

Optical Rotatory Dispersion Studies

LXXIII*. Anomalous Rotatory Dispersion Curves Associated with Acylthioureas. Application to Stereochemical Studies of α -Substituted Carboxylic Acids

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Submitted in honour of the sixtieth birthday of Professor *Arne Fredga*

Optically active carboxylic acids show only plain rotatory dispersion curves through the presently accessible spectral range. In an attempt to obtain Cotton effect curves, a number of "chromophoric" derivatives of carboxylic acids have been investigated. Acylthioureas, readily prepared by successive treatment of a carboxylic acid with thionyl chloride, potassium thiocyanate and a secondary amine, proved to be the most desirable derivatives because of their low intensity ultraviolet absorption maximum near $340\text{ m}\mu$, which gave rise to anomalous rotatory dispersion curves. In general, the sign of the Cotton effect can be related to the absolute configuration (*R* or *S*) of the α -substituted carboxylic acid, but caution has to be exercised because of possible complications associated with free-rotational isomerism.

With very few exceptions, the application of anomalous rotatory dispersion measurements to organic chemical problems dates only to our first publications¹ in 1955 dealing with Cotton effect curves of some steroid ketones. In the intervening six years, over three hundred articles have appeared in which such anomalous rotatory dispersion data have been used for the solution of some organic or biochemical problem and there is no doubt that this method has become part of the organic chemist's armamentarium, notably in the field of

* Paper LXXII, Djerassi, C., Records, R., Bunnenberg, E., Mislow, K. and Moscowitz, A. *J. Am. Chem. Soc.* **84** (1962) 870.

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


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stereochemistry.²⁻⁴ Most of these applications have utilized the carbonyl chromophore, because of its low-intensity absorption maximum near 300 $m\mu$, but in recent years a considerable effort has been expended in our laboratory on converting other functional groups, which are transparent in the 700—250 $m\mu$ region, into readily prepared derivatives with spectral properties giving rise to easily measured Cotton effects. This development of "chromophoric" derivatives for rotatory dispersion work has been quite successful⁵ and in the present paper we should like to describe our results with carboxylic acids.⁶

Extensive rotatory dispersion measurements by Sjöberg⁷ on a variety of optically active carboxylic acids have shown that these substances exhibit only plain dispersion curves. While these curves did prove to be of utility for stereochemical correlations — and certainly are to be preferred over monochromatic rotation measurements at the sodium D line — it was clearly of importance to examine Cotton effect curves of suitable derivatives. Using optically active α -methylbutyric or hydratropic acids as models, a variety of derivatives was examined and we eventually settled on acylthioureas of the type $RCONHC(=S)NR_2$ for the following reasons: (a) as shown in the experimental section, they are easy to prepare; (b) they are usually crystalline derivatives (see Table 6), which are readily purified because of their solubility in alkali and their stability to alumina upon chromatography; (c) in addition to a high intensity ultraviolet absorption maximum near 280 $m\mu$ ($\log \epsilon \sim 4.2$), they exhibit a weaker maximum at 335—345 $m\mu$ ($\log \epsilon \sim 2.4$). It was this last feature, which seemed particularly attractive to us, since this relatively weak absorption band — if proven to be optically active — should lead to measurable Cotton effects.

Experimentally, the optically active acid was transformed into its acid chloride with thionyl chloride and treated immediately in acetone solution with potassium thiocyanate. The resulting acylisothiocyanate was not isolated but was converted directly into the corresponding N,N -disubstituted N' -acylthiourea by reaction with a secondary amine. Using (+)-hydratropic acid as the substrate, the corresponding (+)-hydratropyl morpholino (I), piperidino

Table 1. Rotatory dispersion properties of (+)- (S) -hydratropylthiocarbamides.
R. D. Cotton effect (methanol)

Derivative (R)	Chemical structure			Sign and molecular amplitude
	First extremum	Second extremum	Last reading	
I R = 	$[\alpha]_{374} - 961^\circ$	$[\alpha]_{325} + 2\ 370^\circ$	$[\alpha]_{315} + 1\ 780^\circ$	— 9 160°
II R = 	$[\alpha]_{365} - 944^\circ$	$[\alpha]_{320} + 2\ 490^\circ$	$[\alpha]_{310} + 1\ 940^\circ$	— 9 480°
III R = 	$[\alpha]_{380} - 982^\circ$	$[\alpha]_{312} + 2\ 250^\circ$	$[\alpha]_{305} + 1\ 540^\circ$	— 8 475°
IV R = $N(C_2H_5)_2$	$[\alpha]_{370} - 815^\circ$	$[\alpha]_{320} + 3\ 140^\circ$	$[\alpha]_{310} + 2\ 510^\circ$	— 10 450°

