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4-Acyl-1,2-dimethyl-3H-phenothiazin-3-ones were prepared by the photochemical reaction of 1,2-dimethyl-3H-phenothiazin-3-one with aldehydes. The structures of the newly prepared compounds were determined by elemental analysis, spectroscopic methods (ir, nmr and ms) and comparison with a sample prepared by an alternate route.

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Although some attention has been given to the synthesis of phenothiazone derivatives which are used as enzyme inhibitors, anthelmintics, stabilizers, antioxidants, and indicators (1-11), their relative difficulty of preparation (12-13) has limited the number of compounds which have been examined. In a previous paper (14), the photochemical reaction of 5H-benzo[a]phenothiazin-5-one with aldehydes has been found to give 6-acyl-5H-benzo[a]phenothiazin-5-ones. As part of the general problem of the study of the photochemical reaction of quinone imines with aldehydes, we have extended the investigation to the photochemical reaction of 1,2-dimethyl-3H-phenothiazin-3-one (**1**) with aldehydes (**2a-d**).

Upon irradiation of a benzene solution of 1,2-dimethyl-3H-phenothiazin-3-one (**1**) and aldehydes (**2a-d**) in a Pyrex

vessel using a 100 Watt high-pressure mercury lamp, 4-acyl-1,2-dimethyl-3H-phenothiazin-3-ones (**3a-d**) were obtained. The results are summarized in Table 1. The structures of the photoproducts (**3a-d**) were fully supported by microanalytical results and spectral data. In particular, the nmr spectrum (deuteriochloroform) of **1** exhibited a characteristic singlet at 6.60 ppm due to the olefinic proton, but the spectra of the photoproducts (**3a-d**) of **1** with **2a-d** did not show a characteristic singlet at 6.60 ppm. Therefore, the photochemical addition did occur at the 4-position of **1**. Furthermore, the photoproducts (**3a-c**) were identified by direct comparison with a sample prepared by an alternate route. This route involves the condensation of 2-aminothiophenol (**4**) with an appropriate 2-acyl-5,6-dimethyl-1,4-benzoquinone (**5a-c**)

SCHEME I

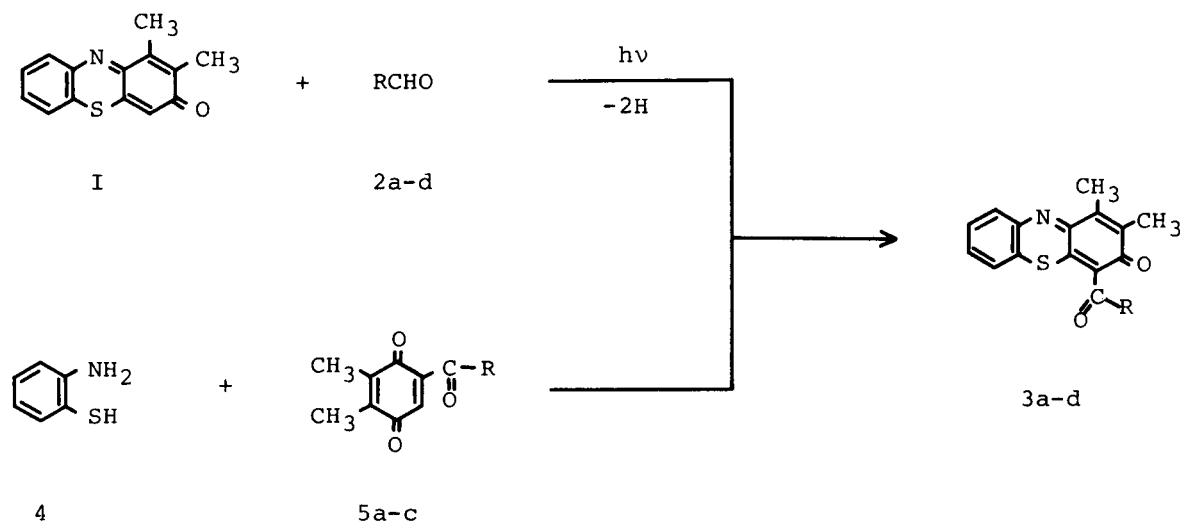
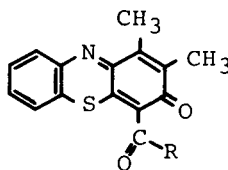
a: R = CH₃c: R = C₃H₇b: R = C₂H₅d: R = C₆H₅

Table 1

4-Acyl-1,2-dimethyl-3H-phenothiazin-3-ones (**3a-d**)

Compound No.	R	Procedure Yield, %	M.p., °C	Molecular Formula	Elemental Analysis Analysis Calcd. (Found)		
					C	H	N
3a	CH ₃	A, 80 (a)	205-207	C ₁₆ H ₁₃ NO ₂ S (283.4)	67.82 (67.62)	4.62 (4.48)	4.94 (4.77)
		B, 45 (b)					
3b	C ₂ H ₅	A, 39 (a)	157-158	C ₁₇ H ₁₅ NO ₂ S (297.4)	68.66 (68.44)	5.08 (4.89)	4.71 (4.50)
		B, 6 (b)					
3c	C ₃ H ₇	A, 31 (a)	122-124	C ₁₈ H ₁₇ NO ₂ S (311.4)	69.43 (69.21)	5.50 (5.35)	4.50 (4.38)
		B, 5 (b)					
3d	C ₆ H ₅	A, 63 (a)	227-228	C ₂₁ H ₁₅ NO ₂ S (345.4)	73.02 (72.84)	4.38 (4.21)	4.05 (3.93)

(a) Yield of product based on 1,2-dimethyl-3H-phenothiazin-3-one consumed. (b) Yield of isolated product.

