SYNTHESIS AND CHIRAL-OPTICAL PROPERTIES OF (+)-3-METHYL-3,4-DIHYDROISOQUINOLINE-1-THIONE*

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(+)-3-Methyl-3,4-dihydroisoquinoline-1-thione was obtained by sulfuration of (+)-3-methyl-3,4-dihydroisoquinolone with phosphorus pentasulfide or by cyclization of (+)-α-benzylethyl isothiocyante under the influence of polyphosphoric acid. Measurements of the rotatory dispersion and circular dichroism showed the presence of two positive Cotton effects due to n→π* and π→π* transitions in the thioamide chromophore, as well as Cotton effects apparently due to π→π* transitions in the aromatic chromophore.

Sulfur-containing compounds are very convenient subjects for spectral studies, inasmuch as the absorption bands of the thio chromophores lie in the longer-wavelength region as compared with the corresponding oxygen-containing chromophores: An n→π* transition in the thiocarbonyl chromophore is observed at 490-500 nm [2, 3], as compared with 325-360 nm in the thioamide chromophore [4]. Compounds that are transparent in the region accessible to measurements have been converted to derivatives that have a Cotton effect (CE) by introduction of a sulfur-containing chromophore, for example, acylthioureas [5, 6] and thioamides [4, 7] for carboxylic acids. The measurements of the rotatory dispersion (RD) and circular dichroism (CD) in these studies were made primarily at 300-600 nm, and a correlation between the sign of the CE induced by the electron transition in the sulfur-containing chromophore and the configuration of the starting compounds was established in a number of cases. The RD and CD of these derivatives and other sulfur compounds in the shorter-wave region have remained virtually unstudied.

In a previous spectral polarimetric study [8] of (+)-3-methyl-3,4-dihydro-1-isoquinolone (I) and the isomeric (–)-4-methyl-3,4-dihydro-1-isoquinolone [9] we showed that they give complex RD curves that represent the superimposition of several Cotton effects caused by π→π* transitions in the aromatic chromophore (250-270, 210, and 190 nm) and n→π* (220 nm) and π→π* (190 nm) transitions in the amide chromophore. All of these transitions lie in a relatively narrow spectral region, and even measurement of the CD did not enable us to resolve them sufficiently distinctly.

Continuing our study of optically active amides, we synthesized and studied the chiral-optical properties of the cyclic thioamide (+)-3-methyl-3,4-dihydroisoquinoline-1-thione (II). Conversion to the thioamide makes it possible, while retaining the chromophore of the benzamide type, to "separate" the electron transitions and expand the spectral regions in which they appear. Isoquinolinethione II, which has not been described in the literature, was obtained by two methods. The first method consisted in treatment of dihydroisoquinolone I [8] with phosphorus pentasulfide in toluene by the method described for 3,4-dihydroisoquinoline-1-thione [10].

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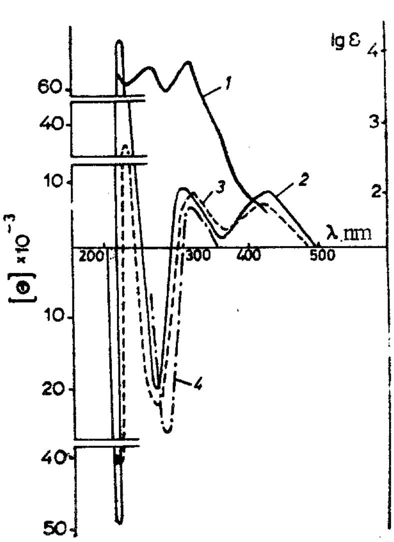


Fig. 1

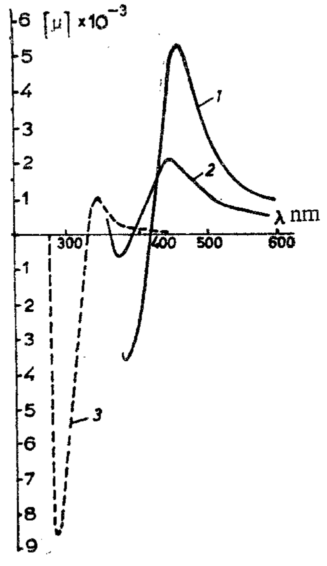
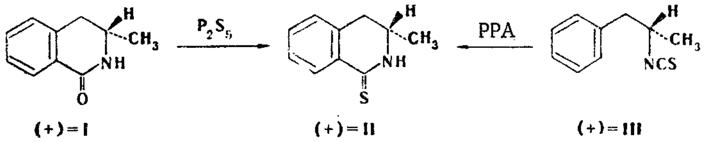