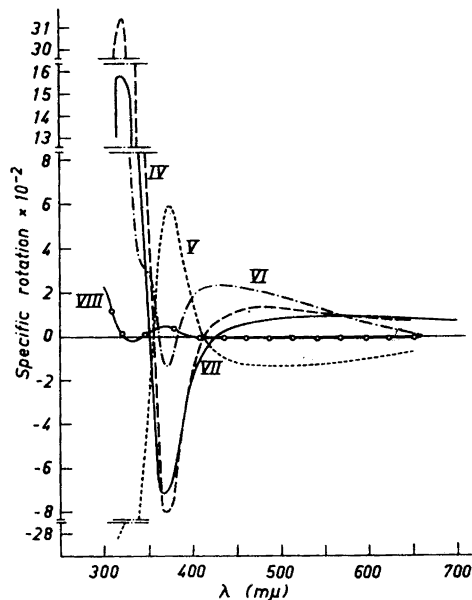
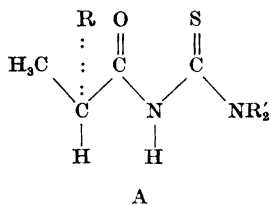


Fig. 1. Optical rotatory dispersion curves (methanol solution) of acylthioureas IV–VIII.

(II), pyrrolidino (III) and diethylamino (IV) thiocarbamides were prepared. As shown in Fig. 1, the (+)-hydratropyl diethylaminothiocarbamide (IV) exhibited a negative Cotton effect of substantial amplitude centered in the 340 $m\mu$ region, thus showing that this low-intensity absorption band is indeed optically active. The nature of the amine is not important, since all four hydratropyl derivatives (I–IV) gave negative Cotton effects of approximately identical amplitude (see Table 1). From a synthetic standpoint, the morpholino (I) and diethylamino (IV) derivatives proved to be the most desirable and these were the ones selected for the remaining acids. Before discussing these results, some general comments bearing on the possible relationship of Cotton effect curves and stereochemistry of such acylthioureas seem pertinent.

The sign and magnitude of the Cotton effect (see Fig. 1) of these acylthioureas is associated with the interaction between the partially unshielded nuclei of the various substituents and the electrons involved in the 340 $m\mu$ transition of the C=S chromophore. The analogous situation with *cyclic* ketones led to generalizations^{2, 4, 8–11} which permit the prediction of the sign and amplitude of Cotton effects of ketones, largely because the spatial relationship between the chromophore and all other substituents is fixed and known. This is obviously not the case with acylthioureas of type A, where theoretically there exists free rotation around all single bonds and where the characteristic feature of the Cotton effect is then made up of the individual contributions of the various free-rotational isomers. Ultimately, this problem can probably be attacked by machine computations¹² but even at the present qualitative stage, some rough generalizations can be made since a considerable number of rotomers will probably be present to only a negligible extent.




As shown in Table 1, variations in the N-dialkyl substituent over the steric range encompassed by I—IV do not affect appreciably the rotomer composition since the Cotton effects of these four hydratropyl derivatives (A, R = C₆H₅) were all negative and of similar amplitude. Free rotation around the two bonds of the central nitrogen will probably also be of little significance, because one and the same rotomer (or rotomer mixture) will be found in virtually all acylthioureas under examination. The most likely arrangement is probably the all-*trans* geometry shown in A, unless the parallel dipoles of the C=O and C=S chromophore favor an alternate arrangement. Since this electrostatic factor is identical in all of the compounds under discussion, it should still lead to roughly the same rotomer composition around the two single bonds of the central nitrogen. This brings us to free rotation around the four bonds connected to the asymmetric carbon atom and it is here that steric factors will play the crucial role. Consequently, differences in the steric requirements of the substituents attached to that carbon atom may lead to variable rotomer mixtures, which may very well result in inversions of the sign of the Cotton effect in spite of the fact that they may possess the same absolute configuration. It is for this reason that any attempted correlation between sign of Cotton effect and absolute configuration be based not on the D and L Fischer convention, but rather on the Cahn-Ingold-Prelog¹³ (*R*) and (*S*) system, which usually takes into account the relative bulk of the substituents around the asymmetric center. Even this system may fall down when a hetero-atom is involved, since it will receive priority¹³ over a much bulkier carbon-linked substituent. An additional complication may arise when a substituent attached to the carbon atom may undergo hydrogen bonding with either the carbonyl oxygen or the hydrogen atom attached to the central nitrogen in (A), whereupon a new rotomer may become dominant. Taking these factors into consideration, we shall now cover the experimental material at our disposal.

