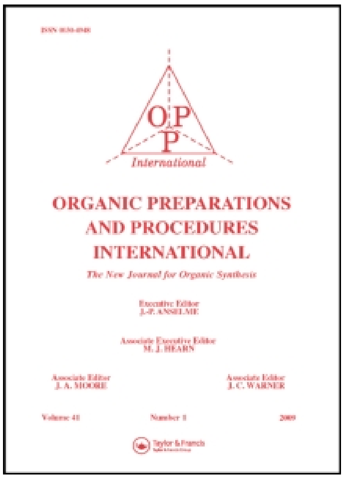

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NOVEL 1,3-DIARYLPYRAZOLINES AND PYRAZOLO[3,4-d]PYRIDAZINES

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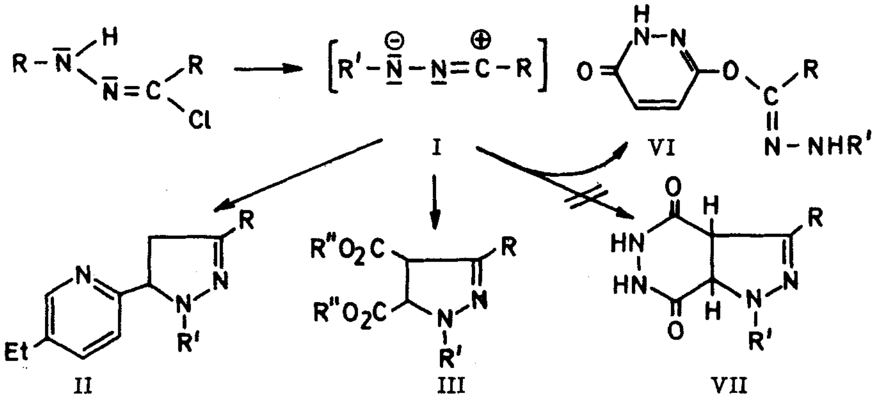
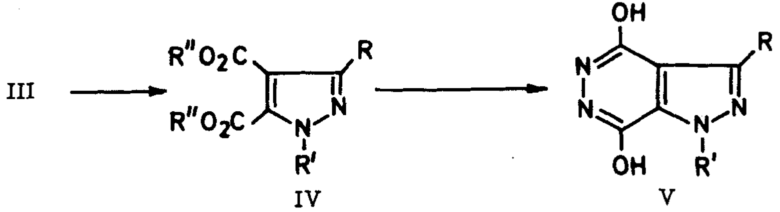
1,3-Dipolar cycloaddition of diarylnitrilimines(I)[1] -prepared *in situ* from N-aryl carbohydrazonoylchlorides[2]- with 5-ethyl-2-vinylpyridine gave the pyrazolines II. With diethyl or dimethyl maleate the corresponding pyrazoline dicarboxylates III were obtained, which after dehydrogenation with chloranil to IV were converted to the pyrazolo[3,4-d]pyridazines V.



IIa, IIIa; R = R' = C_6H_5, R" = C_2H_5; IIb, IIIb, VI: R = R' = 4-ClC_6H_4, R" = C_2H_5; IIc: R = C_6H_5, R' = 4-ClC_6H_4; IId: R = C_6H_5, R' = 3,4-$Cl_2C_6H_5$; IIe: R = 4-ClC_6H_4, R' = C_6H_5; IIIc: R = 2,4-$Cl_2C_6H_3$, R' = C_6H_5, R" = CH_3



IVa, Va: R = R' = C_6H_5, R" = C_2H_5; IVb, Vb: R = R' = 4-ClC_6H_4, R" = C_2H_5; IVc: R = 2,4-$Cl_2C_6H_3$, R' = C_6H_5, R" = CH_3.

Reaction of I with maleic acid hydrazide in DMF did not give the 3a,7a-dihydropyrazolo[2,3-d]pyridazine VII, but the substitution product VI.

EXPERIMENTAL

1,3-Dipolar Additions of Nitrilimines. General Procedure.- To a solution of the N-aryl benzenecarbohydrazonoylchloride (50 mmol) and the dipolarophile (125-250 mmol) in 200 ml dry benzene at reflux, was added 30 ml of purified triethylamine. Triethylamine hydrochloride separated immediately and the reaction mixture was heated at reflux for 30 min. The cooled mixture was filtered and the precipitate, which consisted of 90-98% of the theoretical quantity of $Et_3N{\cdot}HCl$, was washed with benzene. The combined filtrates were washed with water (3 x 250 ml) and dried (Na_2SO_4). Distillation of benzene and excess of dipolarophile gave the crude product, which was purified by distillation of recrystallization.

