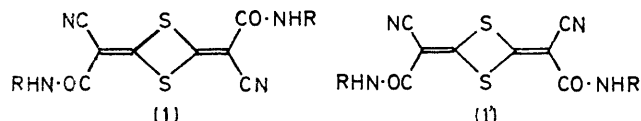


$\alpha\alpha'$ -Dicyano-(1,3-dithiacyclobutane-2,4-diylidene)diacetamides (Desaurins) from Thiazine Derivatives

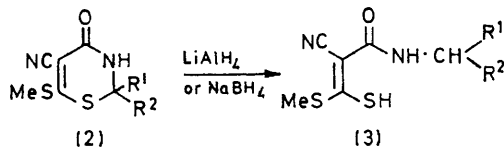
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The title compounds (1) were synthesized in good yields by refluxing *N*-alkyl-2-cyano-3-mercapto-3-methylthioacrylamides (3) with acetic anhydride. Compounds (3) were prepared by a novel hydrogenolysis of 2,2-disubstituted 3,4-dihydro-6-methylthio-4-oxo-2*H*-1,3-thiazine-5-carbonitriles (2) with lithium aluminium hydride or sodium borohydride.

THIS paper deals with a method for synthesizing desaurins † (1) from easily accessible thiazine derivatives (2).² Compound (1; R = H) has been obtained previously by a different route.³ The preparative methods reported so far may be classified roughly into three types: (i) syntheses from enedithiol compounds^{3,4} or dithiocarboxylic acids;⁵ (ii) reactions of active methylene compounds with carbon disulphide;^{1,6} (iii)



- a; R = CH₂Ph
b; R = cyclohexyl
c; R = CHMeEt



- a; R¹ = H, R² = Ph
b; R¹ R² = [CH₂]₅
c; R¹ = Me, R² = Et

miscellaneous methods.⁷ The present method is of type (i).

† Norton originally described a compound of type (1) as a thioketen dimer.^{1a} Meyer^{1b} dubbed the compound of type (1) prepared from deoxybenzoin 'desaurin.'

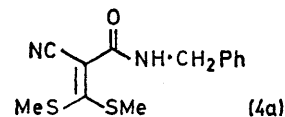
¹ (a) T. Norton and A. Oppenheim, *Ber.*, 1877, **10**, 701; (b) V. Meyer, *ibid.*, 1888, **21**, 353; 1890, **23**, 1571.

² M. Yokoyama, *Bull. Chem. Soc. Japan*, 1971, **44**, 1610.

³ M. Yokoyama, *J. Org. Chem.*, 1970, **35**, 283.

⁴ C. Kelbler and A. Schwarz, *Ber.*, 1912, **45**, 137; R. Gompper and W. Töpfl, *ibid.*, 1962, **95**, 2861.

A novel hydrogenolysis of 2,2-disubstituted 3,4-dihydro-6-methylthio-4-oxo-2*H*-1,3-thiazine-5-carbonitriles (2) with lithium aluminium hydride or sodium borohydride afforded *N*-substituted 2-cyano-3-mercapto-3-methylthioacrylamides (3) by a scission of the S-C(2) bond. The acrylamides (3) were identified by their i.r. and mass spectra and elemental analyses (Experimental section), and by the following evidence. Methylation of compound (3a) afforded the bismethylthio-derivative (4a). The u.v. spectra of the amides (3) [(3a) λ_{max} (EtOH) 230 (log ϵ 3.54), 283 (3.31), and 339 nm (3.65)] were similar to those of the thiazines (2) [(2a) λ_{max} (EtOH) 235 (log ϵ 3.77), 279 (3.93), and 336 nm (3.98)]. The n.m.r. spectrum (CDCl₃) of (3a) showed signals at δ 2.60 (s, SMe), 4.56 (d, CH₂), 6.92br (NH), 7.30 (s, Ph), and 17.0 (s, SH) (this unusual low-field shift shows strong intramolecular hydrogen bonding). The NH and SH signals disappeared on deuterium exchange. Irradiation at δ 6.92 simplified the methylene signal to a singlet; decoupling of the SH signal had no effect on the other peaks.



The amides (3) were converted by refluxing with acetic anhydride into the dithiacyclobutanes (1) in 68–75% yield [overall yield from (2) 22–51%]. The

⁵ A. Schönberg, L. von Vargha, and H. Kaltschmitt, *Ber.*, 1931, **64**, 2582; A. Schönberg, A. Stephenson, H. Kaltschmitt, E. Petersen, and H. Schulten, *ibid.*, 1933, **66**, 237.

⁶ V. Meyer and H. Wege, *Ber.*, 1891, **24**, 3535; P. Petrenko-Kristschenko, *ibid.*, 1892, **25**, 2239.

