acid gave the corresponding cycloadduct in 70-85 % yield.

Compound 11a had mp 183°C, δ ($CDCl_3$) 3.6 (d, J = 9Hz, 2H), 5.1 (t, J = 9Hz, 1H), 6.8 (d, J = 9Hz, 2H), 7.0-7.8 (m, 3H), 8.1 (d, J = 9Hz, 2H) ppm; $\bar{\nu}$ (KBr) 1590 (C=N) cm^{-1}. Anal. Calcd for $C_{14}H_{10}N_4O_2S$: C, 56.37; H, 3.38; N, 18.78. Found: C, 56.21; H, 3.41; N, 18.51.

Compound 11b had mp 297°C, δ ($CDCl_3$) 4.90 (dd, J = 8,13 Hz, 1H), 3.60 (dd, J = 13,18 Hz, 1H), 3.00 (dd, J = 8, 18 Hz, 1H), 6.8 (d, J = 9Hz, 2H), 7.0-7.8 (m, 5H), 8.2 (d, J = 9Hz, 2H) ppm; $\bar{\nu}$ (KBr) 3370, 3180 (NH_2), 1640 (CO) cm^{-1}. Anal. Calcd for $C_{14}H_{12}N_4O_3S$: C, 53.15; H, 3.82; N, 17.71. Found: C, 53.62; H, 3.74; N, 17.43.

Compound 11c had mp 202°C, δ ($CDCl_3$) 2.1 (s, 3H), 3.33 (dd, J = 6,18 Hz, 1H), 3.84 (dd, J = 12, 18 Hz, 1H), 4.8 (dd, J = 6,12 Hz, 1H), 6.9 (d, J = 9Hz, 2H), 7.0-7.7 (m, 3H), 8.15 (d, J = 9Hz, 2H) ppm; $\bar{\nu}$ (KBr) 1720 (CO), 1590 (C=N) cm^{-1}. Anal. Calcd for $C_{15}H_{13}N_3O_3S$: C, 57.13; H, 4.16; N, 13.33. Found: C, 57.34; H, 4.07; N, 12.35.

Compound 12a had mp 180°C, δ ($CDCl_3$) 1.3 (s, 3H), 3.55 (d, J = 18 Hz, 1H), 4.1 (d, J = 18 Hz, 1H), 7.0-8.0 (m, 3H), 7.4 (d, J = 9Hz, 2H), 8.2 (d, J = 9Hz, 2H) ppm, $\bar{\nu}$ (KBr) 1590 (C=N) cm^{-1}. Anal. Calcd for $C_{15}H_{12}N_4O_2S$: C, 57.68; H, 3.87; N, 17.94. Found: C, 57.64; H, 3.82; N, 17.89.

Compound 12b had mp 210°C, δ ($CDCl_3$) 1.7 (s, 3H), 3.7 (s, 3H), 3.25 (d, J = 18Hz, 1H), 4.15 (d, J = 18 Hz, 1H), 6.9 (d, J = 9 Hz, 2H), 7.0-7.6 (m, 3H), 8.15 (d, J = 9Hz, 2H) ppm; $\bar{\nu}$ (KBr) 1740 (CO), 1590 (C=N) cm^{-1}. Anal. Calcd for $C_{16}H_{15}N_3O_4S$: C, 58.35; H, 4.59; N, 12.75. Found: C, 58.11; H, 4.22; N, 12.56.

Compound 14 had mp 212°C, δ ($CDCl_3$) 6.9 (d, J = 9Hz, 2H), 7.0-7.7 (m, 8H), 8.15 (d, J = 9Hz, 2H) ppm; $\bar{\nu}$ (KBr) 2230 (C≡N), 1595 (C=N) cm^{-1}. Anal. Calcd for $C_{20}H_{12}N_4O_2S$: C, 64.51; H, 3.25; N, 15.04. Found: C, 64.42; H, 3.21; N, 14.84.

Compound 16a had mp 208°C, ($CDCl_3$) 4.6 (d, J=6Hz, 1H), 5.7 (d, J = 6Hz, 1H), 6.9 (d, J = 9Hz, 2H), 7.0-7.8 (m, 13 H), 8.15 (d, J = 9Hz, 2H) ppm; $\bar{\nu}$(KBr) 1690 (CO), 1595 (C=N) cm^{-1}. Anal. Calcd for $C_{26}H_{19}N_3O_3S$: C, 68.86; H, 4.23; N, 9.27. Found: C, 68.70; H, 4.15; N, 8.91.

