PYRAZOLOBENZOTHIAZOLES AND THEIR CONVERSION TO CYANINE DYES

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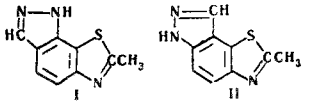
Thiocyanation of 5- and 6-aminoindazoles gives 5-amino-4-thiocyanoindazole and 6-amino-7-thiocyanoindazole. Sodium sulfide reduction of these aminothiocyano derivatives, followed by cyclization with acetic anhydride gives 2-methylpyrazolo[5, 4-g] benzothiazole and 2-methylpyrazolo[4, 5-g]benzothiazole. Dimethyl sulfate alkylation in alkaline solution gives 2, 6-dimethylpyrazolo[5, 4-g]benzothiazole and 2, 8-dimethylpyrazolo[4, 5-g]benzothiazole. Quaternary salts of the latter were used to synthesize symmetrical and unsymmetrical trimethinecyanines, monomethinecyanines, and dimethinemerocyanines containing the thiocyano group, as well as styryl dyes. It is found that 2-methylpyrazolo[4, 5-g]benzothiazole is less basic than 2-methylpyrazolo[5, 4-g]benzothiazole and more basic than unsubstituted benzothiazole.

The present paper presents a continuation of a series of researches which we have carried out on the synthesis of condensed tricyclic heterocyclic compounds, and cyanine dyes derived from them [1]. The present work aimed to prepare new tricyclic heterocyclic compounds: 2-methylpyrazolo[4, 5-g]benzothiazole (I) and 2-methylpyrazolo[5, 4-g]benzothiazole (II):



The starting compound for synthesis of base I was 6-aminoindazole, for synthesis of base II, 5-aminoindazole. They were thiocyanated, and the thiocyano derivatives reduced with sodium sulfide to mercapto derivatives. The latter were then cyclized to the corresponding pyrazolobenzothiazoles (equations 1 and 2 below).

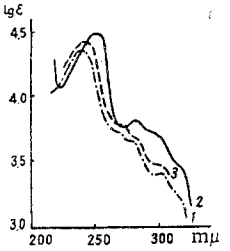


Fig. 1. UV spectra in EtOH. 1) 2-Methylpyrazolo[4, 5-g] benzothiazole; 2) 2, 8-dimethylpyrazolo [4, 5-g]-benzothiazole; 3) 2-methyl-8-ethylpyrazolo[4, 5-g] benzothiazole.

Thiocyanation of aminoindazoles has not hitherto been described. In this reaction the thiocyano group can enter at position 5 or 7 (with 6-aminoindazole), or at position 4 or 6 (with 5-aminoindazole).

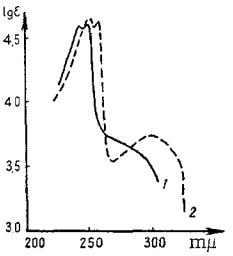
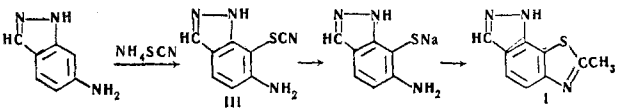


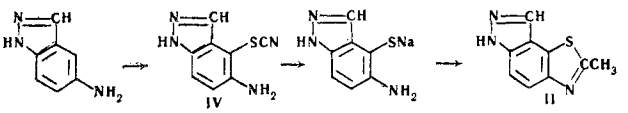
Fig. 2. UV spectra in EtOH. 1) 2-Methylpyrazolo[5, 4-g] benzothiazole; 2) 2, 6-dimethylpyrazolo [5, 4-g]-benzothiazole.

It is known that [2, 3] in electrophilic substitution reactions of 6-aminoindazoles, the substituent enters at position 7, while with 5-aminoindazoles it enters at position 4.

