NITRILES IN ORGANIC SYNTHESIS: SYNTHESIS OF NEW POLYFUNCTIONALLY SUBSTITUTED AROMATIC HYDROCARBONS AND AROMATIC HETEROCYCLES

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Part of our research program is directed to developing new polyfunctionally substituted aromatics as potential agrochemicals[1,2]. Recently, samples of certain biphenyl, substituted aryls and heterocycles were required. Synthetic approaches reported in refs[2 - 5] were utilized (Schemes 1 and 2).

EXPERIMENTAL

All melting points are uncorrected and were measured on electrothermal melting point apparatus. IR Spectra were measured in KBr and ^{1}H NMR spectra were measured on a EM-39090 MHz spectrometer in $CDCl_3$. Microanalytical determinations were performed at microanalysis unit, Cairo University. Physical data of prepared compounds are presented in Tables I and II.

Condensation of 4-Acetylbiphenyl with Malononitrile; Synthesis of 1-(4-Biphenyl)-ethylidenemalononitrile *II*

A mixture of equimolar amounts of 4-acetylbiphenyl (*I*) and malononitrile (0.01 mol) in dry benzene (100 ml), catalytic amount of AcOH (5 ml) and ammonium acetate (5 g) was heated under reflux in a flask fitted with adapter for continual water separation till the calculated amount of water has been collected. The benzene was distilled off and the reaction mixture was then triturated with water to give product *II*.

Reaction of *II* with 4-Acetylbiphenyl Acetylacetone and Cyanamide

An equimolar amount of *II* and *I* or acetylacetone or cyanamide (0.01 mol), respectively, in ethanol (100 ml) together with triethylamine (2 ml) was heated under reflux for 4 h. After cooling, the separated products were collected and recrystallized from the proper solvents to give 2-amino-4,6-di(4-biphenylyl)benzonitrile *III* 2-amino-3-acetyl 4-methyl-6-(4-biphenylyl)benzonitrile *IV* and 2-amino-1,3-dicyano-4-(4-biphenylyl)-5*H*-pyrroline *V*, respectively.

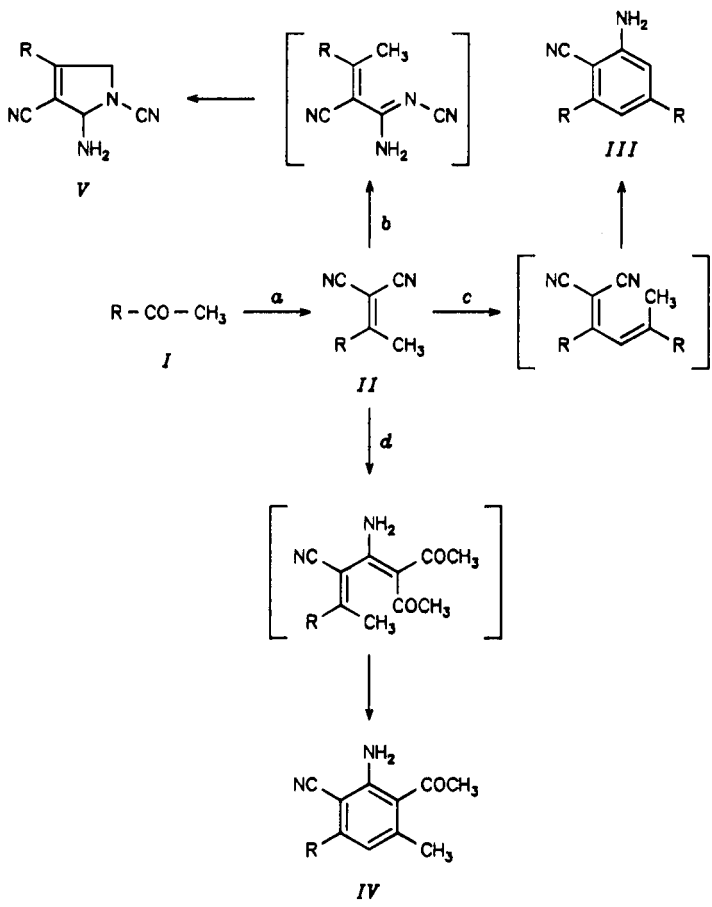
Reaction of *II* with Carbon Disulfide

To a mixture of *II* (0.01 mol) and ethanolic potassium hydroxide (0.02 mol, 100 ml), carbon disulfide (0.012 mol) was added dropwise while stirring at 15 – 20 °C. After complete addition, stirring was continued for

further 4 h. On acidification with concentrated HCl a red precipitate was obtained which on recrystallization gave pale brown crystals of thiopyrane *VII*.