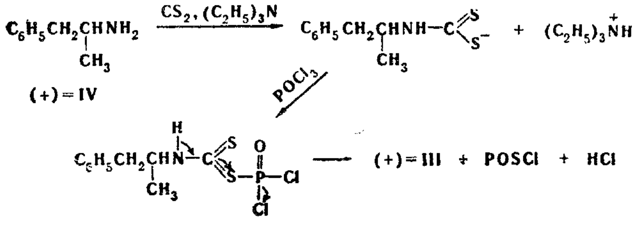
Fig. 2

Fig. 1. UV spectrum in isooctane (1) and CD curves of (+)-3-methyl-3,4-dihydroisoquinoline-1-thione (II) in isooctane (2), alcohol (3), and CF_3COOH (4).

Fig. 2. Rotatory dispersion curves of (+)-3-methyl-3,4-dihydroisoquinoline-1-thione (II) in benzene (1), alcohol (2) and CF_3COOH (3).



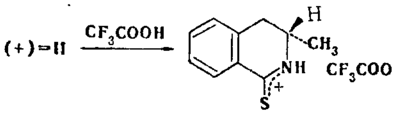
The second method consists in cyclization in the presence of polyphosphoric acid (PPA) of (+)-α-benzylethyl isothiocyanate (III). Optically active isothiocyanate III was synthesized from optically active α-benzylethylamine (IV) through dithiocarbamic acid chlorophosphate ester (V) via the following scheme:



This method, which was proposed in 1965 by Dieter and co-workers [11] for the synthesis of optically inactive isothiocyanates, was modified somewhat in our laboratory [12] as applied to the synthesis of optically active α-phenylethyl isothiocyanate.

The cyclization of (+)-α-benzylethyl isothiocyanate in PPA was carried out by the method described for β-(3,4-dimethoxyphenyl)ethyl isothiocyanate [13]. Inasmuch as this reaction has been described for a compound in which the benzene ring is activated by two methoxy groups, we changed the conditions: We raised the temperature from 75 to 130° and increased the heating time from 1.5 to 6 h and allowed the reaction mixture to stand for another 24 h at room temperature. Under these conditions we were able to obtain II in quantitative yield.

The electronic absorption spectra and the RD and CD curves in various solvents were recorded for isoquinolinethione II. The electronic spectrum of II is similar to the spectrum described in [10] for 3,4-dihydroisoquinoline-1-thione: λ_{max}, nm (log ε): 400 (2.08), 327 (3.75), 300 (shoulder, 3.69), and 262 (3.82) (Fig. 1). In a study of the chiral-optical properties (RD and CD) we observed a positive CE at 405-430 nm (Figs. 1 and 2), the position of which depends markedly on the solvent: A hypsochromic shift from 430 nm in isooctane to 405 nm in alcohol is observed as the solvent polarity increases. The position of this CE and its dependence on the polarity of the solvent make it possible to assign it to an $n \rightarrow \pi^*$ transition in the thioamide chromophore. This CE vanishes on measurement of the RD and CD in CF_3COOH, and this makes it possible to assume disappearance under these conditions of the thioamide chromophore because of the formation of protonated structure IIB:



(+)=IIB

We were unable to measure the RD below 360 nm because of strong absorption. Several Cotton effects are observed in the CD spectra in the shorter-wave region: a positive CE at 320 nm in alcohol (at 310 nm in isooctane), the reason for which is a $\pi \rightarrow \pi^*$ transition in the thioamide chromophore [10]; two negative CE at 262 and 208 nm and a positive CE at 218 nm, which are evidently due to $\pi \rightarrow \pi^*$ transitions in the aromatic chromophore fastened in the cyclic isoquinolinethione system and conjugated with the thioamide chromophore.

EXPERIMENTAL

Measurements of the RD and CD were made with a JASCO J-20 automatic spectropolarimeter and a Cary-60 spectrophotometer with an adapter for circular dichroism in cuvettes with thicknesses of 1, 0.1, and 0.01 cm. The electronic absorption spectra were recorded with a Cary-15 spectrophotometer.