For this reason it can be deduced that thiocyanation of 6-aminoindazole gives 6-amino-7-thiocyanoindazole (III, equations 1), so that the resultant pyrazolobenzothiazole has structure I:



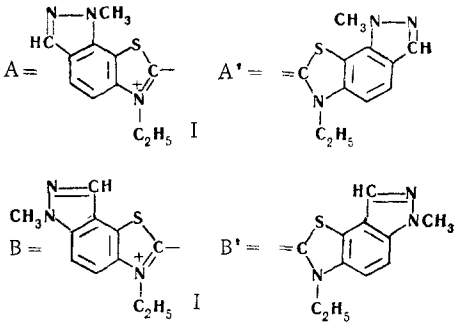
Similarly thiocyanation of 5-aminoindazole gives 5-amino-4-thiocyanoindazole (IV, equations 2), and the second isomeric pyrazolobenzothiazole isolated has the structure II:



Alkylation of indazoles in alkaline solution usually gives 1- and 2-alkylindazoles [4, 5]. The UV spectra of 1-alkylindazoles resemble the absorption spectra of unsubstituted indazoles, and differ greatly from the absorption spectra of 2-alkylindazoles [6].

Alkylation of pyrazolobenzothiazoles with dimethyl and diethyl sulfates in alkaline solution would be expected to give, in the case of base I, two isomeric compounds A and B:

Dyes with Pyrazolobenzothiazole Rings

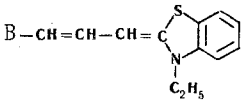
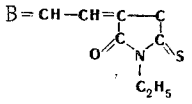
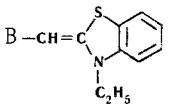
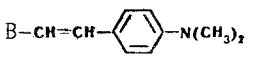


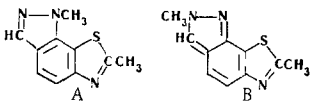
Dye number	Dye structure and name	Mp, ° C	Absorption maximum mμ	Formula	S, % Found	S, % Calculated	Yield, %
VII	A—CH=CH—CH=A′ Bis(3-ethyl-8-methylpyrazolo[4, 5-g] benzothiazole-2)trimethinecyanine iodide	259*	590	$C_{25}H_{25}IN_6S_2$	10.68 10.76	10.66	44
VIII	(3-Ethyl-8-methylpyrazolo[4, 5-g] benzothiazole-2)(3-ethylbenzo-thiazole-2)trimethinecyanine iodide	275	574	$C_{23}H_{23}IN_4S_2$	11.62 11.61	11.72	34
IX	3-Ethyl-5-(3-ethyl-8-methylpyrazolo [4, 5-g]benzothiazole-2-ethylidene)-thiazolidine-2-thione-4-one	>320	548	$C_{18}H_{18}ON_4S_3$	23.68 23.64	23.88	30
X	(3-Ethyl-8-methylpyrazolo[4, 5-g] benzothiazole-2)(3-ethylbenzo-thiazole-2)monomethinecyanine iodide	280	436	$C_{21}H_{21}IN_4S_2$	12.21 12.24	12.30	46
XI	2-p-Dimethylaminostyryl-8-methyl-pyrazolo[4, 5-g]benzothiazole methiodide	242	538	$C_{21}H_{23}IN_4S$	25.65** 25.76	25.91**	55

*Uncorrected mp.

**Iodine content.

Table (cont'd)

