ACTA CHEMICA SCANDINAVICA 16 (1962) 591–598

Isothiocyanates XLII *. Glucocleomin, A New Natural Glucoside, Furnishing (–)-5-Ethyl-5-methyl-2-oxazolidinethione on Enzymic Hydrolysis

ANDERS KJÆR and HELENE THOMSEN

Department of Organic Chemistry, Royal Veterinary and Agricultural College, Copenhagen V, Denmark

Dedicated to Professor *Holger Erdtman* on his 60th birthday

The presence of a new glucoside, *glucocleomin*, in seeds of *Cleome spinosa* Jacq. *(Capparidaceae)* is demonstrated. Acid hydrolysis of glucocleomin produces hydroxylamine whereas enzymic hydrolysis is accompanied by the formation of sulphate, glucose and a 2-oxazolidinethione. On basis of composition, paper chromatography, infra-red and nuclear magnetic resonance spectra the latter is identified as *(–)-5-ethyl-5-methyl-2-oxazolidinethione* with as yet unknown absolute configuration.

The identification is corroborated by synthesis of the heterocyclic hydrolysis product from optically active 1-amino-2-methyl-2-butanol, obtained by resolution of the racemic amino-alcohol with L-mandelic acid. The synthesis of *racemic 5-propyl-* and *5-isopropyl-2-oxazolidinethione* also is described. The combined experimental data provide the basis for a structural formulation of *glucocleomin*. Several botanical sources of glucocleomin are listed.

In a previous communication of this series [1], seed extracts of several species of the family *Capparidaceae* were demonstrated to contain two isothiocyanate-producing glycosides. One of these, glucocapparin, afforded methyl isothiocyanate on enzymic hydrolysis and was subsequently isolated in crystalline form from seeds of *Cleome spinosa* Jacq.[2] It is the purpose of the present paper to describe the structure elucidation of the second glycoside, extracted from the same seed material and constituting an addition to the rapidly growing list of glycosides of this general type [3].

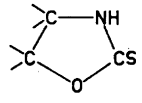
Cleome spinosa Jacq. is a herb of paleotropical distribution, indigeneous to the American continent but naturalized in tropical and subtropical regions

* Part XLI of this series: *Acta Chem. Scand.* **16** (1962) 83.

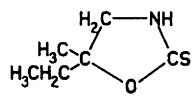
throughout the world. It affords a popular garden annual ('spider flower') and seed material can be obtained commercially *.

Enzymic hydrolysis of the unknown glycoside did not give rise to the formation of steam-volatile products whereas the expected production of sulphate and glucose was confirmed by paperchromatographic methods. Again, acid hydrolysis of a paper eluate of the unknown glycoside yielded hydroxylamine, a characteristic behaviour of all mustard oil-producing glucosides [4]. It was further established that the enzymic reaction was accompanied by the formation of an ether-extractable hydrolysis product, *cleomin*, yielding a blue colour with Grote's reagent and displaying ultra-violet absorption data (λ_{max}^{EtOH} 242 mμ, displaced to 230 mμ in alkali), analogous to those of several 2-oxazolidinethiones, previously recognized as enzymic hydrolysis products of glucosides containing β-hydroxy-substituted side-chains [3,5]. Paperchromatographic comparison of the enzymically produced compound with all formerly known 2-oxazolidinethiones of natural derivation clearly indicated it to be different from these. The combined evidence at this stage indicated that the glycoside present in *C.spinosa* besides glucocapparin was a new glucoside of the ordinary type, for which the designation *glucocleomin* was introduced in accordance with the common practice for naming compounds within this group of natural products [3] (*cf.* footnote p. 594).

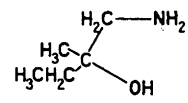
On a preparative scale, a methanolic extract of defatted *C. spinosa* seed powder was subjected to enzymic hydrolysis with a cell-free myrosinase preparation in aqueous citrate buffer at pH 6.4. The mixture was steam-distilled in order to remove methyl isothiocyanate originating from glucocapparin, and the non-volatile hydrolysis product, cleomin, was isolated by continuous ether extraction. After chromatography on alumina and recrystallization from water, cleomin was obtained as a *levo*rotatory, colourless compound, m.p. 52°, possessing the elemental composition $C_6H_{11}NOS$ and exhibiting ultra-violet and infra-red absorption spectra strikingly similar to those of several 2-oxazolidinethiones previously studied in this laboratory and elsewhere [3,5]. Consequently, (I) represents a likely partial structure of cleomin, in which three carbon and ten hydrogen atoms remain to be accomodated.



