Synthesis of New Pyrazolo[1,5-*a*]pyrimidine Derivatives *via* CT-Complexation

Synthese neuer Pyrazolo[1,5*a*]pyrimidin-Derivate über charge-transfer-Komplexe

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Pyrazolo[1,5-*a*]pyrimidines[1] and indanopyrazolo[1,5-*a*]pyrimidines[2] have been synthesized from 3,5-diamino-4-arylazopyrazoles with TCNE and CNIND, respectively, *via* CT-complexation. Due to interesting biological properties of pyrazolopyrimidines[3,4] and in an expansion of our interest on this type of compounds we have utilized 5-substituted-3-amino-2*H*-pyrazole-4-carbonitriles **1-3** as pyrazole derivatives to act as donors in complexation with π-acceptors. The objectives of the present work are to ascertain the effective donating and cyclizing centers in 3,5-diamino-4-arylazopyrazoles on complexation with the electron acceptors[5], and interpretation of the effect of the polyfunctional groups in **1a-e, 3** on the interaction with TCNE and CNIND as π-acceptors.

Upon adding double molar amounts of TCNE to a solution of aminopyrazoles **1-3** in ethyl acetate a green colour of a transient CT-complex was observed which changed gradually to brown. Chromatographic separations gave products **4a-e**.

On the other hand, the donors **1-3** did not form CT-complexes with CNIND in ethyl acetate or CH_2Cl_2. Presumably, this is due to the low electron affinity of CNIND as well as to the cyano group at C-4 in compounds 1-3, which reduces the donating ability of the donors to some extent. However on mixing both CNIND and aminopyrazoles **1-3** in pyridine, an initial CT-complex was formed. Heating the mixture, the CT-complex was followed by immediate chemical reaction which was completed after a few h to form the indanopyrazolo[1,5-*a*]pyrimidines **8**.

The rational for the formation of the indanopyrazolo[1,5-*a*]pyrimidines **8** is presented in Scheme 1: the aminopyrazoles **1-3** and CNIND form a CT-complex in the initial step. The radical ion pair **5** formed upon complete electron transfer is suggested to undergo proton transfer from the NH of the pyrazole ring to pyridine. C-CN bond cleavage in **6** forms intermediate **7**. Elimination of water from **7** forms the indanopyrazolo[1,5-*a*]pyrimidines **8**.

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Experimental Part

Melting points: uncorrected.- UV/VIS spectra: Perkin-Elmer Lambda 2 spectrophotometer using 1.0 cm stoppered silica cells.- IR spectra: Shimadzu 470 spectrophotometer (KBr).- ^{1}H-NMR spectra: Bruker Wp 80 (80 MHz), Bruker WM 400 (400.1 MHz) spectrometers.- Mass spectra: Finnigan 8430 spectrometer at 70 eV.- Elemental analyses: Microanalytical unit at Cairo University.

Table 1: Physical and analytical data of substituted aminopyrazoles **1a-f**

Compound*	m.p °C	Colour	Yield %	Mol.Formula (M.Wt)	Analysis % Found (calcd)		
					C	H	N
1a	177-78	colourless	96	$C_{10}H_9N_5$ (199.22)	60.42 (60.29	4.44 4.55	35.38 35.15)
1b	207-09	colourless	94	$C_{11}H_{11}N_5$ (213.24)	62.15 (61.96	5.39 5.20	32.64 32.84)
1c	181-82	white	95	$C_{11}H_{11}N_5$ (213.24)	61.84 (61.96	5.41 5.20	33.03 32.84)
1d	186-88	white	90	$C_{11}H_{11}N_5O$ (229.24)	57.88 (57.63	4.66 4.84	30.67 30.55)
1e	240-42	white	86	$C_{10}H_8N_5Cl$ (233.66)	51.32 (51.40	3.54 3.45	30.02 29.97)
1f	195-97	grey	82	$C_{12}H_{14}N_6$ (242.28)	59.66 (59.49	5.69 5.82	34.81 34.69)

*All compounds were recrystallized from ethanol/water.