⁷ A. J. Kirby, *Tetrahedron*, 1966, **22**, 3001; M. S. Raasch, *Chem. Comm.*, 1966, 577; E. U. Elam and H. E. Davis, *J. Org. Chem.*, 1967, **32**, 1563; A. W. K. Chan, W. D. Crow, and I. Gosney, *Tetrahedron*, 1970, **26**, 1493.

u.v. and mass spectra of the products (1) are similar to those^{3,8} of other desaurins. The two RNH groups are shown to be magnetically equivalent by the n.m.r. spectra; thus two structures, (1) and (1'), can be considered. Structure (1), which possesses a high degree of symmetry, may be preferred on the grounds that another desaurin has been shown by X-ray crystallography to exist as a structure of this type.⁹

EXPERIMENTAL

Compounds were prepared as previously reported.²

N-Benzyl-2-cyano-3-mercapto-3-methylthioacrylamide (3a).—(a) *Hydrogenolysis with lithium aluminium hydride*. To a mixture of dry ether (ca. 200 ml) and lithium aluminium hydride (2 g, 53 mmol), 3,4-dihydro-6-methylthio-4-oxo-2-phenyl-2H-1,3-thiazine-5-carbonitrile (2a) (4 g, 15 mmol) was added with stirring below 0 °C. After 3 h stirring, the mixture was added dropwise to an excess of water. The ethereal layer was separated and evaporated to afford light yellow material which was recrystallized from acetic acid to give the amide (3a) as colourless needles (3 g, 74%), m.p. 165–166°.

(b) *Hydrogenolysis with sodium borohydride*. To a mixture of water (ca. 150 ml) and compound (2a) (2.5 g, 9 mmol), sodium borohydride (2 g, 53 mmol) and then a small amount of ethanol were added gradually with stirring at room temperature. After 1 h stirring, hydrochloric acid (1 : 1) was added until evolution of hydrogen ceased. The precipitate was collected, washed with water, and dried. Recrystallization from acetic acid gave the amide (3a) (1.3 g, 52%); ν_{\max} (KBr) 3280s (NH), 3010w (benzene CH), 2900w (CH), 2200vs (CN), 1630vs (CO), and 1500s cm⁻¹ (benzene); *m/e* 264 (*M*⁺, 26%), 231 (*M* - SH, 5), 217 (*M* - SCH₃, 44), 106 (NHCH₂Ph, 28), and 91 (CH₂Ph, 100) (Found: C, 54.65; H, 4.55; N, 10.9. C₁₂H₁₂N₂S₂O requires C, 54.55; H, 4.55; N, 10.6%).

The *N-cyclohexyl-* (3b) (50%) by lithium aluminium hydride method) and *N-s-butyl-* (3c) (50% by lithium aluminium hydride method; 32% by sodium borohydride method) analogues were obtained similarly. Compound (3b) had m.p. 131–132° (light yellow needles from acetic acid); ν_{\max} (KBr) 3280s (NH), 2920s, 2830m (CH), 2200s (CN), 1630vs (CO), and 1490m cm⁻¹ (benzene); δ (CDCl₃) 1.36 (4H, m, cyclohexyl 3- and 5-H₂), 1.88 (6H, m, cyclohexyl 2-, 4-, and 6-H₂), 2.60 (3H, s, CH₃), 3.82br (1H, CH), 6.30br (1H, exchangeable, NH), and 16.8 (1H, s, exchangeable, SH); λ_{\max} (EtOH) 227 (log ϵ 4.09), 286 (3.93), and 344 nm (4.36); *m/e* 256 (*M*⁺, 44%), 241 (*M* - CH₃, 20), 223 (*M* - SH, 12), 209 (*M* - SCH₃, 72), 158 (*M* - NHCH[CH₂]₅, 28), 126 (CONHCH[CH₂]₅, 100), and 98 (NHCH[CH₂]₅, 56). Compound (3c) had m.p. 106–107° (colourless needles from ethanol-water); ν_{\max} (KBr) 3250s (NH), 2960m, 2920m, 2850m (CH), 2200s (CN), and 1625vs cm⁻¹ (CO); δ (CDCl₃) 0.98 (3H, t, *J* 8 Hz, -CH₃), 1.12 (3H, d, *J* 6 Hz, CH₃), 1.60 (2H, quint, *J* 8 Hz, CH₂-CH₃), 2.62 (3H, s, CH₃), 4.00 (1H, m, CH), 6.10br (1H, NH), and 16.82 (1H, s, SH); λ_{\max} (EtOH) 229 (log ϵ 3.74), 288 (3.65), and 341 nm (4.09); *m/e* 230 (*M*⁺, 90%), 215 (*M* - CH₃, 7), 202 (*M* - CO, 7), 183 (*M* - SCH₃, 100), 158 (*M* - NHCHMeEt, 10), and 72 (NHCHMeEt, 30).