I



II



III

Substitution of (I) with propyl- or isopropyl-groupings in 5-position could be ruled out upon comparison of the infra-red spectra of cleomin with those of synthetic samples of these previously unknown substitutes, but also through the higher R_F-values observed on paper chromatography of the 5-substituted propyl-derivatives. Several analogies[5] suggested that the unknown 4-substituted

* The seed material employed in the present studies was purchased from E. Benary, Hann.-Münden, Germany, under the name *Cleome pungens* Willd. (synonym for *C. spinosa* Jacq.). On paperchromatographic evidence two glucosides were likewise reported by Schultz and Wagner [14] in *C. pungens*.

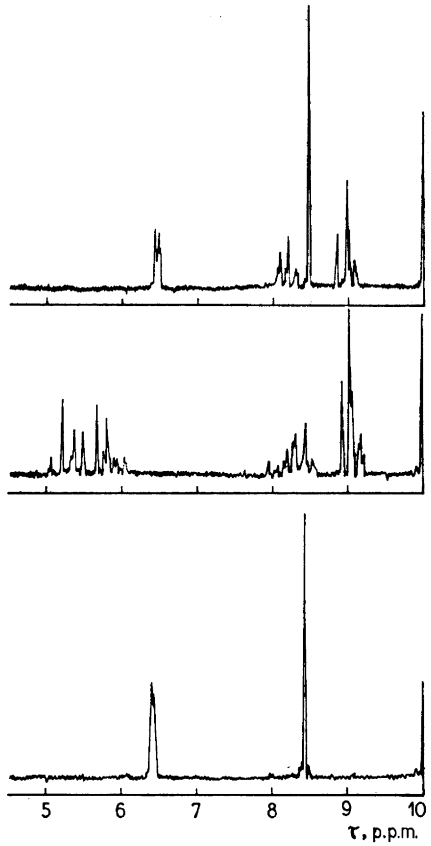


Fig. 1. Proton resonance spectra (60 Mc) of: upper curve: cleomin (II)[(−)-5-ethyl-5-methyl-2-oxazolidinethione]; middle curve: 4-ethyl-2-oxazolidinethione; lower curve: 5,5-dimethyl-2-oxazolidinethione. Solvent: $CDCl_3$.

propyl-isomerides would possess even higher R_F-values and hence could be disregarded as well. The syntheses of the racemic *5-propyl-* and *5-isopropyl-2-oxazolidinethione* were performed by reaction of the appropriate amino-alcohols with thiocarbonyl chloride in the customary way, as described in the experimental section.

A choice between the six possible di-(or tri)-substitutes could be made on basis of n.m.r. spectra (Fig. 1) *. The strong singlet at τ 8.46 precludes structures with hydrogen in both 4- and 5-position, whereas the absence of a doublet at τ 8.5—9.0 is incompatible with structures containing three methyl groups as substituents. Of the remaining possibilities, *viz.* 4-ethyl-4-methyl- and 5-ethyl-5-methyl-2-oxazolidinethione, the former can be excluded since no absorption occurs at τ 5—6, the range for the (5)-CH_2-O-multiplet, as evident from the n.m.r. spectrum of 4-ethyl-2-oxazolidinethione (Fig. 1). The n.m.r. data of

* Nuclear magnetic resonance (n.m.r.) spectra were kindly determined by Varian Associates, Zürich, on an A-60 instrument and are reported here in τ values relative to tetramethylsilane (τ 10.0, Fig. 1).

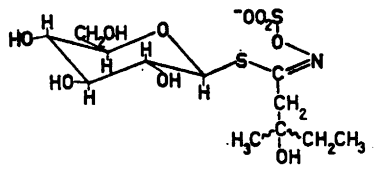
cleomin are, on the other hand, in perfect agreement with those expected for structure (II), the multiplet at τ 6.45 being assignable to the (4)-CH_2-protons as supported by comparison with the n.m.r. spectrum of 5,5-dimethyl-2-oxazolidinethione (Fig. 1).

Corroboration of this conclusion was provided through infra-red studies. Whereas the solid-phase IR-spectrum of cleomin differed significantly from that of (±)-5-ethyl-5-methyl-2-oxazolidinethione, previously prepared in this laboratory [6], the two compounds gave, as expected, identical infra-red spectra in solution.

