67. 4-*Pyrones. Part II.*[1] *Action of Alkylamines on 2-Methyl- and 2-Styryl-naphtho*[1,2-b]-4-*pyrones and on 2,6-Distyryl-4-pyrones and their Sulphur Analogues.*

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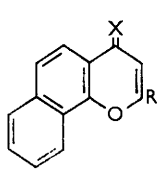
The reaction of the pyrones and thiopyrones named in the title with alkylamines depends on the alkalinity of the medium and on the $-T$ effect of the carbonyl and the thiocarbonyl group. 2-Methylnaphtho[1,2-*b*]-4-pyrone gives an amino-ketone, the corresponding thiopyrone undergoes degradation to 2-acetyl-1-naphthol *N*-alkylimine. 2-Styrylnaphtho[1,2-*b*]-4-pyrone and -thiopyrone give a double condensation product; the 2,6-distyryl derivatives do not react with amines.

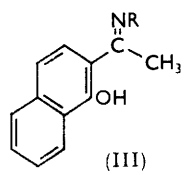
2-Styrylnaphtho[1,2-*b*]-4-pyrone and -thiopyrone and their derivatives were prepared from the 2-methyl compound and araldehydes by the method of Schönberg *et al.*[2] but attempts to effect this condensation with ketones, *e.g.*, acetone, acetophenone, benzophenone, in alkaline or acid media failed.

In a previous paper[3] two of us have shown that 2,6-disubstituted 4-pyrones and

(I) X=O. (II) X=S.

a: R = Me
b: R = CH:CHPh
c: R = CH:CH·C_6H_4Me-*p*
d: R = CH:CH·C_6H_4Cl-*p*
e: R = CH:CH·C_6H_4·OMe-*p*



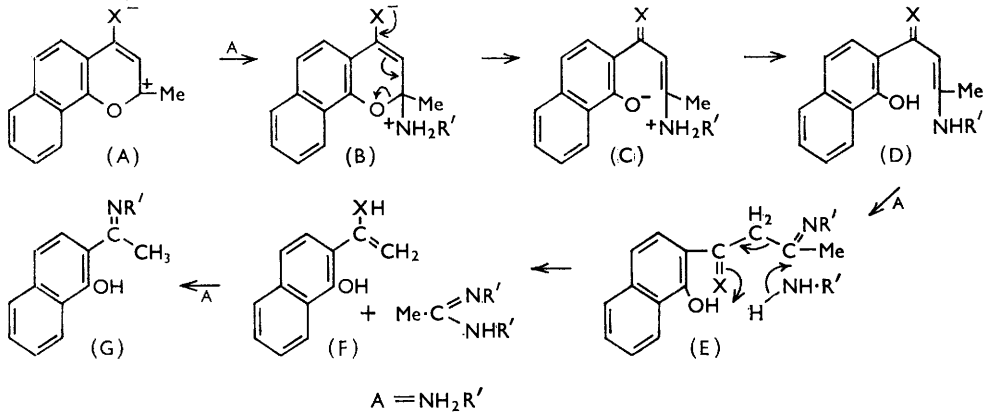


(III)

-thiopyrones react with alkylamines to give the corresponding *N*-alkylpyridones. On the other hand, Sammour,[4] treating 2-methylnaphtho[1,2-b]-4-pyrone with alkylamines,

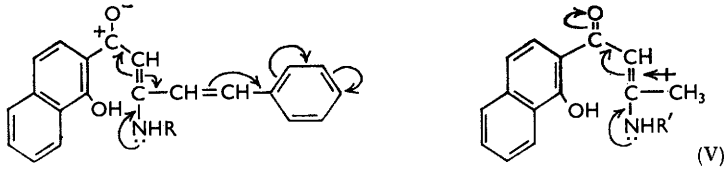
[1] Part I, *J. Amer. Chem. Soc.*, 1960, **82**, 4344.
[2] Schönberg, Fateen, and Sammour, *J. Amer. Chem. Soc.*, 1956, **78**, 4689.
[3] Elkaschef and Nosseir, *J. Amer. Chem. Soc.*, 1960, **82**, 4344.
[4] Sammour, *J. Org. Chem.*, 1958, **23**, 1222.

obtained the corresponding alkylaminoallyl ketones. We confirmed Sammour's work with methylamine and the pyrone, obtaining 1-hydroxy-2-naphthyl methylaminopropenyl ketone; butyl- and benzyl-amine in benzene also gave the compounds claimed by him. But the thiopyrone with these amines afforded 2-acetyl-1-naphthol *N*-alkylimines (III), and thence on acid hydrolysis afforded 2-acetyl-1-naphthol. We postulate the mechanism shown in the annexed scheme (X = S).



