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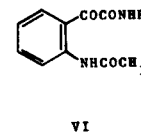
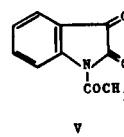
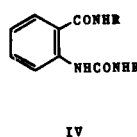
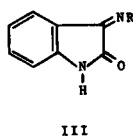
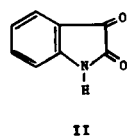
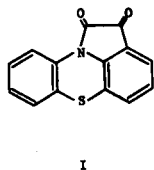
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The title compound I reacts with aliphatic amines producing ring-opened keto-amides of structure VII and with anilines forming imines of structure VIII.

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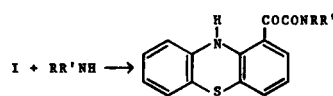
As part of our program of synthesizing new phenothiazine derivatives, we have been exploring the chemical transformations of 1,2-dioxo-1,2-dihydropyrrolo[3,2,1-*kl*]phenothiazine (I) (1). We were prompted to initiate our investigations along lines based upon the chemistry of a structurally similar isatin (II) (2). It is reported that isatin reacts with equimolar quantities of primary amines giving cyclic imines III (3-5), whereas an excess of cycloalkyl amines leads to ring-opened amides having structure IV (5). The reaction of *N*-acetyl isatin (V) with primary amines (including anilines) also leads to ring opening, but results in the formation of keto-amides of structure VI (6).



The title compound I undergoes reactions dependent upon the type and not the quantity of amine employed. Treatment of I with an equivalent or excess of primary or secondary aliphatic amines leads in high yield to keto-amides VIIa-g, while treatment with anilines results in imine (VIII) formation. Compounds VIIa-g are included in Table I and compounds VIIIa-b in Table II. The spectral data are consistent with the assigned structures.

In view of the mechanistic implications of the initial attack of primary amines at the amide carbonyl of *N*-acetyl isatin (V) and I, one could consider IX as a possible alternative to structure VIII. Assuming behavior analogous to that of V (6), however, one would predict ring opening to occur in the reaction of I with anilines. The well

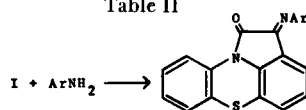
Table I



Compound	R	R'	M.p. (a)	Yield %	Formula	Analysis (b) Calcd./Found	Ir (Potassium Bromide), cm ⁻¹
VIIa	<i>n</i> -C ₄ H ₉	H	95-96	90	C ₁₈ H ₁₈ N ₂ O ₂ S	326.1100 326.1118	3260 1655 1630
VIIb	Benzyl	H	143-144	92	C ₂₁ H ₁₆ N ₂ O ₂ S	360.0934 360.0961	3230 1650 1630
VIIc	Cyclopentyl	H	130-132	89	C ₁₉ H ₁₈ N ₂ O ₂ S	338.1100 338.1060	3270 1650 1630
VIIId	Cyclohexyl	H	156-157	86	C ₂₀ H ₂₀ N ₂ O ₂ S	352.1247 352.1241	3230 1650 1630
VIIId	C ₂ H ₅	C ₂ H ₅	119-121	88	C ₁₈ H ₁₈ N ₂ O ₂ S	326.1100 326.1100	3270 1650 1635
VIII f	(CH ₂) ₄ -		144-145 (c)	91	C ₁₈ H ₁₆ N ₂ O ₂ S	324.0934 324.0946	3280 1640 (d)
VII g	(CH ₂) ₂ O(CH ₂) ₂ -		154-155	94	C ₁₈ H ₁₆ N ₂ O ₃ S	340.0883 340.0983	3290 1650 1630

(a) Recrystallized from hexane-ethyl acetate unless otherwise noted. (b) High resolution mass spectrum. (c) Recrystallized from methanol. (d) Center of unresolved multiple absorption.

Table II

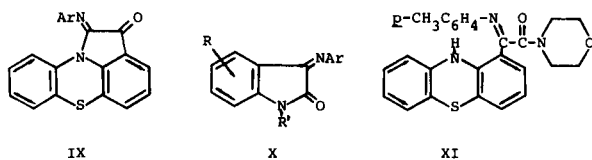


Compound	Ar	M.p. (a)	Yield %	Formula	Analysis (b) Calcd./Found	Ir (Potassium Bromide), cm^{-1}
VIIIa	C_6H_5	168 dec.	83	$\text{C}_{20}\text{H}_{12}\text{N}_2\text{OS}$	328.0673 328.0717	1755 1625
VIIIb	$p\text{-CH}_3\text{C}_6\text{H}_4$	166 dec.	88	$\text{C}_{21}\text{H}_{14}\text{N}_2\text{OS}$	342.0828 342.0863	1770 1630

(a) Recrystallized from hexane. (b) High resolution mass spectrum.

documented (2) formation of anils (X) from isatins also lends support to structure VIII.

Additional evidence for structure VIII is provided by the reaction of VIIIb with morpholine leading to ring opening and the formation of XI. The hydrolysis of XI in aqueous acetone readily afforded keto-amide VIIg.



EXPERIMENTAL

The ir spectra were obtained on a Perkin-Elmer model PE 137 spectrophotometer and the high resolution mass spectra on a Varian MAT CH-5 mass spectrometer. All melting points are uncorrected.

Reaction of I with Aliphatic Amines.

A mixture of I with an equivalent or excess of amine in sufficient chloroform or benzene to dissolve them was allowed to stand at room temperature for 1 hour. After removal of excess amine by washing with 5% hydrochloric acid, the compounds in Table I were obtained by evaporation of the solution to dryness followed by recrystallization from the appropriate solvent.

Reaction of I with Anilines.

A mixture of I with an excess of the aniline in sufficient benzene to dissolve them was heated at reflux until the consumption of I was shown to be complete by tlc (ca., 24 hours). After evaporation of the benzene, the products were purified by preparative thick layer chromatography (silica gel; hexane-ethyl acetate 2.5:1) followed by recrystallization from hexane.

Reaction of VIIIb with Morpholine (XI).

A solution of 170 mg. of VIIIb and 50 mg. of morpholine in 10 ml. of *p*-xylene was heated at reflux for 2 hours. After cooling,

the mixture was washed with 10 ml. of 5% hydrochloric acid, dried over magnesium sulfate and the solvent removed at reduced pressure. The residue was purified by preparative thick layer chromatography (silica gel; hexane-ethyl acetate-methanol 6:2:1) followed by recrystallization from carbon disulfide-pentane (1:1) giving 145 mg. (68%) of orange needles, m.p. 134.5-136.5; ir (potassium bromide): 1635 cm^{-1} ; pmr (100 MHz, deuteriochloroform): δ 11.76 (s, 1H), 7.30-6.44 (m, 11H), 3.72-2.72 (m, 8H), 2.38 (s, 3H).

Anal. Molecular Weight Calcd. for $\text{C}_{25}\text{H}_{23}\text{N}_3\text{O}_2\text{S}$, 429.1511. Found (high resolution mass spectrum), 429.1511.

Hydrolysis of XI (VIIg).

A solution of 100 mg. of XI and 10 mg. of *p*-toluenesulfonic acid in 10 ml. of 5% aqueous acetone was heated at reflux for 4 hours. After cooling, the solution was evaporated to dryness. The residue was redissolved in 10 ml. of chloroform, washed with 5% hydrochloric acid, dried over magnesium sulfate, filtered and evaporated to dryness. The resulting dark red solid was recrystallized from hexane-ethyl acetate affording 65 mg. (82%) of VIIg, m.p. $154\text{-}155^\circ$.

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