A synthesis of cleomin (II) was achieved in the following way. (±)-1-Amino-2-methyl-2-butanol (III), prepared from the cyanohydrin of methyl ethyl ketone as formerly described in this series [6], was resolved through diastereoisomeric salts. Preliminary attempts to effect the resolution by means of (−)-2-(2-naphthoxy)-propionic acid *, successfully employed by Fourneau and Ribas [7] in the resolution of the analogous 1-dimethylamino-2-methyl-2-butanol, were unavailing. Mandelic acid, however, proved to be useful for the desired resolution. The amino-alcohol enantiomer giving a *levo*rotatory neutral oxalate was liberated from the least soluble salt with L(+)-mandelic acid.

On reaction with thiocarbonyl chloride, the active amino-alcohol (III) was converted into (−)-*5-ethyl-5-methyl-2-oxazolidinethione* (II), which proved identical with cleomin, both with regard to sign and magnitude of rotation, m.p. and mixed m.p., as well as ultra-violet, infra-red and n.m.r. spectra. Experimental work is in progress to establish the absolute configuration of cleomin.

No attempts have been made to isolate the parent glucoside, glucocleomin, but the above structure determination of cleomin provides the clue to its structure. Since it has been repeatedly demonstrated [3,5] that enzymically produced 2-oxazolidinethiones arise from cyclization of initially formed 2-hydroxy-substituted isothiocyanates, and in view of the behaviour of glucocleomin towards enzymic and acid hydrolysis, it appears safe to conclude that the glucoside ion ** possesses the structure (IV) with as yet unknown stereochemistry in the side-chain.



IV

* This acid was conveniently prepared by resolution of the racemate with (+)-2-amino-1-phenylpropane ('dextroamphetamine') according to a proposal of Matell [8] (*cf.* the experimental part).

** Recently, Ettlinger and Dateo [23] suggested the trivial name 'glucosinolate' (*cf.* Greek *σινατ-ελαιον*, mustard oil) for the *S*-β-D-1-glucopyranosyl-formthiohydroximic acid-*O*-sulphonate ion whence all hitherto encountered glucosides of this class derive. In this semisystematic nomenclature, which is considered practical in view of the rapidly growing number of such uniformly constituted glucosides, the glucocleomin ion would be *2-hydroxy-2-methylbutyl-glucosinolate*.

Formally, the new glucoside is closely related to glucoconringiin, a natural glucoside undergoing hydrolysis to 5,5-dimethyl-2-oxazolidinethione [9-11]. As discussed in a recent communication from this laboratory [5], compounds involved in the well-known metabolism of valine, isoleucine and leucine may conceivably function as precursors in the biogenesis of isothiocyanate glucosides containing branched side-chains.

Besides *Cleome spinosa* Jacq. previously published paperchromatographic data [1] indicate seeds of the following *Cleome* species to be sources of glucocleomin: *C. arabica* L., *C. arborea* Bss., *C. gigantea* L., *C. speciosissima* Deppe., *C. viscosa* L., *C. graveolens* Rafin. and *C. trachysperma* (Torr. *et* Gray) Pax *et* K. Hoffm. Other seed specimens containing glucocleomin according to paper chromatography are: *Cleome ornithopoides* L., *C. machycarpa* Rafin., *C. integrifolia* Torr. *et* Gray, *C. serrata* Jacq. and *Crataeva Tapia* L. Whereas no glucocleomin is detectable in seeds of the common caper, *Capparis spinosa* L., fresh green leaves of the same species was found to contain the new glucoside. It is interesting to note that glucocleomin in all of the above listed sources is accompanied by glucocapparin.

Recently, glucocleomin also has been identified in this laboratory as a constituent of seeds of the Indian tree *Putranjiva Roxburghii* Wall., belonging to the family *Euphorbiaceae* and reputed as a source of isothiocyanate glucosides. The results of these studies will be presented in a forthcoming communication [13].

EXPERIMENTAL

Melting points are uncorrected and determined in capillary tubes in liquid baths equipped with fully immersed thermometers. Rotations are measured in 1 dm tubes. Analytical samples are dried *in vacuo* at room temperature over calcium chloride.