N-Benzyl-2-cyano-3,3-bismethylthioacrylamide (4a).—To aqueous methanol (1 : 1; 50 ml) containing the amide (3a) (0.5 g, 1.3 mmol) and sodium hydroxide (0.2 g, 5 mmol), dimethyl sulphate (5 g, 40 mmol) was added with stirring at room temperature. The mixture was set aside at room temperature for 2 days. The resulting needles were collected, washed with ethanol, and recrystallized from acetic acid-water (yield 0.3 g, 83%); m.p. 85–86°; ν_{\max} (KBr) 3350s, 3280s (NH), 3040w (benzene CH), 2910w (CH), 2200s (CN), and 1635vs cm⁻¹ (CO); δ (CDCl₃) 2.46 (3H, s, CH₃), 2.62 (3H, s, CH₃), 4.52 (2H, d, *J* 3 Hz, CH₂), 6.48br (1H, NH), and 7.24 (5H, s, C₆H₅) (irradiation at δ 6.48 simplified the methylene signal to a singlet); *m/e* 278 (*M*⁺, 5%), 263 (*M* - CH₃, 20), 231 (*M* - SCH₃, 44), 184 (*M* - 2SCH₃, 19), 106 (NHCH₂Ph, 18), and 91 (CH₂Ph, 100).

NN'-Dibenzyl- $\alpha\alpha'$ -dicyano-(1,3-dithiacyclobutane-2,4-diyldene)diacetamide (1a).—A mixture of the amide (3a) (2 g, 7.5 mmol) and acetic anhydride (17 g, 0.16 mol) was refluxed for 15 min and set aside for 1 day. The solution was then added to ethanol (10 ml) and poured into water (ca. 200 ml) to afford a light brown powder. Recrystallization from acetic acid gave light yellow plates (1a) [0.1 g, 69%; overall yield from (2a) 51%], m.p. 248–249°; ν_{\max} (KBr) 3260vs (NH), 3050m (benzene CH), 2920m (CH), 2210vs (CN), 1650vs (CO), and 1600w cm⁻¹ (benzene); δ [(CD₃)₂SO] 4.34 (4H, d, *J* 3 Hz, CH₂), 7.28 (10H, s, C₆H₅), and 9.20 (2H, d, *J* 3 Hz, NH); λ_{\max} (EtOH) 320sh (log ϵ 3.91), 334 (4.16), and 349.5 nm (4.19); *m/e* 432 (24%, *M*⁺), 326 (5, *M* - NHR), 298 (2, *M* - CONHR), 216 [100, (NC)(RNHCO)CS], 188 [18, (NC)(RNH)CS], and 106 (62, RNH) (Found: C, 60.65; H, 3.7; N, 12.85; S, 14.6. C₂₂H₁₆N₄S₂O₂ requires C, 61.1; H, 3.75; N, 12.95; S, 14.85%).

The *NN'-dicyclohexyl-* (1b) [75%; overall yield from (2b) 38%] and *NN'-di-s-butyl-* (1c) [68%; overall yield from (2c) 22%] analogues were prepared similarly. Compound (1b) had m.p. 221–222° (light yellow plates from acetic acid); ν_{\max} (KBr) 3320s (NH), 2920s, 2840s (CH), 2200s (CN), and 1640vs cm⁻¹ (CO); δ (CDCl₃) 1.28 (4H, m, cyclohexyl 3- and 5-H₂), 1.76 (6H, m, cyclohexyl 2-, 4-, and 6-H₂), 3.80br (2H, CH), and 5.92 (2H, d, *J* 4 Hz, NH); λ_{\max} (EtOH) 320sh (log ϵ 4.39), 334 (4.61), and 349.5 nm (4.64); *m/e* 416 (100%, *M*⁺), 318 (70, *M* - NHR), 290 (13, *M* - CONHR), 208 [60, (NC)(RNHCO)CS], 180 [13, (NC)(RNH)CS], and 98 (35, RNH). Compound (1c) had m.p. 234–235° (light yellow plates from acetic acid); ν_{\max} (KBr) 3320vs (NH), 2960m, 2920m, 2860m (CH), 2210s (CN), and 1640vs cm⁻¹ (CO); λ_{\max} (EtOH) 318 (log ϵ 3.60), 333 (3.85), and 347 nm (3.88); *m/e* 364 (53%, *M*⁺), 292 (100, *M* - NHR), 264 (2, *M* - CONHR), 182 [60, (NC)(RNHCO)CS], 154 [55, (NC)(RNH)CS], and 72 (2, RNH).

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⁸ P. Yates and T. R. Lynch, *Canad. J. Chem.*, 1968, **46**, 365.

⁹ T. R. Lynch, I. P. Mellor, S. C. Nyburg, and P. Yates, *Tetrahedron Letters*, 1967, 373.