The first group of optically active acids is related to the hydratropic acid derivatives (I—IV, Table 1) in that the asymmetric center has attached to it a small alkyl group (methyl or ethyl), hydrogen and an aromatic system. As shown in Fig. 1 as well as Tables 1 and 2, all of these acylthioureas IV—VIII exhibit a Cotton effect of sign opposite to that of the conventional D line rotation. In each instance, a *negative Cotton effect corresponds to the (S) and a positive Cotton effect to the (R) configuration*.¹³

The second group (IX—XIV) differs from the first in that a hetero-atom (oxygen or sulfur) or a methylene group (IX) is inserted between the aromatic moiety and the asymmetric carbon atom. As can be seen from Fig. 2 and Table 2, the above generalization still holds in that all members with the (*S*)

Table 2. Rotatory dispersion properties of primary acyl morpholino and diethylamino carbamides.

Substance (R = NHC(=S)NEt ₂) (X = NHC(=S)N )	Absolute con-figuration	R. D. Cotton effect (methanol)					
		Sign	First extremum	Second extremum	Last reading	Lit. Reference to acid	
$\begin{array}{c} \text{COR} \\ \\ \text{C}_6\text{H}_5-\text{C}-\text{H} \\ \\ \text{C}_2\text{H}_5 \end{array}$	(V) ^a	(R)	+	[α] ₃₇₂ + 594°	—	[α] ₃₂₀ - 2800°	(-) ¹⁴
$\begin{array}{c} \text{COR} \\ \\ \text{H}-\text{C}-1\text{-naphthyl} \\ \\ \text{CH}_3 \end{array}$	(VI)	(S)	-	[α] ₃₇₀ - 136°	—	[α] ₃₃₀ + 757°	(+) ¹⁵
$\begin{array}{c} \text{COX} \\ \\ \text{H}-\text{C}-2\text{-naphthyl} \\ \\ \text{CH}_3 \end{array}$	(VII)	(S)	-	[α] _{367.5} - 715°	[α] ₃₂₀ + 1580°	[α] _{312.5} + 1060°	(+) ¹⁶
$\begin{array}{c} \text{COR} \\ \\ \text{H}-\text{C}-\text{S} \text{---} \text{C}_6\text{H}_4 \\ \\ \text{CH}_3 \end{array}$	(VIII)	(R)	+	[α] ₃₇₀ + 44°	[α] ₃₃₀ - 20°	[α] ₃₀₀ + 224°	(+) ¹⁷
$\begin{array}{c} \text{COR} \\ \\ 2\text{-naphthyl}-\text{CH}_2-\text{C}-\text{H} \\ \\ \text{CH}_3 \end{array}$	(IX) ^b	(R)	+	[α] ₃₇₀ + 907°	[α] ₃₁₃ - 2790°	[α] ₃₀₅ - 2560°	(-) ^{18,19}
$\begin{array}{c} \text{COR} \\ \\ \text{H}-\text{C}-\text{O}-\text{C}_6\text{H}_4\text{-}p\text{-CH}_3 \\ \\ \text{CH}_3 \end{array}$	(X)	(R)	+	[α] ₃₆₀ + 720°	[α] ₃₁₀ - 195°	[α] ₃₀₀ + 870°	(+) ¹⁹
$\begin{array}{c} \text{COR} \\ \\ \text{H}-\text{C}-\text{O}-\text{C}_6\text{H}_4\text{-}p\text{-Cl} \\ \\ \text{CH}_3 \end{array}$	(XI)	(R)	+	[α] ₃₆₅ + 582°	[α] ₃₁₅ - 146.5°	[α] ₃₁₀ - 69°	(+) ²⁰
$\begin{array}{c} \text{COR} \\ \\ o\text{-Cl}-\text{C}_6\text{H}_4\text{-O}-\text{C}-\text{H} \\ \\ \text{CH}_3 \end{array}$	(XII)	(S)	-	[α] ₃₅₀ - 602°	—	[α] ₃₂₀ - 294°	(-) ²¹
$\begin{array}{c} \text{COR} \\ \\ 2\text{-naphthyl}-\text{O}-\text{C}-\text{H} \\ \\ \text{CH}_3 \end{array}$	(XIII)	(S)	-	[α] ₃₆₅ - 1420°	[α] ₃₃₀ - 557°	[α] ₃₁₀ - 365°	(-) ²²
$\begin{array}{c} \text{COR} \\ \\ \text{H}-\text{C}-\text{S}-\text{C}_6\text{H}_5 \\ \\ \text{CH}_3 \end{array}$	(XIV)	(R)	+	[α] ₃₅₀ + 113°	[α] ₃₃₅ + 57°	[α] ₃₁₀ + 191°	(+) ¹⁹