Compound 16b had mp 192°C, δ($CDCl_3$) 2.4 (s, 3H), 4.6 (d, J = 6Hz, 1H), 5.7 (d, J=6Hz, 1H), 6.8-8.2 (m, 16 H), ppm; $\bar{\nu}$(KBr) 1685 (CO), 1595 (C=N) cm^{-1}. Anal. Calcd for $C_{27}H_{21}N_3O_3S$: C, 69.36; H, 4.53; N, 8.99. Found: C, 69.21; H, 4.41; N, 8.61.

Compound 16c had mp 238°C, δ ($CDCl_3$) 3.8 (s, 3H), 4.55 (d, J = 6Hz, 1H), 5.7 (d, J = 6Hz, 1H), 6.8-8.3 (m, 16H) ppm; $\bar{\nu}$ (KBr) 1680 (CO), 1590 (C=N) cm^{-1}. Anal. Calcd for $C_{27}H_{21}N_3O_4S$: C, 67.07; H, 4.38; N, 8.69. Found: C, 67.14; H, 4.21; N, 8.45.

Compound 16d had mp 274°C, δ ($CDCl_3$) 4.4 (d, J = 6Hz, 1H), 5.7 (d, J = 6Hz, 1H), 6.8-8.3 (m, 16H) ppm; $\bar{\nu}$ (KBr) 1690 (CO), 1595 (C=N) cm^{-1}. Anal. Calcd for $C_{26}H_{18}ClN_3O_3S$: C, 63.99; H, 3.72; N, 8.61. Found: C, 63.98; H, 3.68; N, 8.53.

Compound 16e had mp 280°C, δ($CDCl_3$) 4.53 (d, J = 6Hz, 1H), 5.77 (d, J = 6Hz, 1H), 6.8-8.3 (m, 16H) ppm; $\bar{\nu}$ (KBr) 1695 (CO), 1590 (C=N) cm^{-1}. Anal. Calcd for $C_{26}H_{18}N_4O_5S$: C, 62.64; H, 3.64; N, 11.24. Found: C, 62.41; H, 3.41; N, 11.12.

1-(p-Nitrophenyl)-3-(2-thienyl)pyrazole derivatives 22a-f. General Method - To an ethanolic sodium ethoxide solution (prepared from sodium metal (0.1 g, 0.005 g atom) and absolute ethanol (20 ml)) was added the appropriate active methylene compound (0.005 mole) with stirring. To the resulting solution, the hydrazidoyl chloride 5a (1.4 g, 0.005 mole) was added at room temperature. The mixture was stirred for 24 h during which the chloride 5a dissolved and the crude pyrazole 22 precipitated. The latter was collected, washed with water, dried and crystallized from ethanol or acetic acid as outlined.

Compound 22a had mp 133°C, (C_2H_5OH), δ ($CDCl_3$) 2.3 (s, 3H), 3.3 (s, 3H), 6.8 (d, J = 9Hz, 2H), 7.0-7.6 (m, 3H), 8.15 (d, J = 9Hz, 2H) ppm; $\bar{\nu}$ (KBr) 1660 (CO) cm^{-1}. Anal. Calcd for $C_{16}H_{13}N_3O_3S$: C, 58.70; H, 4.00; N, 12.84. Found: C, 58.50; H, 4.02; N, 12.77.

Compound 22b had mp 170°C (C_2H_5OH), δ ($CDCl_3$) 6.8-8.3 (m) ppm; $\bar{\nu}$(KBr) 1665 (CO). Anal. Calcd. for $C_{26}H_{17}N_3O_3S$: C, 69.17; H, 3.80; N, 9.31. Found: C, 69.41; H, 3.65; N, 9.41.

Compound 22c had mp 220°C (CH_3COOH), δ (DMSO) 6.6-8.3 (m) ppm; $\bar{\nu}$ (KBr) 1330, 1150 (-SO_2-) cm^{-1}. Anal. Calcd for $C_{25}H_{17}N_3O_4S$: C, 61.59; H. 3.51; N, 8.62. Found: C, 61.45; H, 3.45; N, 8.52.

Compound 22d had mp 144°C (C_2H_5OH), δ ($CDCl_3$) 1.4 (t, J = 7Hz, 3H), 2.6 (s, 3H), 4.4 (q, J=7Hz, 2H), 6.8 (d, J = 9Hz, 2H), 7.0-7.9 (m, 3H), 8.15 (d, J = 9Hz, 2H) ppm; $\bar{\nu}$(KBr) 1690 (CO) cm^{-1}. Anal. Calcd for $C_{17}H_{15}N_3O_4S$: C, 57.13; H, 4.23; N, 11.75. Found: C, 56.92; H, 3.92; N, 11.76.

Compound 22e had mp 238°C (CH_3COOH), δ ($CDCl_3$) 2.4 (s, 3H), 6.7-8.4 (m, 13 H) ppm; $\bar{\nu}$ (KBr)

3240 (NH), 1670 (CO), 1595 (C=N) cm^{-1}. Anal. Calcd for $C_{21}H_{16}N_4O_3S$: C, 62.35; H, 3.99; N, 13.85. Found: C, 62.22; H, 3.85; N, 13.74.