Evidence favouring this mechanism was sought as follows: The 2-methylnaphtho[1,2-*b*]-4-thiopyrone did not react with methylamine hydrochloride in the presence of sodium acetate, a fact previously observed for 2,6-disubstituted 4-thiopyrones.[5] Hydrolysis of the 2-methylnaphthopyrone (Ia) or its sulphur analogue (IIa) with sodium hydroxide afforded 2-acetyl-1-naphthol, which condensed with alkylamines to give the corresponding ketimines (III).

The reaction between alkylamines and the naphtho-pyrone or -thiopyrone depends on both the alkalinity of the amine and the $-T$ effect of the carbonyl or thiocarbonyl group. Thus, while 2-methylnaphtho[1,2-*b*]-4-pyrone oxime or benzylimine, with a weak $-T$ effect, does not react with alkylamines, the 2-methylnaphthopyrone undergoes ring cleavage with the same reagents (cf. A ⟶ D; X = O) and is degraded by sodium hydroxide.



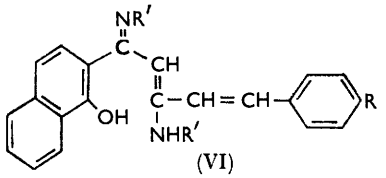
2-Methylnaphtho[1,2-*b*]-4-thiopyrone, with a strong $-T$ effect, is degraded even by alkylamines, but with the less alkaline benzylamine it gives the 4-pyrone benzylimine. The 2-styrylnaphtho-pyrones (Ib and d) and -thiopyrones (IIb, d, and e), on the other hand, undergo only ring cleavage, to give the ketones (IV) (cf. A ⟶ D; X = O).

2-4'-Methoxystyrylnaphtho[1,2-*b*]-4-pyrone (Ie), in contrast to its sulphur analogue (IIe), did not react with alkylamines owing to compensation of the positive charge at positions 2 and 6 (cf. reaction of 2,6-di-*p*-methoxyphenyl-4-pyrone with alkylamines [3]). The same styryl-pyrones and -thiopyrones with stronger alkaline reagents, *e.g.*, sodium hydroxide or ethoxide,[2] undergo degradation by the mechanism A ⟶ F (H_2O instead of NH_2R'), to give 2-acetyl-1-naphthol and cinnamic acid.

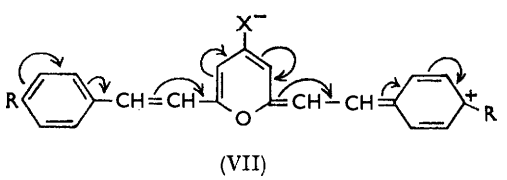
The ketones (V) do not react further with the amine, owing to the inductive effect of the methyl group and the mesomeric effect of the amino-group; but withdrawal of

[5] Elkaschef and Nosseir, unpublished work.

electrons by the styryl group in the ketone (IV) permits nucleophilic attack of the amino-group to give a double condensation product (VI), which has been separated from the reaction mixture. 2,6-Distyryl-4-pyrones and -thiopyrones (VII and derivatives: X = O or S), on the other hand, do not react with the amines, owing to distribution of the positive charge over the molecule.



(VI)



(VII)

2-Methylnaphtho[1,2-*b*]-4-pyrone with hydroxylamine gives an isoxazole,[2] but the naphthothiopyrones (IIa—e) react normally, giving oximes.

Experimental

Some analyses were done by the Unit of Microanalysis, N.R.C., Cairo.