^a 80 % optical purity.

^b 88 % optical purity.

configuration exhibit a negative Cotton effect, while the reverse holds true for the (*R*) enantiomers. It is interesting to note from Fig. 2 that in three instances the sign of the Cotton effect coincides with that of the sodium D line rotation,

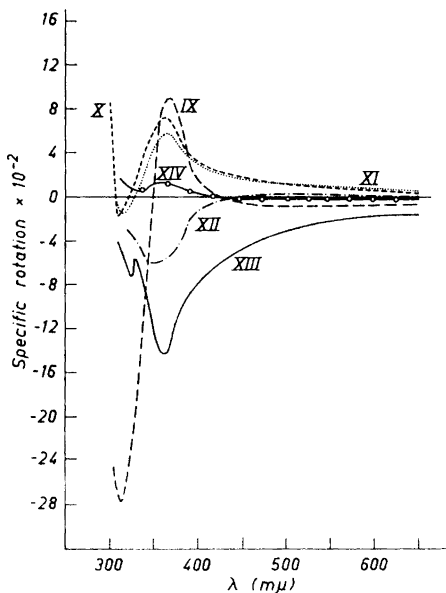


Fig. 2. Optical rotatory dispersion curves (methanol solution) of acylthioureas IX—XIV.

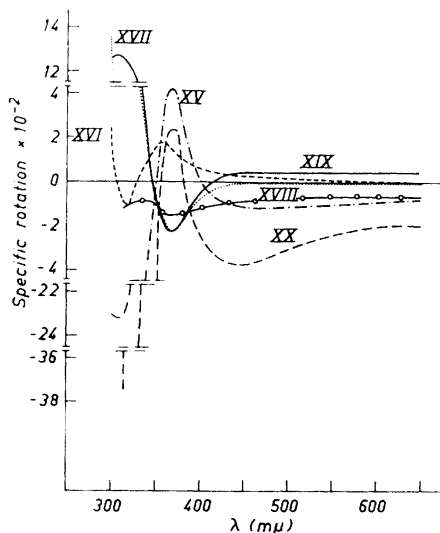


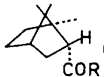

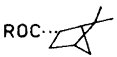

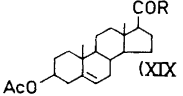
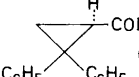
Fig. 3. Optical rotatory dispersion curves (methanol solution) of acylthioureas XV—XX.

while this is not the case in the others (IX, XII, XIV). This illustrates again the great advantage of considering the sign of Cotton effects rather than that of a single wavelength rotation, especially the sodium D line.

The next group of acids (XV—XX in Table 3) differs from the first two in one very important respect, namely that it includes a secondary carboxyl group attached directly to a ring. With one exception (XVIII), the members with the (*S*)-configuration of the carboxyl-bearing asymmetric center exhibit a negative Cotton effect, while a positive Cotton effect is associated with the (*R*)-configuration. The single anomaly XVIII is in our opinion due to a particular rotomer, which is favored in this highly strained, bicyclic system. It is likely that in such a rotomer, some of the more distant ring carbons may be brought in sufficient proximity to the C=S chromophore so as to exert an important rotational contribution. These more distant carbon atoms are, of course, not considered in the (*S*) and (*R*) notation, which is concerned only with the substituents directly connected to the asymmetric carbon atom.

