

On phthalides and 1,3-indandiones. LII.

Reactions of 3,6-dithia-3,4,5,6-tetrahydrophthalic anhydride with methyl derivatives of nitrogen-containing heterocycles

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It has been found that the condensation of 3,6-dithia-3,4,5,6-tetrahydrophthalic anhydride or phthalic anhydride with mono-, di-, and trimethyl derivatives of nitrogen-containing heterocycles gives the corresponding 2-substituted indandiones or their dithia analogs. The structure of the formed compounds has been determined on the basis of their n.m.r. and i.r. spectra. It has been found that only monoderivatives of the respective indandiones are formed.

A relatively readily available 3,6-dithia-3,4,5,6-tetrahydrophthalic anhydride [1] (dithiaphthalic anhydride) led us to its applications as a carbonyl component in reactions of the aldol type. In our previous works it was used as a carbonyl component in reactions with arylacetic acids using the Gabriel modification of the Perkin and Oglialoro synthesis [2]. It was also found that it reacts with anhydrides of aliphatic or malonic acids [3].

In this paper we present the results of reactions of dithiaphthalic anhydride with methyl derivatives of different nitrogen-containing heterocycles.

From among anhydrides of dicarboxylic acids it was phthalic [4–7] and naphthoic anhydrides [8, 9] which were used in reactions with methyl derivatives of nitrogen-containing heterocycles. Some of the formed phthalones are used in the dyestuff industry.

Dithiaphthalic anhydride was allowed to react with mono-, di-, and trimethyl derivatives of nitrogen-containing heterocycles. In reactions with di- and trimethyl derivatives only one methyl group reacted even in case a great excess of the carbonyl component was used (Table 2). The use of nitrobenzene as in [7, 10] did not much affect either the total yield or the reaction time in our case. In addition, the isolation of the product using this solvent was more laborious.

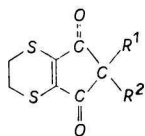
In addition to the preparation of the products listed in Table 1, dithiaphthalic anhydride was allowed to react with 3-methylisoquinoline and 2,3-dimethylquinoxaline. With these heterocycles the reactions did not proceed; but they did not react with phthalic anhydride either.

Phthalic anhydride was found to be reactive toward 4-methylpyridine, though the authors [7] stated the contrary; but dithiaphthalic anhydride was unreactive.

By column chromatography of the reaction products only the compounds of the indandione type were separated. Its structure was confirmed by determining the n.m.r. and i.r. spectra. Phthalide, described in reactions of phthalic anhydride with 2-methylpyridine by [5, 11] was not obtained.

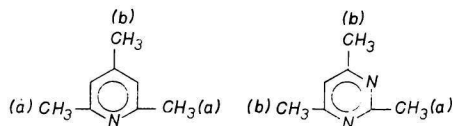
Two position isomers can be formed in the reaction of phthalic and dithiaphthalic anhydrides with 2,4-dimethylpyridine, 2,4,6-trimethylpyridine, and 2,4,6-trimethyl-

Table 1
Characterization of the prepared substances



Compound	R ¹	R ²	Formula <i>M</i>	Calculated/found					M.p. [°C]	Yield [%]	$\bar{\nu}_{as}(C=O)$ [cm ⁻¹]	$\bar{\nu}_s(C=O)$ [cm ⁻¹]
				% C	% H	% N	% S	% Br				
<i>I</i>	2-Pyridyl	H	C ₁₂ H ₉ O ₂ N ₁ S ₂ 263	54.73	3.44	5.32	24.35	—	271—272	32.8	1634	1673
				54.51	3.39	5.15	24.01	—				
<i>II</i>	2-(6-Methylpyridyl)	H	C ₁₃ H ₁₁ O ₂ N ₁ S ₂ 277.36	56.29	3.99	5.05	23.12	—	213—215	26.3	1640	1678
				56.42	4.11	4.94	23.46	—				
<i>III</i>	2-(4-Methylpyridyl)	H	C ₁₃ H ₁₁ O ₂ N ₁ S ₂ 277.36	56.29	3.99	5.05	23.12	—	281—283	22.9	1629	1672
				56.42	4.11	4.94	23.46	—				
<i>IV</i>	2-(4,6-Dimethylpyridyl)	H	C ₁₄ H ₁₃ O ₂ N ₁ S ₂ 291.39	57.70	4.49	4.80	21.99	—	261—263	21.0	1642	1672
				57.52	4.53	4.59	21.47	—				
<i>V</i>	4-(2,6-Dimethylpyrimidinyl)	H	C ₁₃ H ₁₂ O ₂ N ₂ S ₂ 292.38	53.40	4.13	9.58	21.93	—	278—279	21.3	1635	1690
				53.21	4.02	9.77	21.68	—				
<i>VI</i>	2-Quinolyl	H	C ₁₆ H ₁₁ O ₂ N ₁ S ₂ 313.4	61.32	3.53	4.47	20.46	—	277—278	36.2	1638	1680
				60.97	3.44	4.61	20.47	—				
<i>VII</i>	2-Pyridyl	Br	C ₁₂ H ₈ O ₂ N ₁ S ₂ Br 342.24	42.11	2.36	4.09	18.71	23.35	184—185	62.6	1703	1744
				41.98	2.27	4.23	18.53	23.61				
<i>VIII</i>	2-(6-Methylpyridyl)	Br	C ₁₃ H ₁₀ O ₂ N ₁ S ₂ Br 356.26	43.82	2.82	3.93	18.00	22.43	179—181	51.5	1701	1742
				43.45	2.69	3.67	17.81	22.81				
<i>IX</i>	2-Quinolyl	NO ₂	C ₁₆ H ₁₀ O ₄ N ₂ S ₂ 358.40	53.63	2.79	7.82	17.87	—	167—169 decomp.	54.8	1706	1752
				53.18	2.61	7.98	18.01	—				