Methyl- and ethyl-amine were 33% aqueous solutions. Light petroleum used had b. p. 70—80°

Styrylnaphtho-pyrone and -thiopyrones.—(*a*) To a solution of 2-methylnaphtho[1,2-*b*]-4-pyrone (Ia) (3·0 g.) in ethanol (20 c.c.) a solution of sodium ethoxide (from 0·4 g. of sodium) and *p*-chlorobenzaldehyde (2·4 g.) in ethanol (20 c.c.) was added. The mixture was left at room temperature for 2 days, then filtered. The solid product (Id) (5·5 g.), 2-4′-*chlorostyrylnaphtho*-[1,2-b]-4-*pyrone*, formed yellow crystals, m. p. 198°, from benzene–alcohol and gave an orange colour in concentrated sulphuric acid and a greenish fluorescence under ultraviolet light (Found: C, 76·3; H, 3·9; Cl, 10·7. $C_{21}H_{13}ClO_2$ requires C, 75·9; H, 3·9; Cl, 10·5%).

(*b*) 2-Methylnaphtho[1,2-*b*]-4-thiopyrone (IIa) (1·0 g.) and *p*-chlorobenzaldehyde (1·0 g.) in absolute ethanol (20 c.c.) containing 4 drops of piperidine were refluxed for 6 hr. 2-4′-*Chlorostyrylnaphtho*[1,2-b]-4-*thiopyrone* (0·8 g.) that separated formed from benzene violet crystals, m. p. 258° (decomp.), giving an orange colour in concentrated sulphuric acid (Found: S, 8·8. $C_{21}H_{13}ClOS$ requires S, 9·2%).

(*c*) The 4′-methylthiopyrone, obtained similarly and crystallised from benzene, had m. p. 235° (orange solution in sulphuric acid) (Found: C, 80·5; H, 5·0; S, 9·4. $C_{22}H_{16}OS$ requires C, 80·5; H, 4·9; S, 9·8%).

Action of Methylamine on 2-Methylnaphtho-[1,2-b]-4-*pyrone.*—2-Methylnaphtho[1,2-*b*]-4-pyrone (Ia) (1·0 g.) and methylamine (10 c.c.) in ethanol (50 c.c.) were refluxed for 8 hr. 2-(3-Methylaminobut-2-enoyl)-1-naphthol (0·5 g.) that separated on cooling formed from ethanol yellow crystals, m. p. 163°, that gave a green colour with ethanolic ferric chloride and an orange colour in concentrated sulphuric acid (Found: C, 74·6; H, 6·4; N, 5·8. $C_{15}H_{15}NO_2$ requires C, 74·7; H, 6·2; N, 5·8%).

Butylamine and benzylamine gave analogous products indentified by mixed m. p.s.[4]

Table 1.

2-Substituted naphtho[1,2-*b*]-4-pyrone oximes (I; X = N·OH).

2-Subst.	M. p.	Yield (g.)	Formula	Found: N, %	Reqd.: N, %
Me	182°	0·3	$C_{14}H_{11}NO_2$	6·2	6·2
CH:CHPh	210	0·4	$C_{21}H_{15}NO_2$	4·3	4·5
CH:CH·C_6H_4Me-*p*	256	0·3	$C_{22}H_{17}NO_2$	4·1	4·3
CH:CH·C_6H_4Cl-*p*	244	0·35	$C_{21}H_{14}ClNO_2$	4·0	4·0
CH:CH·C_6H_4·OMe-*p*	230	0·25	$C_{22}H_{17}NO_3$	4·0	4·1

Action of Hydroxylamine Hydrochloride on 2-Methyl- and 2-Styryl-naphtho[1,2-b]-4-*thio-pyrone.*—To the thiopyrone (0·5 g.) in ethanol (50 c.c.) were added hydroxylamine hydrochloride (0·7 g.) and sodium acetate (0·7 g.) in water (1 c.c.). The mixture was refluxed for 5 hr., cooled, and diluted with water. The solid yellow *oximes* that separated crystallised from ethanol (cf. Table 1); they gave a yellow colour in concentrated sulphuric acid.