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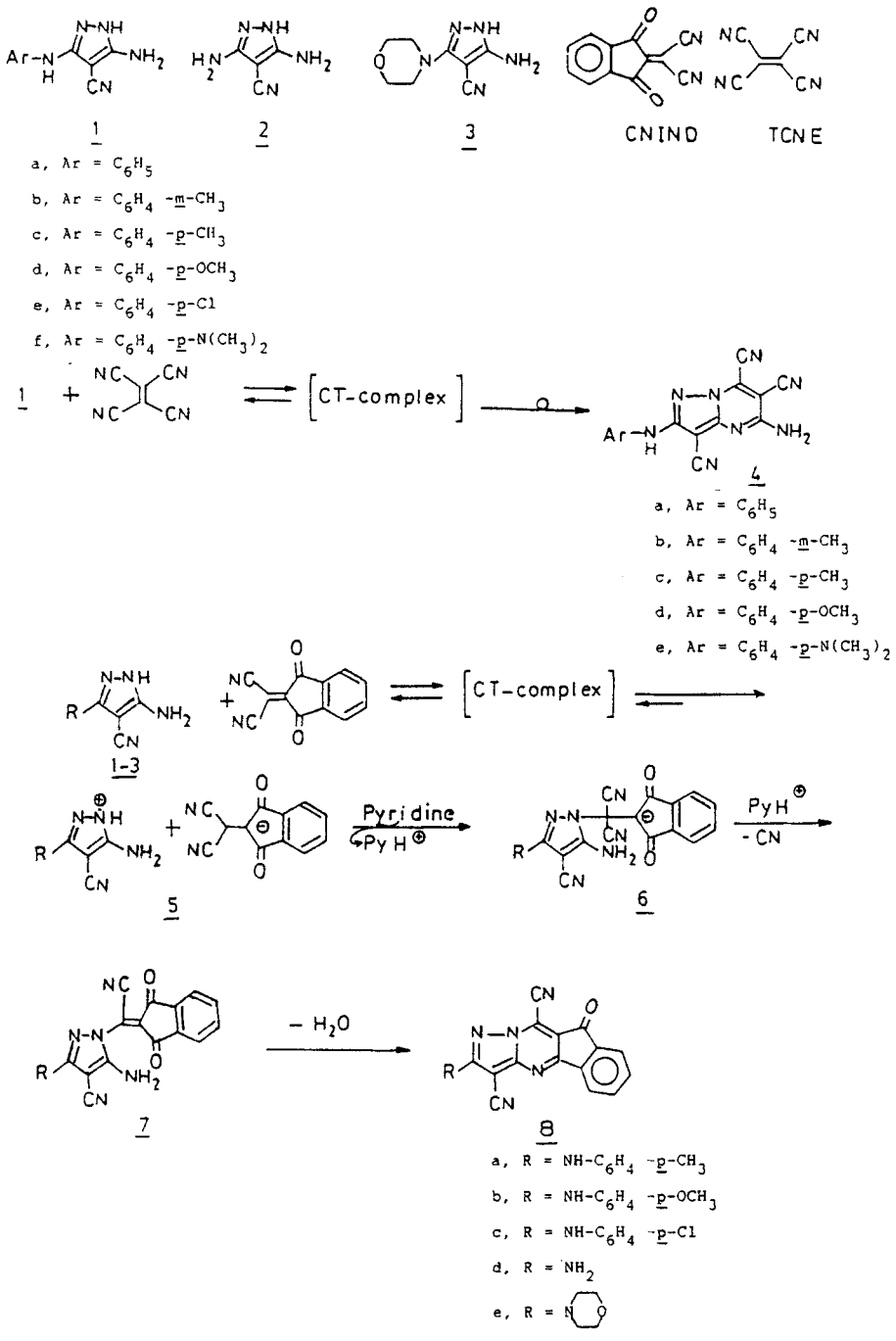

Scheme 1

Table 2: λ_{max}* of the CT-complexes between TCNE and substituted aminopyrazoles 1a-f in ethyl acetate at 25°C.

Compound	λ max nm	Compound	λ max nm
1a	670	1d	760
1b	685	1e	648
1c	720	1f	778

Data of Table 2 are taken from ref. 5, except **1f**.

2-(Dicyanomethylene)indane-1,3-dione (CNIND) was prepared according to *Chatterijee*[6]. 5-Substituted-3-amino-2*H*-pyrazole-4-carbonitriles **1-3** (two of which have been reported in lit.[7,8]) were prepared as follows: A mixture of equimolar amounts of dimethylmercapto-2,2-dicyanoethylene and the appropriate amine was stirred under reflux for 1/2 h. The solvent was evaporated and the residue was recrystallized from ethanol/water. The reaction product was refluxed with hydrazine hydrate in ethanol for 11/2 hours to give the donors **1a-f** (Table 1).- **1a-f**: IR (KBr): $\tilde{\nu}$ = 3460-3200 (NH, NH_2), 2220-2210 cm^{-1} (CN).- ^{1}H-NMR ([D_6]DMSO): δ = 11.20-11.00 (s, br, 1H, pyrazole-NH), 8.52-8.05 (s, br, 1H, HN-Ar), 7.55-6.65 (Ar-H); 6.15-6.30 (s, br, 2H, NH_2).