Table 2

Proton signals of methyl groups [δ]

Compound	<i>a</i>	<i>b</i>
2,6-Dimethylpyridine	2.42	—
<i>II</i>	2.39	—
2,4-Dimethylpyridine	2.43	2.22
<i>III</i>	—	2.27
2,4,6-Trimethylpyridine	2.35	2.20
<i>IV</i>	2.33	2.22
2,4,6-Trimethylpyrimidine	2.45	2.16
<i>V</i>	2.45	2.30

pyrimidine: in the first two cases by reaction of the methyl group in positions 2 (6) and 4 respectively. 2,4,6-Trimethylpyrimidine has nonequivalent groups in positions 2 and 4 (6). In both cases only one position isomer was formed. By comparing the n.m.r. spectra of the starting methyl derivatives of nitrogen-containing heterocycles and the

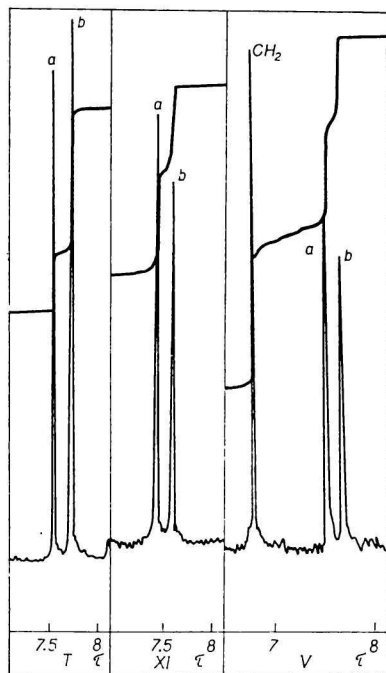
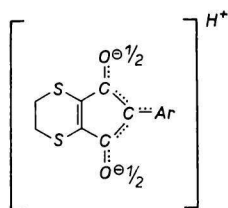


Fig. 1. NMR spectra. Resonance signals of protons of methyl groups of 2,4,6-trimethylpyrimidine (T) and of the compounds *V* and *XI*.

products formed it was found (from disappearance of the resonance signal or from the change in the ratio of integrated intensities of the signals of methyl groups; Table 2) that in the case of 2,4-dimethylpyridine and 2,4,6-trimethylpyridine the methyl group reacted in position 2 (6). In the case of 2,4,6-trimethylpyrimidine it reacted in position 4 (6) (Fig. 1). 2-Phenyl-1,3-indandiones exist in chloroform in the diketo form. In the region of the C=O stretching vibrations they show two bands at 1700–1770 cm⁻¹ assigned to the asymmetrical and symmetrical vibrations of the C=O group [12]. 2-Phenyl-dithiaindandiones display a similar spectrum in the region of the C=O vibrations [2]. From the prepared derivatives of 2-pyridyl and 2-quinolyldithiaindandiones only the compounds VII, VIII, and IX display two bands above 1700 cm⁻¹, *i.e.* the compounds in which hydrogen is replaced by bromine or nitro group. These three compounds appear in the diketo forms in chloroform also in the solid state. The prepared 2-heteroaryldithiaindandiones do not occur in the typical diketo form since the bands of asymmetrical and symmetrical C=O stretching vibrations appear in the range 1634–1681 cm⁻¹. Neiland and Kroge [13] ascribe such wavenumbers of the C=O groups to the derivatives of 1,3-indandione which have strongly polarized C=O groups. Electron-acceptor effect of the pyridine or the quinoline ring will be manifested by the acidity of hydrogen in position 2 (Scheme 1).



Scheme 1

Analogously to 2-(*p*-nitrophenyl)- or 2-(*p*-trimethylammoniumphenyl)-1,3-indandione [13], also the derivatives of 2-pyridyl- or 2-quinolyldithiaindandione form an intermolecular grouping. That it is the intermolecular grouping both in the solid state and in the chloroform medium and not an intramolecular hydrogen bond between the O–H group of the enol form of the diketone and the nitrogen of heterocycle is shown by the fact that the prepared compounds do not display their characteristic maximum in the region of the OH stretching vibrations. Similarly it does not concern a betaine structure since in the region of NH stretching vibrations no characteristic maximum occurs. The prepared 2-(4-pyridyl)-1,3-indandione having the nitrogen atom of heterocycle in *para* position, which excludes the intramolecular interaction, shows similar i.r. spectrum [$\bar{\nu}_{as}(C=O) = 1625 \text{ cm}^{-1}$, $\bar{\nu}_s(C=O) = 1667 \text{ cm}^{-1}$] to that of the derivatives of 2-pyridyl- and 2-quinolyldithiaindandiones. This also supports the assumption that the grouping of the prepared compounds is intermolecular. Neither bromination nor nitration of these compounds is easy and the products of bromination contain bromine in most cases in nonstoichiometric ratios.