Only three optically active acids were available (XXI—XXIII in Table 4) in which the carboxyl function is tertiary and it is not possible to state, therefore, whether the above emphasized correlation of sign of Cotton effect with (*R*) or (*S*) configuration will hold in such acids. The derivatives of the pair of diterpene acids, O-acetyl podocarpic acid (XXI) and dehydroabiatic acid (XXII) do follow the generalization; whether this is fortuitous cannot be determined at this stage, but in any event this result should be useful for absolute configurational assignments among related diterpenes. The cyclopropane

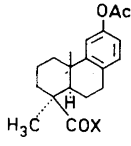
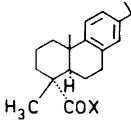
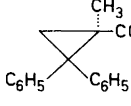
Table 3. Rotatory dispersion properties of secondary (ring attached) acyl diethylamino carbamides.

Substance (R=NHC(=S)NEt ₂)	Absolute con- figuration	R. D. Cotton effect (methanol)				
		Sign	First extremum	Second extremum	Last reading	Lit. Reference to acid
 (XV)	(R)	+	[α] ₃₆₈ + 420°	[α] ₃₁₅ - 2325°	[α] ₃₀₀ - 2295°	(-)-endo ²³
 (XVI)	(R)	+	[α] ₃₆₈ + 181°	[α] ₃₂₀ - 105°	[α] ₃₀₀ + 232°	(+)-endo ²⁴
 (XVII)	(S)	-	[α] ₃₇₀ - 227°	-	[α] ₃₀₀ + 1375°	(+)-2α ²⁵
 (XVII)	(R)	-	[α] ₃₇₅ - 155°	[α] ₃₄₀ - 89°	[α] ₃₁₅ - 126°	(-)-2β ²⁵
 (XIX)	(S)	-	[α] ₃₇₄ - 222°	[α] ₃₁₃ + 1263°	[α] ₃₁₀ + 1250°	²⁶
 (XX)	(R)	+	[α] ₃₇₁ + 262°	-	[α] ₃₁₅ - 3720°	(-) ²⁷

carboxylic acid derivative XXIII evidently possesses the same absolute configuration as the lower homolog XX as determined²⁷ by quasi-racemate and rotatory dispersion studies. Consequently, the negative Cotton effect (Fig. 4) of this (*R*)-acid derivative XXIII suggests the presence of a different rotomer composition in XXIII as compared to XX, which is not unreasonable as the presence of the tertiary methyl group may also affect the preferred spatial orientation of the phenyl groups.

The last group of acylthioureas collected in Table 5 (XXIV—XXX) contains several examples, which illustrate the borderline area where such rotatory dispersion results may be used only with caution for stereochemical work. Most of them should be considered as *sui generis* for the time being until additional closely related examples become available. First, there arises the question as to the limiting distance³² (between the thiourea chromophore and the asymmetric center) which still gives rise to a Cotton effect. A comparison between the α -methylbutyric (XXIV) and β -methylvaleric (XXV) acid derivatives or between the 3β -acetoxy- Δ^5 -bisor- (XXVIII) and nor (XXIX)-choleryl thioureas suggests that insertion of a single methylene function is already sufficient to practically obliterate the Cotton effect, only a slight irregularity being noticeable (see Fig. 5) in the β -substituted derivatives. That this does not necessarily follow, however, is illustrated in the 3β -acetoxy- Δ^5 -choleryl

Table 4. Rotatory dispersion properties of tertiary acyl dialkylamino carbamides.

Substance (R = NHC(=S)NEt ₂) (X = NHC(=S)N ₆ O)	Absolute con- figuration	R. D. Cotton effect (methanol)				
		Sign	First extremum	Second extremum	Last reading	Lit. Reference to acid
 (XXI)	(S)	-	[α] ₃₇₈ + 87°	-	[α] ₃₁₅ + 681°	28
 (XXII)	(R)	+	[α] _{367.5} + 168°	-	[α] ₃₁₅ - 509°	29
 (XXIII)	(R)	-	[α] ₃₆₉ - 439°	-	[α] ₃₀₂ + 1610°	(+) ²⁷

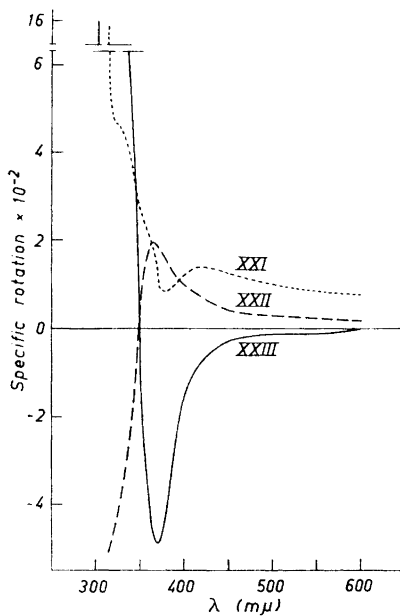


Fig. 4. Optical rotatory dispersion curves (methanol solution) of acylthioureas XXI—XXIII.