Table 2

Spectroscopic Data of 4-Acyl-1,2-dimethyl-3H-phenothiazin-3-ones (**3a-d**)

Compound No.	Mass	Infrared Spectrum cm ⁻¹	¹ H Nmr Spectrum (deuteriochloroform) ppm
3a	283 (M ⁺)	2915, 2820, 1630 (C=O), 1595, 1415, 1295, 765	2.21 (s, 3H), 2.52 (s, 3H), 2.72 (s, 3H), 7.38-8.16 (m, 4H, arom.)
3b	297 (M ⁺)	2945, 2880, 1630 (C=O), 1608, 1430, 1295, 775	1.02-1.37 (t, 3H), 2.17 (s, 3H), 2.47 (s, 3H), 2.91-3.35 (q, 2H), 7.36-8.05 (m, 4H, arom.)
3c	311 (M ⁺)	2930, 2870, 1630 (C=O), 1602, 1420, 1290, 778	0.77-1.18 (t, 3H), 1.30-2.09 (m, 2H), 2.20 (s, 3H), 2.52 (s, 3H), 2.98-3.30 (t, 2H), 7.44-8.13 (m, 4H, arom.)
3d	345 (M ⁺)	2925, 2860, 1665 (C=O), 1595, 1445, 1305, 770	2.19 (s, 3H), 2.58 (s, 3H), 7.30-8.16 (m, 9H, arom.)

to furnish the corresponding 4-substituted-1,2-dimethyl-phenothiazin-3-ones (**3a-c**) in 15% aqueous hydrochloric acid. Compounds **3a-d** were prepared in 31-80% yields by the photochemical reaction of **1** with **2a-d**. On the other hand, compound **3a** was obtained in 45% yield by the condensation of **4** with **5a**, whereas compounds **3b,c** were formed under the same condition in poor yields.

The present report offers a facile method for the photochemical synthesis of 4-acyl-1,2-dimethyl-3H-phenothiazin-3-ones from readily available starting material.

EXPERIMENTAL

Melting points were determined on a Yanagimoto micromelting apparatus and are uncorrected. The infrared spectra were recorded on a Jasco DS 701G spectrometer. Absorption frequencies are reported in reciprocal centimeters. Nuclear magnetic resonance spectra were determined on a Hitachi R-20B spectrometer using tetramethylsilane as an internal reference. Chemical shifts are quoted in parts per million (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Mass spectra were determined on a Hitachi M-52 spectrometer.

1,2-Dimethyl-3H-phenothiazin-3-one (**1**).

A solution of 2-aminothiophenol (**4**) (1.25 g., 10 mmoles) in 15%

aqueous hydrochloric acid (50 ml.) was gradually added with stirring to a solution of 2,3-dimethyl-1,4-benzoquinone (1.4 g., 10 mmoles) in ethanol (250 ml.), and the mixture was stirred at room temperature for 20 hours. Iron(III) chloride hexahydrate (10.8 g., 40 mmoles) was then added with stirring and the mixture was set aside overnight. The precipitate was collected, washed well with water, and recrystallized from ethanol-water to give 1.2 g. of **1** as red needles, m.p. 191-192°; ms: m/e 241 (M⁺); ir (potassium bromide): 1615 cm⁻¹ (C=O); nmr (deuteriochloroform): δ 2.13 (s, 3H), 2.44 (s, 3H), 6.60 (s, 1H), 7.28-7.94 (m, 4H, arom.).

Anal. Calcd. for C₁₆H₁₁NOS: C, 69.68; H, 4.59; N, 5.80. Found: C, 69.42; H, 4.34; N, 5.69.

General Procedure A for the Photochemical Synthesis of 4-Acyl-1,2-dimethyl-3H-phenothiazin-3-ones (**3a-d**).

1,2-Dimethyl-3H-phenothiazin-3-one (**1**) (0.15 g., 0.6 mmole) and an aldehyde (**2**) (1 ml.) were dissolved in benzene (50 ml.). The solution was irradiated in a Pyrex glass tube for 7 hours from outside by means of 100 Watt high-pressure mercury arc lamp in a nitrogen atmosphere through a 7 cm-thick layer of cold water (0-5°) and then bubbled with air for several minutes. After the removal of the solvent under reduced pressure, the residue was chromatographed on a silica gel column using benzene-ethylacetate (10:1) as an eluent. The photoproducts (**3**) thus obtained were further purified by recrystallization from ethanol-water.

General Procedure B for the Preparation of 4-Acyl-1,2-dimethyl-3H-phenothiazin-3-ones (**3a-c**).

The compounds **3a-c** were prepared by condensation of **4** with an appropriate 2-acyl-5,6-dimethyl-1,4-benzoquinone (**5a-c**) just as was **1**.

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