Table 3: Physical and analytical data of pyrazolo[1,5-*a*]pyrimidines **4a-f** and indanopyrazolo[1,5-*a*]pyrimidines **8a-e**.

Compound	Colour	m.p. (°C)	Yield %	Solvent of recrystallization	Mol.formula (M Wt)	Analysis % Found (calcd) C	H	N	Cl
4a	pale yellow	293-95	59	Ethyl acetate	$C_{15}H_8N_8$ (300.28)	59.84 (60.00	2.74 2.69	37.22 37.32)	
4b	yellow	325-26	67	Ethanol	$C_{16}H_{10}N_8$ (314.31)	61.31 (61.14	3.32 3.21	35.59 35.65)	
4c	yellow	306-08	63	Ethanol	$C_{16}H_{10}N_8$ (314.31)	60.93 (61.14	3.36 3.21	35.81 35.65)	
4d	orange	dec.299	61	Acetonitrile	$C_{16}H_{10}N_8O$ (330.31)	58.31 (58.18	2.97 3.05	34.12 33.92)	
4e	grey	339-41	74	Acetic acid	$C_{17}H_{13}N_9$ (343.35)	59.63 (59.47	3.74 3.82	36.92 36.72)	
8a	orange	350-52	64	DMF	$C_{22}H_{12}N_6O$ (376.38)	70.37 (70.21	3.09 3.21	22.51 22.33)	
8b	reddish-brown	344-46	68	Acetonitrile	$C_{22}H_{12}N_6O_2$ (392.38)	67.49 (67.34	2.96 3.08	21.58 21.42)	
8c	orange	321-23	62	DMF	$C_{21}H_9N_6ClO$ (396.80)	63.71 (63.57	2.18 2.29	21.33 21.18)	9.07 8.93
8d	yellow	> 360	54	Ethanol	$C_{15}H_6N_6O$ (286.25)	63.08 (62.94	2.25 2.11	29.17 29.36)	
8e	orange	> 360	59	Ethanol	$C_{19}H_{12}N_6O_2$ (356.34)	63.86 (64.04	3.22 3.39	23.70 23.58)	

Reaction of TCNE with 5-substituted-3-amino-2H-pyrazole-4-carbonitrile **1a-f**

To a solution of 256 mg (0.002 mol) TCNE in 10 ml dry ethyl acetate, the aminopyrazole (0.001 mol) in 20 ml dry ethyl acetate was added dropwise with stirring at 25 °C. The reaction colour changes gradually from green or blue to brown. Stirring was continued for 48 h. The mixture was concentrated and the residue was tlc-chromatographed (tolouene/ethyl acetate (1:1)). Extraction and recrystallization from the suitable solvent afforded compounds **4a-e** (Table 3).

4a-e: IR (KBr): $\tilde{\nu}$ = 3400-3220 (NH, NH_2), 2220 cm^{-1} (CN).- ^{1}H-NMR ([D_6]DMSO): δ (ppm) = 9.13-8.96 (s, br, 2H, NH_2 pyrimidine), 8.38-8.00 (s, br, 1H, HN-Ar), 7.66-6.65 (Ar-H).

Reaction of CNIND with 5-substituted-3-amino-2H-pyrazole-4-carbonitrile **1-3**

To a solution of CNIND (416 mg, 0.002 mol) in 20 ml dry pyridine, the aminopyrazole (0.001 mol) in 10 ml dry pyridine was added dropwise with stirring. The mixture was heated gently without increasing the temp. above 100 °C for 3 h. The solvent was removed and the residue was washed with ethanol to remove the residual pyridine. The residue was tlc-chromatographed (toluene/ethyl acetate (5:1)). Extraction and recrystallization from an appropriate solvent afforded products **8a-e** (Table 3).

8a-e: IR (KBr): $\tilde{\nu}$ = 3400-3320 (NH), 2220-2210 (CN), 1715-1695 cm^{-1} (CO).- ^{1}H-NMR ([D_6]DMSO): δ (ppm) = 8.43-8.14 (s, br, 1H, HN-Ar for **8a-c**), 8.40 (s, br, 2H, NH_2 for **8d**), 4.15 (s, 4H and 3.75 s, 4H, morph. CH_2 for **8e**), 8.00-7.00 (Ar-H for **8a-c**), 8.10-7.75 (Ar-H for **8d,e**).

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