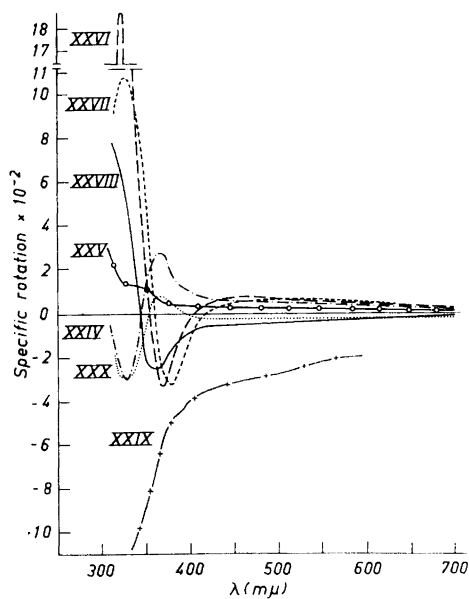
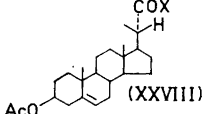
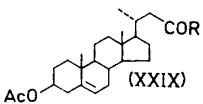
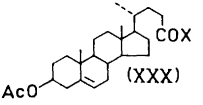


Fig. 5. Optical rotatory dispersion curves of acylthioureas XXIV—XXVII, XXIX and XXX (methanol solution) and XXVIII (dioxane solution).

Table 5. Rotatory dispersion properties of some miscellaneous acylthioureas.

Substance (R = NHC(=S)NEt ₂) (X = NHC(=S)N $\begin{array}{c} \diagup \\ \diagdown \end{array}$ O)	Absolute con- figuration	R. D. Cotton effect (methanol)				
		Sign	First extremum	Second extremum	Last reading	Lit. Reference to acid
$\begin{array}{c} \text{COX} \\ \\ \text{CH}_3-\text{C}-\text{H} \\ \\ \text{C}_2\text{H}_5 \end{array} \quad (\text{XXIV})$	(S)	+	$[\alpha]_{370} + 266^\circ$	$[\alpha]_{330} - 311^\circ$	$[\alpha]_{310} - 67^\circ$	(+) ³⁰
$\begin{array}{c} \text{CH}_2\text{COR} \\ \\ \text{CH}_3-\text{C}-\text{H} \\ \\ \text{C}_2\text{H}_5 \end{array} \quad (\text{XXV})$	(S)	See Fig. 5	—	—	$[\alpha]_{310} + 328^\circ$	(+) ³¹
$\begin{array}{c} \text{COX} \\ \\ \text{H}-\text{C}-\text{OAc} \\ \\ \text{CH}_3 \end{array} \quad (\text{XXVI})$	(R)	—	$[\alpha]_{370} - 340^\circ$	$[\alpha]_{322.5} + 1875^\circ$	$[\alpha]_{317} + 1700^\circ$	(-) ³⁰
$\begin{array}{c} \text{COR} \\ \\ \text{AcO}-\text{C}-\text{H} \\ \\ \text{C}_6\text{H}_5 \end{array} \quad (\text{XXVII})$	(S)	—	$[\alpha]_{370} - 337^\circ$	$[\alpha]_{320} + 1080^\circ$	$[\alpha]_{315} + 933^\circ$	(+) ³⁰
 (XXVIII)	(S)	— ^a	$[\alpha]_{362} - 263^\circ$	—	$[\alpha]_{312.5} + 789^\circ$	26
 (XXIX)	(R)	See Fig. 5	—	—	$[\alpha]_{335} - 108^\circ$	26
 (XXX)	(R)	+	$[\alpha]_{365} + 74^\circ$	$[\alpha]_{320} - 289^\circ$	$[\alpha]_{315} - 193^\circ$	26

^a In dioxane solution.

thiourea (XXX), where the asymmetric center is located in the γ -position and where a Cotton effect is again observed (Fig. 5). It is very likely, therefore, that in XXX there exist rotomers in which the C=S chromophore is in substantial proximity to some of the asymmetric centers of rings C and/or D, thus resulting in a Cotton effect. Further work with optically active acids is indicated in which the distance of the asymmetric center from the thiourea functionality is varied, before generalizations can be made on the relation of distance with disappearance of Cotton effect.