Action of Alkylamines on 2-Methylnaphtho[1,2-b]-*4-thiopyrone.*—The thiopyrone (IIa) (0·5 g.) in ethanol (50 c.c.) with methyl-, ethyl- (10 c.c.), or butyl-amine (3 c.c.) was refluxed for 8 hr. The solid imine (III) that remained on evaporation of the solvent was crystallised from light petroleum (cf. Table 2). These compounds gave a deep green colour with ferric chloride and a yellow colour in concentrated sulphuric acid. Benzylamine in ethanol or benzene gave the *pyrone benzylimine* which gives reddish-brown colour in concentrated sulphuric acid and no colour with ferric chloride.

TABLE 2.

2-Acetyl-1-naphthol alkylimines (III).

			Found (%)				Required (%)		
R	M. p.	Yield (g.)	C	H	N	Formula	C	H	N
Me	142°	0·3	78·2	6·8	7·0	$C_{13}H_{13}NO$	78·4	6·6	7·0
Et	126	0·4	78·8	7·4	6·9	$C_{14}H_{15}NO$	78·8	7·1	6·6
Bu	106	0·3	79·5	8·1	5·7	$C_{16}H_{19}NO$	79·6	7·9	5·8
(CH_2Ph	217 *	0·24	84·6	5·7	4·7	$C_{21}H_{17}NO$	84·3	5·7	4·7)

* This product is the pyrone benzylimine.

Hydrolysis of the Imines (III).—The imine (0·5 g.) was refluxed with 17% hydrochloric acid (25 c.c.) for 0·5 hr. The first three of Table 2 afforded 2-acetyl-1-naphthol [6] (0·3 g.), m. p. and mixed m. p. 103°. The benzyl derivative was unchanged.

Hydrolysis of the Naphtho-pyrones and -thiopyrones by Sodium Hydroxide.—The pyrone (Ia) or thiopyrone (IIa) (0·5 g.) was refluxed in aqueous-ethanolic 20% sodium hydroxide (25 c.c.) for 4 hr. The mixture was filtered while hot, cooled, and acidified with dilute hydrochloric acid. The solid that separated and crystallised from ethanol proved to be 2-acetyl-1-naphthol, m. p. and mixed m. p. 103°.

Reaction of Alkylamines with 2-Acetyl-1-naphthol.—The ketone (0·5 g.) was heated for 6 hr. in ethanol (25 c.c.) with the alkylamine (10 c.c. for methyl- or ethyl-amine, 3 c.c. for butyl-amine). The crystals remaining on evaporation recrystallised from light petroleum and proved to be the imines recorded in Table 2. Yields were quantitative.

Benzylamine gave a similar *imine* (III; R = CH_2Ph), m. p. 147° (from ethanol) (Found: C, 83·4; H, 6·2; N, 5·2. $C_{19}H_{17}NO$ requires C, 82·9; H, 6·2; N, 5·1%).

2-Methylnaphtho[1,2-*b*]-4-pyrone oxime and benzylimine were unchanged when boiled with methylamine in alcohol for 6 hr. So was the thiopyrone (IIa) when boiled for 8 hr. in alcohol with methylamine hydrochloride and sodium acetate.

Reaction of 2-Styrylnaphtho[1,2-b]-*4-pyrones and -thiopyrones with Alkylamines.*—Each pyrone (Ib, c, d, or e) or thiopyrone (IIb, c, d, or e) (1·0 g.) was refluxed for 8 hr. in ethanol with methyl- or ethyl- (10 c.c.) or benzyl-amine (5 c.c.). The oil remaining on evaporation solidified under benzene. Recrystallised from benzene–alcohol it gave yellow crystals of the *amino-imine* (VI) that gave a yellow colour with concentrated sulphuric acid and a green colour in alcoholic ferric chloride (cf. Table 3).

TABLE 3.

2-(3-Alkylamino-1-alkylimino-5-arylpenta-2,4-dienyl)-1-naphthols (VI) obtained from the naphtho-pyrones (I) or -thiopyrones (II).