Compound 22f had mp 200°C (CH_3COOH), δ ($CDCl_3$) 6.7-8.3 (m) ppm; ν̄ (KBr) 2220 (C≡N), 1595 (C=N) cm^{-1}. Anal. Calcd for $C_{20}H_{12}N_4O_2S$: C, 64.50; H, 3.25; N, 15.04. Found: C, 64.41; H, 3.11; N, 15.21.

1-(p-Nitrophenyl)-3-(2-thienyl)-5-aminopyrazole derivatives (27a-c). General Method - These were prepared by the same general procedure described for synthesis of 22a-f using equimolecular amounts of the hydrazidoyl chloride 5a and the appropriate active methylene nitrile (5 mmole each) in ethanol in the presence of sodium ethoxide (5 mmole). The crude product was crystallized from ethanol or acetic acid as specified.

Compound 27a had mp 181°C (C_2H_5OH), δ ($CDCl_3$) 1.4 (t, J = 7Hz, 3H), 4.38 (q, J = 7Hz, 2H), 5.7 (s, 2H), 6.8 (d, J = 9Hz, 2H), 7.0-7.9 (m, 3H), 8.2 (d, J = 9Hz, 2H) ppm; ν̄ (KBr) 3420, 3320 (NH_2), 1650 (CO) cm^{-1}. Anal. Calcd for $C_{16}H_{14}N_4O_4S$: C, 53.62; H. 3.94; N, 15.63. Found: C, 53.51; H, 4.00; N, 15.47.

Compound 27b had mp 212°C (CH_3COOH), δ (DMSO) 5.75 (s, 2H), 6.7-8.4 (m, 12 H) ppm; ν̄ (KBr) 3300, 3270 (NH_2), 1650 (CO) cm^{-1}. Anal. Calcd for $C_{20}H_{15}N_5O_3S$: C, 59.25; H, 3.73; N, 17.27. Found: C, 59.14; H, 3.65; N, 17.10.

Compound 27c had mp 255°C(CH_3COOH), δ (DMSO) 5.71 (s, 2H), 6.8 (d, J = 9Hz, 2H), 7.0-7.8 (m, 8H), 8.2 (d, J = 9Hz, 2H) ppm; ν̄ (KBr) 3370, 3300 (NH_2), 2205 (C≡N) cm^{-1}. Anal. Calcd for $C_{14}H_9N_5O_2S$: C, 54.01; H, 2.91; N, 22.50. Found: C, 54.51; H, 2.68; N, 22.41.

Reactions of hydrazidoyl halides (5a,b) with nucleophiles. Synthesis of hydrazone derivatives 7-9. General Method - Equimolecular amounts of 5a or 5b and the appropriate nucleophile (NaCN, $NaOC_6H_5$, $NaSC_6H_5$, $NaSO_2C_6H_5$, NaN_3, morpholine or phenyl hydrazine) were stirred in ethanol (40 ml) for 24 h at room temperature. The crude substitution product, that precipitated, was collected, washed with water and crystallized from the suitable solvent.

Compound 7a had mp 190°C (CH_3COOH), δ ($CDCl_3$) 8.4 (s, 1H), 8.2 (d, J = 9Hz, 2H), 7.0-7.7 (m, 3H), 6.8 (d, J = 9Hz, 2H) ppm; ν̄ (KBr) 3260 (NH), 2210 (C≡N) cm^{-1}. Anal. Calcd for $C_{12}H_8N_4O_2S$: C, 59.98; H, 3.35; N, 23.32. Found: C, 60.01; H, 3.41; N, 23.23.

Compound 7b had mp 175°C (CH_3COOH), δ (DMSO) 8.3 (s, 1H), 8.1 (d, J = 9Hz, 2H), 7.1-7.7 (m, 8H), 6.8 (d, J = 9Hz, 2H) ppm; ν̄ (KBr) 3280 (NH), 1210 (ArO) cm^{-1}. Anal. Calcd for $C_{17}H_{13}N_3O_3S$: C, 60.17; H, 3.86; N, 12.38. Found: C, 60.21; H, 3.74; N, 12.52.

Compound 7c had mp 146°C (C_2H_5OH), δ ($CDCl_3$) 6.8 (d, J = 9Hz, 2H), 7.1-7.7 (m, 8H), 8.1 (d, J = 9Hz, 2H), 8.5 (s, 1H) ppm; ν̄ (KBr) 3300 (NH), cm^{-1}. Anal. Calcd for $C_{17}H_{13}N_3O_2S_2$: C, 57.45; H, 3.69; N, 11.82. Found: C, 57.32; H, 3.44; N, 11.71.