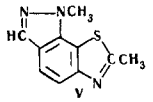
Dye number	Dye structure and name	Mp, ° C	Absorption maximum mμ	Formula	S, %		Yield, %
					Found	Calculated	
XII	B—CH=CH—CH=B' Bis(3-ethyl-6-methylpyrazolo [5, 4-g]benzothiazole-2) triemethinecyanine iodide 	279	588	$C_{25}H_{25}IN_6S_2$	10.49 10.56	10.66	36
XIII	(3-Ethyl-6-methylpyrazolo[5, 4-g] benzothiazole-2)(3-ethylbenzo-thiazole-2)trimethinecyanine iodide 	210	573	$C_{23}H_{23}IN_4S_2$	11.47 11.49	11.72	30
XIV	3-Ethyl-5(3-ethyl-6-methylpyrazolo [5, 4-g]benzothiazole-2-ethylidene)-thiazolidine-2-thione-4-one 	285	544	$C_{18}H_{18}ON_4S_3$	23.79 23.69	23.88	37
XV	(3-Ethyl-6-methylpyrazolo[5, 4-g] benzothiazole-2)(3-ethylbenzo-thiazole-2)monomethinecyanine iodide 	274	436	$C_{21}H_{21}IN_4S_2$	12.21 12.24	12.30	39
XVI	2-p-Dimethylaminostyryl-6-methyl-pyrazolo[5, 4-g]benzothiazole methiodide	240	532	$C_{21}H_{23}IN_4S$	24.14** 24.16	24.14**	51



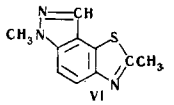
A B

However, chromatography of aluminum oxide enabled only one alkylation product to be isolated either in the case of base I, or in the case of base II.

It is possible to conclude, from the fact that the UV absorption spectrum plot of I resembles that of its alkylation product (Fig. 1), that alkylation of I gives 2,8-dimethylpyrazolo[4,5-g]benzothiazole (V).



V



VI

Similarly, the UV absorption spectra of base II and its alkylation products are alike (Fig. 2); hence the alkylation product of II is 2,6-dimethylpyrazolo-[5,4-g]benzothiazole (VI).

Heating V and VI with dimethyl sulfate, ethyl tosylate, or ethyl iodide, gives monoquaternary salts, from which the cyanine dyes given in the table were synthesized in the usual way.

The data in the table show that the absorption maxima of dyes from base I are slightly displaced towards the long wavelength region compared with those of the dyes from base II. Both series of dyes absorb in the region of wavelengths longer than is the case for the isomeric dyes with thiazolobenzimidazole rings [7]. Dye VII is less basic than dye XII. The basicities of these dyes were assessed according to A, a quantity characterizing ease of decoloration of cyanine dyes by hydrochloric acid [8]. For XII, A = 1.1, while VII is only 21% decolorized by 1.7 mole HCl per liter of aqueous ethanolic solution. This is due to the difference between the structures of I and II. I has a CN group at position 6 in the benzothiazole ring which draws electrons from the nitrogen atom of the thiazole ring, so that I is less basic than benzothiazole. Base II has a nitrogen atom with a lone pair of electrons conjugated with the nitrogen atom of the thiazole ring, so that II is more basic than benzothiazole.

EXPERIMENTAL

6-Amino-7-thiocyanoindazole (III). A solution of 2.6 ml (0.05 mole) bromine in 40 ml MeOH saturated with NH_4Br was added dropwise, over a period of an hour, to 6.65 g (0.05 mole) 6-aminoindazole [9], and 11.4 g (0.015 mole) NH_4CHS dissolved in 50 ml MeOH cooled to −5° to −10° C, with stirring. The mixture was stirred for 1 hr longer, the precipitate filtered off, washed with water, then with EtOH, and dried in a vacuum-desiccator. Recrystallized from dioxane-benzene (1:1), mass 5 g (53%), colorless needles, turning pink in air. Found: S 16.45; 16.55%. Calculated for $C_8H_6N_4S$: S 16.38%.

2-Methylpyrazolo[4,5-g]benzothiazole (I). 8g (0.042 mole) III was gradually added to a solution of 20.4 g (0.085 mole) sodium sulfide in 15 ml water which was stirred, and held at 60°−70° C. The colorless solution obtained was heated for a further 10 min at 80°, filtered, and 20 ml Ac_2O added to the filtrate. The mixture was heated for 3 hr on a boiling water-bath, cooled, and neutralized with ammonia. The precipitate of I formed was recyrstallized from EtOH (charcoal). Mass 6.2 g (78%), colorless needles, mp 252°−253° C (decomp). Found: S 16.79; 16.86%. Calculated for $C_9H_7N_3S$: S 16.92%.