Of the four acylthioureas in this group (XXIV, XXVI—XXVIII) with an asymmetric center in the α -position, two do not obey the earlier noticed relationship between sign of Cotton effect and the (R) or (S) configuration. These two exceptions are the derivatives of (+)- α -methylbutyric acid (XXIV) and

of (—)-O-acetyllactic acid (XXVI) and it is interesting to note that when one of the alkyl substituents in these two acids XXIV and XXVI is replaced by phenyl (XXIV *vs.* IV or V; XXVI *vs.* XXVII) then the standard behavior is regained. Two tentative explanations can be offered for this anomaly: (a) the rotomer compositions in the two aliphatic examples (XXIV and XXVI) are quite different from those in their aromatic counterparts; (b) the rotatory contribution of an aromatic substituent is so much stronger³³ than that of a methyl or ethyl group, that even a relatively small proportion of a given rotomer, in which the C=S chromophore is in close proximity to the aromatic moiety, governs the sign of the Cotton effect. Obviously many more examples of diversely substituted acylthioureas would have to be examined before a firm conclusion could be reached on this point.

Even at this early stage, it is obvious that the examination of "chromophoric" derivatives is quite profitable and may lead to a number of useful applications. In the narrowest sense, derivatives of the type described in the present paper may be used for stereochemical correlations among closely related series (*e.g.* α -arylpropionic or butyric acids), while ultimately subtle conformational points relating to rotomer equilibria may be settled by such an approach. Before this stage is reached, it is necessary to prepare such derivatives of a wide variety of acids (or other substrates⁹), the absolute configuration of which has been determined by some other means. It seems quite appropriate that our initial results be published in a journal issue dedicated to Prof. Arne Fredga, in whose laboratory so many of the presently used acids have been resolved¹⁵⁻²² and where their absolute configurations have been determined by the quasi-racemate method, which has been pioneered so effectively in the Uppsala laboratories.³⁴

EXPERIMENTAL

With one exception (XXVIII), all rotatory dispersion curves were measured in methanol solution (*c.* 0.1–0.04) with a Rudolph automatically recording spectropolarimeter. We are indebted to Mrs. Ruth Records for assistance with these measurements and to Messrs. E. Meier and J. Consul for the microanalyses.

Preparation of acylthioureas. As all thirty derivatives listed in Table 6 were prepared by essentially the same procedure, details are given for only one example (IV):

A mixture of 200 mg of (+)-hydratropic acid (m.p. 31–32°, $[\alpha]_D + 80.7^\circ$ (EtOH)) resolved through the strychnine salt³⁵) and 1.5 ml of thionyl chloride was heated at 80° for 2 h, the excess reagent was removed under reduced pressure, dry benzene was added and the evaporation process repeated. The resulting acid chloride was dissolved in 4 ml of dry acetone and added slowly to an ice-cold solution of 250 mg of finely powdered potassium thiocyanate (dried at 100°/0.1 mm) in 7 ml of acetone, the entire operation being conducted in a carefully dried apparatus with complete exclusion of moisture. After stirring for 30 min at room temperature, the flask was cooled in ice and a solution of 0.5 ml of diethylamine in 4 ml of acetone added slowly. The mixture was left overnight in the refrigerator, the potassium chloride was filtered and the acetone evaporated. The residual oil was extracted in the cold with 0.4 M sodium hydroxide solution, which left undissolved the diethylamide of hydratropic acid, formed as a by-product. The alkaline extracts were acidified, extracted with ether, washed with water, dried and evaporated. The crystalline residue (240 mg) was chromatographed on 30 g of Merck neutral alumina (activity II) and hydratropyl diethylaminothiocarbamide (IV) was eluted with benzene-ether (4:6); yield 203 mg, m.p. 125–127°. Recrystallization from benzene-hexane provided the analytical specimen with m.p. 130–131°, $\lambda_{\max}^{\text{CHCl}_3}$ 2.99, 5.88, 6.56, 6.85–7.1 μ , $\lambda_{\max}^{\text{MeOH}}$ 1.

Table 6. Physical and analytical properties of acylthioureas.