Compound 7d had mp 160°C (C_2H_5OH), δ ($CDCl_3$) 7.6-8.3 (m, 12 H), 8.6 (s, 1H) ppm, ν (KBr) 3300 (NH), 1330, 1150 (-SO_2Ar) cm^{-1}. Anal. Calcd for $C_{17}H_{13}N_3O_4S_2$: C, 52.70; H, 3.38; N, 10.85. Found: C, 52.61; H, 3.51; N, 10.61.

Compound 7e had mp 130°C (C_2H_5OH), δ ($CDCl_3$) 6.8 (d, J = 9Hz, 2H), 7.0-7.8 (m, 3H), 8.15 (d, J=9Hz, 2H), 8.5 (s, 1H) ppm; ν (KBr) 3240 (NH), 2120 (N_3) cm^{-1}. Anal. Calcd. for $C_{11}H_8N_6O_2S$: C, 45.82; H, 2.80; N, 29.15. Found: C, 45.74; H, 2.70; N, 29.12.

Compound 8 had mp 147°C (C_2H_5OH), δ ($CDCl_3$) 3.15 (dd, 4H), 3.6 (dd, 4H), 6.8 (d, J = 9Hz, 2H), 7.1-7.8 (m, 3H), 8.15 (d, J = 9Hz, 2H), 8.5 (s, 1H) ppm, ν (KBr) 3300 (NH) cm^{-1}. Anal. Calcd for $C_{15}H_{16}N_4O_3S$: C, 54.20; H, 4.85; N, 16.85. Found: C, 54.50; H, 4.71; N, 16.41.

Compound 9 had mp 195°C (C_2H_5OH), δ ($CDCl_3$) 6.79 (d, J = 9Hz, 2H), 8.1 (d, J = 9Hz, 2H), 7.0-7.8 (m, 10 H), 8.45 (s, 1H) ppm; ν (KBr) 3280 (NH) cm^{-1}. Anal. Calcd for $C_{17}H_{15}N_5O_2S$: C, 57.78; H. 4.28; N, 19.82. Found: C, 57.61; H, 4.22; N, 19.76.

REFERENCES

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2. For reviews see (a) A. S. Shawali and C. Parkanyi, J. Heterocycl. Chem., 17, 833 (1980); (b) A. S. Shawali, Heterocycles, 20, 2239 (1983); (c) R. N. Butler and F. L. Scott, Chem. Ind. (London), 1216 (1970); (d) H. Ulrich, The Chemistry of Imidoyl Halides, Plenum Press, New York, N. Y., 1968, p. 173.
3. A. O. Abdelhamid, H. M. Hassaneen, and A. S. Shawali, J. Heterocycl. Chem., 22, 453 (1985).
4. G. Newkome and W. W. Paudler, Contemporary Heterocyclic Chemistry, Wiley, New York, N.Y., 1982, pp. 171-174.
5. G. Kaugers, US Patent 3,745,215 (1973); Chem. Abstr., 79, 78412 m (1973).
6. H. M. Habib, Proc. Egypt. Bot. Soc., 3, 328 (1982).
7. Zh. V. Molodykh, B. I. Buzykin, M. A. Kudrina, L. P. Sysoeva, N. G. Gazetdinova, I. D. Neklesova, and Yu. P. Kitaev, Khim. Farm. Zh., 14, 33 (1980); Chem. Abstr., 93, 94943e (1980).
8. L. Emmel and G. Heubach, Farbwerke Hoechst Ger. Offen. 2,017,762 (1972); 2,017,761 (1972); Chem. Abstr., 76, P 45971 c, P 33935 f (1972).
9. P. Wolkoff, Can. J. Chem., 53, 1333 (1975).
10. W. Fliege, R. Huisgen, J.S. Clovis, and H. Knupfer, Chem. Ber., 116, 3039 (1983).
11. (a) G. Butt, J. Climi, P. M. Hooben, and R. D. Topson, Spectrochimica Acta, 36A, 521 (1980); (b) J. P. Jessen and H. W. Thompson, ibid, 13, 217 (1958).

12. G. Bianchi, R. Gandolfi, and C. D. DeMichelli, J. Chem. Res. (S) 6 (1981); ibid. (M), 0135 (1981).

13. R. Huisgen, H. Knupfer, R. Sustman, G. Wallbillich and V. Weberndorfer, Chem. Ber., 100, 1580 (1967).

14. P. Caramella and K. N. Houk, J. Am. Chem. Soc., 98, 6397 (1976).

15. H. M. Hassaneen, R. H. Hilal, N. M. Elwan, A. Harhash, and A. S. Shawali, J. Heterocycl. Chem., 21, 1013 (1984).

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