Subst. in (VI)				Found (%)			Required (%)	
R	R′	M. p.	Yield (g.) †	N	Cl	Formula	N	Cl
(H)	Me	210° *	0·6 (I), 0·9 (II)	7·7	—	$C_{23}H_{22}N_2O$	8·2	—
Cl	,,	215 *	0·9 (I, II)	6·8	9·0	$C_{23}H_{21}ClN_2O$	7·3	9·3
OMe	,,	205 *	0 (I), 1·0 (II)	7·4	—	$C_{24}H_{24}N_2O_2$	7·5	—
(H)	Et	187	0·6 (I), 1·0 (II)	7·6	—	$C_{25}H_{26}N_2O$	7·6	—
Cl	,,	234	1·0 (I), 0·6 (II)	6·4	8·1	$C_{25}H_{25}ClN_2O$	6·9	8·8
OMe	,,	236	0 (I), 1·0 (II)	7·1	—	$C_{26}H_{26}N_2O_2$	7·0	—
(H)	CH_2Ph	224 *	0·6 (I), 1·0 (II)	5·8	—	$C_{35}H_{30}N_2O$	5·7	—
Cl	,,	212 *	0·8 (I), 1·0 (II)	5·6	6·5	$C_{35}H_{29}ClN_2O$	5·6	6·7
OMe	,,	216	0 (I), 1·0 (II)	5·4	—	$C_{36}H_{32}N_2O_2$	5·4	—

* With decomp. † 0 denotes no reaction.

[6] Wittig, Bangert, and Richter, *Annalen*, 1926, **446**, 155.

TABLE 4.

2,6-Distyryl-4-pyrone (VII; X = O) and -thiopyrone (VII; X = S) and their *pp'*-disubstituted derivatives.

Subst., R	M. p.	Cryst. from	Yield (g.)	Found (%) C	Found (%) H	Formula	Required (%) C	Required (%) H
Pyrones								
(H)	168°	Aq. EtOH	1·0	83·9	5·4	$C_{21}H_{16}O_2$	84·0	5·4
OMe	199	EtOH	1·0	76·7	5·8	$C_{23}H_{20}O_4$	76·7	5·6
Me	192	EtOH	1·0	84·2	6·2	$C_{23}H_{20}O_2$	84·1	6·1
Cl	238	C_6H_6–EtOH	1·0	68·1	3·9	$C_{21}H_{14}Cl_2O_2$ *	68·3	3·8
Thiopyrones				S			S	
(H)	244	C_6H_6–EtOH	1·0	10·0		$C_{21}H_{16}OS$	10·1	
OMe	191	C_6H_6–EtOH	1·0	8·6		$C_{23}H_{20}O_3S$	8·5	
Me	217	C_6H_6	1·2	8·8		$C_{23}H_{20}OS$	9·3	

* Found: Cl, 18·9. Required: Cl, 19·2%.

Reaction of the naphthopyrone (Ib or d), but not of the thiopyrone, as above with butylamine (3 c.c.) gave 2-(3-*butylamino*-1-*butylimino*-5-*phenylpenta*-2,4-*dienyl*)-1-*naphthol* (VI; R = H, R' = Bu) (0·58 g.), m. p. 188° (Found: C, 81·7; H, 8·2; N, 6·6. $C_{29}H_{34}N_2O$ requires C, 81·7; H, 8·0; N, 6·6%), and its p-*chloro-analogue* (VI; R = Cl, R' = Bu) (0·9 g.), m. p. 216° (Found: C, 76·2; H, 7·1; N, 6·5; Cl, 8·1. $C_{29}H_{33}ClN_2O$ requires C, 75·6; H, 7·2; N, 6·1; Cl, 7·7%).

Condensation of 2,6-*Dimethyl*-4-*pyrone or -thiopyrone with Aromatic Aldehydes.*—2,6-Dimethyl-4-pyrone (1·0 g.), dissolved in a small quantity of absolute ethanol, was treated at room temperature with alcoholic sodium ethoxide (2 mol.) and then the aldehyde (2 mol.). The solution was kept for 48 hr. at room temperature. The product which usually separated was dissolved in ethanol; acidification with dilute hydrochloric acid precipitated the distyrylpyrone or -thiopyrone (VII) which was then recrystallised (see Table 4). These products were unchanged on treatment with alkylamines.

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