(+)-3-Methyl-3,4-dihyroisoquinoline-1-thione (II). A) A 0.76-g (0.0034 mole) sample of P_2S_5 was added to a solution of 0.5 g (0.003 mole) of (+)-3-methyl-3,4-dihydro-1-isoquinolone (I), obtained in 55% yield from N-[(+)-(α-benzylethyl)]urethane by the method we previously described in [8], to 20 ml of absolute toluene, after which the mixture was refluxed for 30 min (chromatographic monitoring showed that no starting material was present in the reaction mixture after 15 min). The toluene solution was then cooled and decanted, and 10 ml of chloroform was added to the residue. The chloroform mixture was refluxed for a few minutes, after which the chloroform was decanted. Extraction with chloroform was repeated several times, after which all of the extracts were combined, and the solvent was removed by distillation to give 0.25 g (46%) of (+)-3-methyl-3,4-dihydroisoquinoline-1-thione (II) with mp 164° (from benzene–heptane). Found: C 67.6; H 6.20%. $C_{10}H_{11}NS$. Calculated: C 67.7; H 6.2%.

B) (+)-α-Benzylethyl Isothiocyanate (III). A solution of 9.3 g (0.122 mole) of CS_2 in 20 ml of absolute ether was added dropwise slowly with stirring to a cooled (to –5°) mixture of 13.5 g (0.1 mole) of (+)-α-benzylethylamine (IV) and 30 g (0.3 mole) of freshly distilled dry ethylamine in 100 ml of absolute ether, after which the mixture was allowed to stand overnight. The resulting precipitate was triturated to a powder, the mixture was cooled to –5°, and 15.4 g (0.1 mole) of freshly distilled $POCl_3$ was added dropwise with stirring. The mixture was then allowed to stand overnight, and the resulting precipitate was removed by filtration and washed with ether. The ether solution was washed with saturated sodium bicarbonate solution and water and dried with Na_2SO_4. The ether was removed by distillation, and the residue was distilled to give (+)-α-benzylethyl isothiocyanate (III) with bp 111° (1-2 mm), n_D^{18} 1.5746, and d_4^{20} 1.0517 in 60% yield. Found: C 67.7; H 6.4%. $C_{10}H_{11}NS$. Calculated: C 67.7; H 6.2%. UV spectrum in isooctane: λ_{max} (log ε) 252 nm (3.17). RD in isooctane (c 0.087) [M]°: 204 (600 nm), 307 (500), 532 (400), 848 (350), and 1687 (300).

A mixture of 3.3 g (0.018 mole) of (+)-α-benzylethyl isothiocyanate (III) and 95 g of PPA was heated with stirring at 130° for 6 h, after which it was allowed to stand overnight. It was then decomposed with ice water and extracted with chloroform, and the extract was washed with water, sodium bicarbonate solution, and water, and dried with $MgSO_4$. The chloroform was removed by distillation, and the residue was recrystallized from benzene–heptane to give 3.3 g (100%) of (+)-3-methyl-3,4-dihydroisoquinoline-1-thione (II) with mp 164°. No melting-point depression was observed for a mixture of this product and a sample obtained from (+)-3-methyl-3,4-dihydro-1-isoquinolone.

RD in acetonitrile (c 0.095) [M]°: 521 (600 nm), 3539 (442, peak), 0 (407), –2273 (380, valley), –372 (360); in chloroform (c 0.066): 593 (600), 4420 (439, peak), 0 (408), –5390 (380, valley), –5060 (375); in dimethyl sulfoxide (c 0.077): 457 (600), 2880 (447, peak), 0 (407), –1555 (380, valley), 0 (369), 4576 (362, peak), 0 (328), –9140 (302, valley), –11,000 (278, valley), 0 (264); in acetone (c 0.061): 584 (600), 3730 (451, peak), 0 (414), –2550 (380, valley), –1575 (366); in dioxane (c 0.093): 115 (600), 6110 (460, peak), 0 (421), –4810 (385, valley), –2290 (372).

CD in isooctane (c 0.01) [θ]°: 8350 (430 nm), 8700 (310), –21,000 (265-267), 67,000 (218), and –52,000 (208).

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