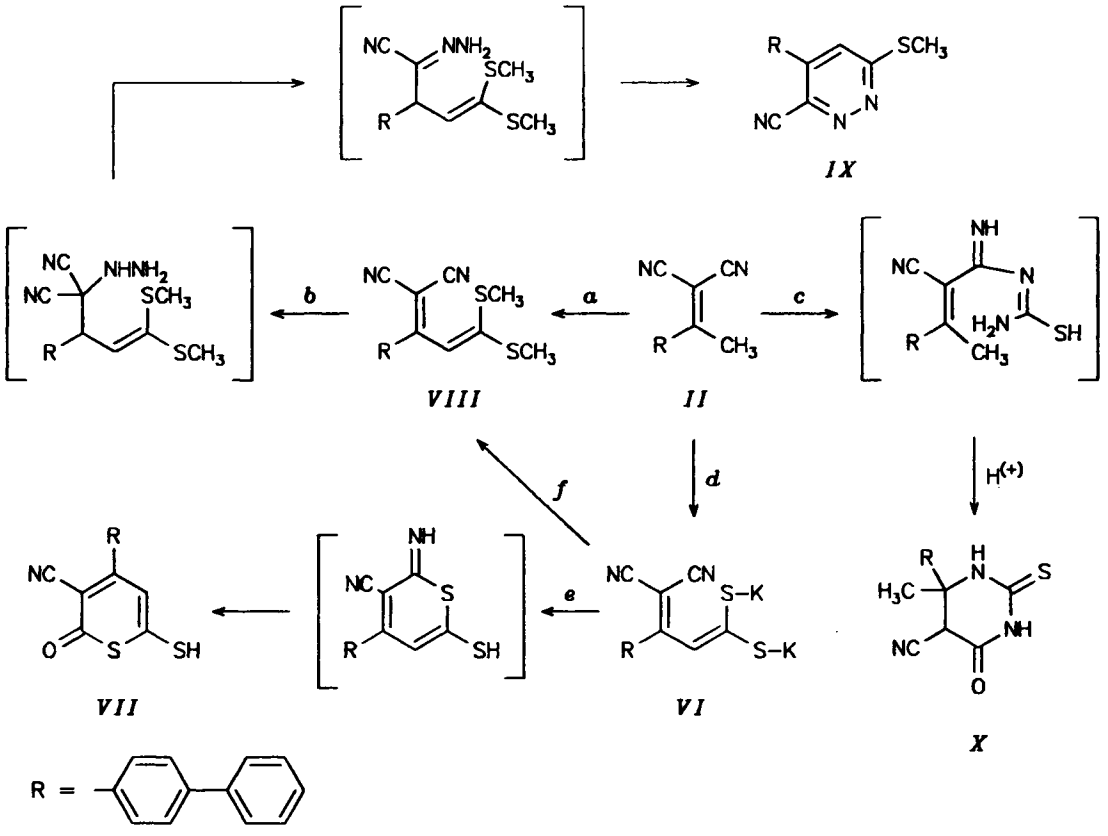
Synthesis of Compound *VIII*

Method A: To a stirred solution of *VI* (0.01 mol) in ethanol (100 ml) methyl iodide (0.022 mol) was added in portions while stirring at room temperature. After complete addition, stirring was continued for further half



a) $CH_2(CN)_2$; *b)* NH_2CN; *c)* *I*; *d)* $CH_2(COCH_3)_2$

SCHEME 1



a) 1. CS_2, KOH; 2. CH_3I. *b)* N_2H_4. *c)* $SC(NH_2)_2$, $NaOC_2H_5$. *d)* CS_2, KOH. *e)* aq. HCl. *f)* CH_3I

SCHEME 2

an hour, then ethanol was distilled off and the residue was triturated with water three times to give a viscous oil with green fluorescence.