Dehydrogenation of III with Chloranil. Dimethyl (or diethyl)1,3-diarylpyrazole-4,5-dicarboxylates (IV).- A solution of III (80 mmol) and chloranil (80 mmol) in 70 ml DMF was heated at reflux for 30 minutes. The cooled solution was diluted with 600 ml ether, decanted, and washed with 2N KOH (4 x 150 ml), 2N HCl (150 ml) and water (150 ml). Drying ($CaCl_2$) and evaporation of the solvent gave the crude product, which was recrystallized.

4,7-Dihydroxy-1,3-diphenylpyrazolo[3,4-d]pyridazine (Va).- A solution of 15.0 g (41.1 mmol) of IVa and 35.0 g hydrazine hydrate in 20 ml ethanol was heated at reflux for 3.5 hrs. The crystallized product was filtered and combined with the precipitate that formed upon acidification of the filtrate to give 12.1 g (96.0%) crude product. A small portion was re-

			Elemental Analysis Calcd Found		
Cmpd	Yield (%)	mp (°C) (recryst. solvent)	C	H	N
IIa	46	yellow oil,	80.70	6.46	12.83
		bp 160°/0.1 mm	80.93	6.33	12.98
IIb	98	143-145°	66.67	4.83	10.60
		(ligroin)	66.93	4.91	10.52
IIc	78	115-118°	73.02	5.57	11.61
		(ligroin)	72.89	5.62	11.42
IId	48	116-119°	66.67	4.83	10.60
		(ligroin)	66.63	4.92	10.92
IIe	79	117-119°	73.02	5.57	11.61
		(methanol)	73.17	5.62	11.73
IIIa[1]	91	41-49°	68.84	6.05	7.65
		bp 160°/0.07 mm	68.54	6.03	7.56
IIIb[1]	93	148-150°	57.94	4.63	6.44
		(ethanol)	57.92	4.68	6.38
IIIc[2]	95	116-118°	56.04	3.96	6.88
		(methanol)	56.14	4.03	6.92
IVa	84	85.5-87.5°	69.22	5.53	7.69
		(methanol)	69.05	5.63	7.55
IVb	60	101-103°	58.21	4.19	6.47
		(methanol)	58.10	4.19	6.44
IVc	72	145-147°	56.04	3.96	6.88
		(ethanol)	56.14	4.03	6.92

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1. Diethyl maleate as dipolarophile. 2. Dimethyl fumarate as dipolarophile.

crystallized from acetic acid to yield colorless needles, mp. 339-342°.

Anal. Calcd for $C_{17}H_{12}N_4O_2$: C, 67.10; H, 3.97; N, 18.41.
Found: C, 66.65; H, 4.12; N, 18.12.

1,3-Di-(4-chlorophenyl)-4,7-dihydroxypyrazolo[3,4-d]pyridazine (Vb) was prepared in a similar fashion to yield colorless crystals from acetic acid (86%), mp. 327° (sublimation).

Anal. Calcd for $C_{17}H_{10}Cl_2N_4O_2$: C, 54.71; H, 2.70; N, 15.01.
Found: C, 54.44; H, 2.80; N, 14.89.

α-(3-Hydroxypyridazin-6-yl-oxy)-4-chlorobenzaldehyde-4-chlorophenylhydrazone (VI).- To a solution of maleic acid hydrazide (5.6 g, 50 mmol) and N-(4-chlorophenyl)-4-chlorobenzenecarbohydrazonoyl chloride (15.0 g, 50 mmol) in 100 ml reagent grade DMF at 100°, was added triethylamine (28.0 ml) and the reaction mixture kept at this temperature for 90 min. The cooled mixture was filtered. The filtrate was concentrated in vacuo and the residue dissolved in methylene chloride (500 ml). The solution was extracted with 2N KOH (4 x 250 ml). The combined alkaline extracts were washed with CH_2Cl_2 (2 x 150 ml) and acidified with 2N HCl to yield 9.7 g (52%) of a yellow precipitate which was washed with dil. HCl and water. Recrystallization from ethanol (charcoal) gave 6.1 g yellow crystals, mp 254-257°.

Anal. Calcd for $C_{17}H_{12}Cl_2N_4O_2$: C, 54.42; H, 3.22; N, 14.93.
Found: C, 54.20; H, 3.30; N, 14.86.

REFERENCES

1. R. Huisgen, M. Seidel, G. Wallbillich and H. Knupfer, Tetrahedron, 17, 3 (1962).
2. G. Kaugars. E. G. Gemrich and V. L. Rizzo, J. Agr. Food Chem., 21 647 (1973).