Substance	m.p. (Kofler)	Empirical formula	Calc.		Found	
			C	H	C	H
I	134–135°	C ₁₄ H ₁₈ N ₂ O ₂ S	60.40	6.52	60.23	6.45
II	102–103°	C ₁₅ H ₂₀ N ₂ OS	65.22	7.30	65.10	7.31
III	144–145°	C ₁₄ H ₁₈ N ₂ OS	64.06	6.91	64.12	6.96
IV	130–131°	C ₁₄ H ₂₀ N ₂ OS	63.58	7.62	63.63	7.65
V	131–132°	C ₁₅ H ₂₂ N ₂ OS	64.75	7.97	64.69	8.10
VI	111–112°	C ₁₈ H ₂₂ N ₂ O ₂ S	68.77	7.05	68.75	6.96
VII	141–142°	C ₁₈ H ₂₀ N ₂ O ₂ S	65.83	6.14	65.64	6.19
VIII	118–119°	C ₁₆ H ₂₀ N ₂ O ₂ S	59.97	6.29	59.84	6.46
IX	88–90°	C ₁₉ H ₂₄ N ₂ OS	69.45	7.36	69.55	7.12
X	116–117°	C ₁₅ H ₂₂ N ₂ O ₂ S	61.22	7.53	61.29	7.58
XI	150–151°	C ₁₄ H ₁₉ ClN ₂ O ₂ S	53.41	6.08	53.69	5.95
XII	95–96°	C ₁₄ H ₁₉ ClN ₂ O ₂ S	53.41	6.08	53.53	5.82
XIII	119–120°	C ₁₈ H ₂₂ N ₂ O ₂ S	65.45	6.71	65.49	6.56
XIV	66–68°	C ₁₄ H ₂₀ N ₂ O ₂ S	56.71	6.80	56.96	6.91
XV	123–124°	C ₁₆ H ₂₈ N ₂ OS	64.82	9.52	64.93	9.43
XVI	101–102°	C ₁₅ H ₂₆ N ₂ OS	63.83	9.29	63.83	9.14
XVII	oil	C ₁₄ H ₂₄ N ₂ OS	62.63	9.01	63.01	9.19
XVIII	92–93°	C ₁₄ H ₂₄ N ₂ OS	62.63	9.01	63.18	9.10
XIX	128–130°	C ₂₇ H ₄₂ N ₂ O ₂ S	68.32	8.92	68.28	8.81
XX	131–132°	C ₂₁ H ₂₄ N ₂ OS	71.55	6.86	71.30	6.89
XXI	176–177°	C ₂₄ H ₃₂ N ₂ O ₄ S	64.83	7.25	64.79	7.17
XXII	102–104°	C ₂₅ H ₃₆ N ₂ O ₂ S	70.05	8.47	70.38	8.39
XXIII	162–164°	C ₂₂ H ₂₆ N ₂ OS	72.08	7.15	72.13	7.11
XXIV	126–127°	C ₁₀ H ₁₈ N ₂ O ₂ S	52.15	7.88	52.44	7.87
XXV	73–74°	C ₁₁ H ₂₂ N ₂ OS	57.34	9.63	57.25	9.49
XXVI	129–130°	C ₁₀ H ₁₆ N ₂ O ₄ S	46.14	6.19	45.98	5.76
XXVII	131–132°	C ₁₅ H ₂₀ N ₂ O ₃ S	58.43	6.41	58.76	6.41
XXVIII	218–219°	C ₂₉ H ₄₄ N ₂ O ₄ S	67.40	8.58	67.69	8.13
XXIX	175–176°	C ₃₀ H ₄₆ N ₂ O ₃ S	69.74	9.36	69.97	9.04
XXX	109–110°	C ₂₁ H ₄₆ N ₂ O ₄ S	68.50	8.89	68.71	9.01

279 and 340 m μ , log ϵ 4.13 and 2.49. The infrared band at 5.88 μ and the two ultraviolet absorption maxima served as the best spectroscopic criteria for the various thioureas; their homogeneity was also always checked by thin-layer chromatography on silica gel using benzene-ethyl acetate (5:1) or benzene-ether (4:1) as solvent.

Acknowledgement. We are indebted to the various investigators listed in the bibliography and especially to Prof. A. Fredga and Dr. B. Sjöberg for many of the optically active acids used as starting material. We also acknowledge with pleasure a stimulating discussion with Prof J. Meinwald (Cornell University) as well as the financial support provided by grant No. CRTY-5061 from the *National Cancer Institute* of the *National Institutes of Health, U. S. Public Health Service.*

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Received December 15, 1961.