The difference of asymmetrical and symmetrical C=O stretching vibrations lie approximately in the same interval as is the case with a great majority of 2-phenyl-1,3-indandiones [12]. The i.r. spectra of phthalones prepared by the authors [8] are very similar to those of 4,7-dithiaphthalones prepared by us. The wavenumber of the C=O symmetrical

stretching vibration increased by about 10–15 cm^{-1} in the case of 2-(2,6-dimethyl-4-pyrimidyl)dithiaindandione (V) and in a similar derivative of 1,3-indandione (XI); it is likely caused by the presence of another nitrogen atom in the six-membered heterocyclic ring. The C=C band of the 3,6-dithiacyclohexene ring is located in the region of 1540–1550 cm^{-1} ; this being in agreement with [2].

Experimental

Melting points were measured on a Kofler hot stage. Characterization of the prepared indandiones is in Table 1.

N.m.r. spectra were measured in deuteriated chloroform solutions of 5% concentrations at 80 MHz on a Tesla BS 487 A apparatus. TMS (3 volume %) was used as standard. The spectra were measured at 24°C. Reading accuracy of the chemical shift was ± 0.01 p.p.m. Infrared spectra were obtained on a UR-20 Zeiss spectrophotometer in the 1500–1800 cm^{-1} and 3200–3700 cm^{-1} regions in nujol and in chloroform. Wavenumber reading accuracy was $\pm 2 \text{ cm}^{-1}$. The polystyrene foil was used as a calibration standard.

2-Heteroaryl-4,7-dithia-4,5,6,7-tetrahydro-1,3-indandiones (I–VI)

3,6-Dithia-3,4,5,6-tetrahydrophthalic anhydride (0.015 mole), the respective methyl derivative of the nitrogen-containing heterocycle (0.015 mole), and fused ZnCl_2 (0.5 g) were heated at 190–200°C for 5 hours. After cooling, the solid was ground and washed with ether. Dark powder was extracted with chloroform and chromatographed on a silica gel column. Chloroform was used as elution agent. The unchanged dithiapthalic anhydride forming a yellow strip moved quickly whereas the final product forming a carmine red strip was obtained by evaporating the eluate and by crystallization of chloroform–ether.

2-Bromo-2-heteroaryl-4,7-dithia-4,5,6,7-tetrahydro-1,3-indandiones (VII and VIII)

The corresponding indandione (0.01 mole) was dissolved in chloroform (50 ml). Bromine (0.01 mole) was added while stirring at room temperature. The reaction mixture was let stand overnight. The obtained hydrobromide was sucked off, washed with a small amount of cold water and 5% NaOH. Bromo derivatives were crystallized from chloroform.

2-Nitro-2-(2-quinolyl)-4,7-dithia-4,5,6,7-tetrahydro-1,3-indandione (IX)

2-(2-Quinolyl)-4,7-dithia-4,5,6,7-tetrahydro-1,3-indandione was shaken with 57% HNO_3 for 1 minute at room temperature. Then the reaction mixture was poured into water, filtered, washed with water, and dried. Crystallization from benzene.

2-(2-Pyridyl)-1,3-indandione (X)

Phthalic anhydride (0.015 mole), 4-methylpyridine (0.015 mole), nitrobenzene (2.5 ml), and fused ZnCl_2 (0.5 g) were heated while stirred at 200–210°C for 6 hours. The solid was washed with ether, dissolved, and crystallized from ethanol. Brick red crystals of 2-(4-pyridyl)-1,3-indandione were obtained. Yield 28.2%, m.p. 330–332°C.

Calculated: 75.32% C, 4.06% H, 6.27% N; found: 75.11% C, 4.01% H, 6.20% N. $\bar{\nu}_{\text{as}}(\text{C}=\text{O}) = 1625 \text{ cm}^{-1}$, $\bar{\nu}_{\text{s}}(\text{C}=\text{O}) = 1667 \text{ cm}^{-1}$.

2-(2,6-Dimethyl-4-pyrimidinyl)-1,3-indandione (XI)

The title compound was prepared similarly as the compounds *I–VI*. Chromatography on silica gel with chloroform. Yield 31.7% of theory; m.p. 270–271°C.

Calculated: 71.41% C, 4.79% H, 11.10% N; found: 71.19% C, 4.62% H, 10.89% N. $\bar{\nu}_{\text{as}}(\text{C}=\text{O}) = 1636 \text{ cm}^{-1}$, $\bar{\nu}_{\text{s}}(\text{C}=\text{O}) = 1688 \text{ cm}^{-1}$.

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