Method B: To solution of *II* (0.01 mol) in stirred dimethylformamide (100 ml) at room temperature, potassium hydroxide (0.022 mol) was added, then carbon disulfide (0.012 mol) followed by addition of methyl iodide (0.025 mol) in portions. Stirring was continued for further 3 h, then DMF was distilled off to leave a residue which on trituration with water gave a viscous oil *VIII* that was used directly for the next step.

Reaction of *VIII* with Hydrazine Hydrate

An equimolar amount of *VIII* and hydrazine hydrate in ethanol (100 ml) and triethylamine (1 ml) was stirred at room temperature for 5 h and left overnight. On filtration and recrystallization gave pyridazine *IX*.

Reaction of *II* with Thiourea

To a mixture of *II* (0.01 mol) and sodium ethoxide (0.011 mol) in ethanol (100 ml), thiourea (0.01 mol) was added, then heated under reflux for 6 h. After cooling and neutralization with cold dilute hydrochloric acid, the product *X* was obtained.

TABLE I
List of newly synthesized compounds

Compound	M. p., °C Cryst. solvent	Colour	Formula (M. w.)	Calculated / Found			
				% C	% H	% N	% S
II	161	light yellow	$C_{17}H_{12}N_2$	83.58	4.95	11.46	–
	ethanol		(244.3)	83.6	5.0	11.5	–
III	105	pale brown	$C_{31}H_{22}N_2$	88.12	5.24	6.62	–
	ethanol		(422.5)	88.0	5.3	6.4	–
IV	153	buff cryst.	$C_{22}H_{18}ON_2$	80.96	5.55	8.58	–
	ethanol		(326.4)	81.1	5.5	8.6	–
V	135	ochre cryst.	$C_{18}H_{14}N_4$	75.44	4.92	19.56	–
	benzene/pet. ether		(286.3)	75.6	4.9	19.6	–
VII	106	pale brown cryst.	$C_{18}H_{11}NOS_2$	67.26	3.44	–	19.95
	ethanol		(321.4)	67.3	3.4	–	20.1
IX	99	pale yellow cryst.	$C_{18}H_{13}N_3S$	71.26	4.31	13.84	10.56
	ethanol		(303.4)	71.3	4.2	13.9	10.6
X	96	pale yellow cryst.	$C_{18}H_{15}N_3OS$	67.27	4.7	13.07	9.97
	methanol		(321.4)	67.3	4.6	12.0	10.0

TABLE II
IR and ^1H NMR spectra for newly prepared compounds

Compound	ν_{max}, cm^{-1}	δ, ppm
II	2 225 (CN), 2 220 (CN)	2.3 – 2.5, 3 H (CH_3); 7.5 – 8, 9 H (biphenyl)
III	2 220 (CN), 3 450 – 3 340 (NH_2)	7.4 – 7.6 and 7.65 – 8.1, 20 H (2 C_6H_5 – C_6H_4 + C_6H_2); 8.3 – 8.4, 2 H (NH_2)
IV	1 690 (C=O), 2 220 (CN), 3 520 – 3 440 (NH_2)	2.6, 3 H (CH_3); 3.1, 3 H ($COCH_3$); 7.2, 1 H (benzene); 7.4 – 7.8, 9 H (biphenyl)
V	2 190, 2 210 (2 CN), 3 580 – 3 410 (NH_2)	2.9, 2 H (NH_2); 3.3, 2 H (CH_2); 6.85, 1 H (CH); 7.4 – 7.8, 9 H (biphenyl)
VII	1 690 (C=O), 2 225 (CN), 2 620 (SH)	5.35, 1 H (CH, thiopyran 5(H)); 7.3 – 7.8, 9 H (biphenyl)
IX	1 635 (C=N), 2 215 (CN\), 3 350 (NH)	2.55, 3 H (S-CH_3); 6.7, 1 H (4(H) pyridazine); 7.4 – 7.7, 9 H (biphenyl)
X	1 690 (C=O), 2 210 (CN)	2.6, 3 H (CH_3); 6.1, 1 H (4(H) pyrimidine); 7.3 – 7.6, 9 H (biphenyl); 8 – 8.2, 2 H (NH_2)

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