5-Aminoindazole [5] was thiocyanated under the conditions described for 6-aminoindazole. Yield of impure IV 73%. Crystallization from EtOH or other solvent is accompanied by isomerization to an aminothiazole derivative characterized by a high mp (309°), and insolubility in aqueous sodium sulfide solution. Found: S 16.58; 16.52%. Calculated for $C_8H_6N_4S$: S 16.83%.

2-Methylpyrazolo[5,4-g]benzothiazole (II). This was prepared from crude IV by reduction with aqueous sodium sulfide followed by cyclization in Ac_2O, similarly to I. Colorless needles, yield 46%, mp 188° C (ex EtOH). Found: S 16.79; 16.69%. Calculated for $C_9H_7N_3S$: S 16.92%.

2,8-Dimethylpyrazolo[4,5-g]benzothiazole (V). 1.9 g (0.01 mole) 2-methylpyrazolo[4,5-g]benzothiazole (I) was added to a solution of 1 g KOH in 25 ml dry EtOH. The resultant solution was stirred, and 2.5 g (0.02 mole) Me_2SO_4 added, then the whole refluxed for 1 hr on a water-bath. After cooling the precipitate was filtered off, washed with EtOH, and the solvent vacuum-distilled off from the filtrate. The liquid residue was dissolved in $CHCl_3$, and run through an Al_2O_3 column. No isomers could be detected. After distilling the eluate, the liquid left solidified on standing. Snow-white crystals (ex petrol ether), mass 0.85 g (42%), mp 103°−104° C. Found: S 15.80; 15.88; N 20.67; 20.57%, Calculated for $C_{10}H_9N_3S$: N 20.68; S 15.76%. Picrate: pale yellow needles (ex EtOH), mp 196° C. Found: N19.62; 19.53%. Calculated for $C_{16}H_{12}N_6O_7S$: N 19.44%.

2-Methyl-8-ethylpyrazolo[4,5-g]benzothiazole was prepared similarly to V, from base I and Et_2SO_4. Colorless needles (ex petrol ether), yield 60%, mp 81° C. Found: S 15.47; 15.55%. Calculated for $C_{10}H_9N_3S$; S 15.76%. Picrate: yellow needles (ex EtOH). mp 172° C, Found: N 18.59; 18.78%. Calculated for $C_{17}H_{14}N_6O_7S$: N 18.83%.

2,6-Dimethylpyrazolo[5,4-g]benzothiazole (VI) was prepared similarly to V, from base II and Me_2SO_4. Yield 61%, colorless needles (ex petrol ether), mp 103° C. Found: S 15.47; 15.55%. Calculated for $C_{10}H_9N_3S$: S 15.76%. Picrate: yellow needles (ex EtOH), mp 214° C. Found: N 19.20; 19.26%. Calculated for $C_{16}H_{12}N_3O_7S$: N 19.44%.

2,8-Dimethylpyrazolo[4,5-g]benzothiazole ethiodide was prepared by heating together for 3 hr, equi-

molecular amounts of V and ethyl tosylate, at 120°–130° C, and then converting the tosylate to the iodide in the usual way. Colorless plates (ex EtOH), yield 65%, mp 251° C. Found: I 37.05; 37.08%. Calculated for $C_{11}H_{12}IN_3S$: I 36.81%.

2,6-Dimethylpyrazolo[5,4-g]benzothiazole perchlorate was prepared similarly to V tosylate. Found: Cl 10.96; 11.04%. Calculated for $C_{12}H_{14}ClN_3 \cdot O_4S$: Cl 10.71%.

2,6-Dimethylpyrazolo[5,4-g]benzothiazole ethiodide prepared by heating VI with EtI in a sealed tube for 6 hr, yield 73%.

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