Paperchromatographic analysis. A 20 μl aliquot of a 70 % methanol extract (1.0 ml) of finely ground seeds (0.1 g) of *Cleome spinosa* Jacq. was chromatographed on paper with glucotropaeolin as a reference compound in the solvent system butanol: ethanol: water (4:1:4). Besides much glucocapparin (R_B*0.26), a somewhat weaker spot of glucocleomin was observed with an R_B-value of 0.63. Two additional, faint spots with R_B-values of 1.36 and 1.88 indicated the presence of two minor glycosides in the same seed extract.

The total 70 % methanol extract of a 5 g seed sample was evenly distributed along the starting lines of two sheets of Whatman paper No. 3 MM and chromatographed in the above solvent system. The glucocleomin-zones were located by spraying of edge cuts with $AgNO_3/NH_3$ and separately eluted with water. The residue from the eluate of the first sheet was hydrolyzed with 20 % HCl (3 ml) at 50° for 2.5 h. Next day, the hydrolysis residue was chromatographed in methanol : 6 N HCl (7:3), and the formation of hydroxylamine was demonstrated on spraying with picryl chloride [4]. The eluate from the second sheet (100 μl) was subjected to enzymic hydrolysis with a sulphate-free myrosinase preparation. After 1 h, the liberation of sulphate could easily be demonstrated by means of barium acetate. Paper chromatography in *n*-BuOH:EtOH:H_2O (4:1:4) and *n*-BuOH:pyridine:H_2O (6:4:3) served to confirm the concomitant formation of glucose.

Isolation and properties of cleomin. Seeds of *Cleome spinosa* Jacq. (1 kg) were portionwise disintegrated and defatted in a Waring blendor in a total of 3.2 l of carbon tetrachloride. The seed cake was refluxed for 1 h with fresh solvent (3 l) and this operation was repeated once. The dry seed powder (645 g) was extracted by refluxing with three successive 3.5 l-portions of 70 % methanol. The combined filtrates were concentrated *in vacuo*

* *i.e.* the ratio between the distances travelled by the compound and glucotropaeolin, respectively[14].

to remove methanol (end volume 1.4 l) and an orange precipitate was removed by filtration through Celite.

The filtrate was diluted to 4 l and buffered by addition of 150 ml of a 1 M solution of trisodium citrate, containing 3 g of citric acid per l. A cell-free myrosinase solution (100 ml), prepared from white mustard flour, was added together with a small quantity of ascorbic acid [15], and the enzymic hydrolysis was allowed to proceed at room temperature for 24 h. The mixture was then steam-distilled to remove methyl isothiocyanate, a total of 3 l of distillate being collected. After removal of a dark precipitate by filtration, the residue from the steam-distillation was saturated with sodium chloride and subjected to continuous extraction with ether for 24 h.

Cleomin was subsequently transferred from the ether extract to 0.1 N NaOH (400 ml). The aqueous phase was brought to pH 6.5 with hydrochloric acid and the product was retransferred to ether by continuous extraction for 24 h.

The dried ether solution was concentrated to a yellow oil (1.6 g) from which the Grote-positive fraction was quantitatively extracted with hot water. The solid contained in the combined aqueous extracts (1.37 g) was now extracted with several portions of benzene to bring all cleomin into solution. This was then allowed to flow through a column of neutral alumina (65 × 32[o] mm) retaining considerable amounts of extraneous matter. The column was washed with benzene (400 ml) and eluted with the same solvent containing 0.5 % of methanol. The cleomin-containing fractions were pooled and concentrated to dryness. The residue (700 mg) was taken up in hot water, a small quantity of insoluble material was filtered off, and the solution was cooled whereupon slightly yellow crystals separated (270 mg). These were recrystallized twice from water with a little charcoal to give an analytical specimen of *cleomin* (40 mg) as dense, colourless rhombs, m.p. 50—51°, $[\alpha]_D^{24}$—25.4° (*c* 1.0, H_2O). (Found: C 49.34; H 7.78; N 9.62. Calc. for $C_6H_{11}NOS$: C 49.62; H 7.64; N 9.65). The ultra-violet spectrum in ethanol had the following characteristics: λ_{max} 243 mμ (ε 19500), λ_{max} 204 mμ (ε 6650) and λ_{min} 218 mμ (ε 3000), in good agreement with previously reported data for 2-oxazolidinethiones [3]. The infra-red spectrum (in KBr) exhibited conspicuous bands at 3140 vs, 3020 m, 2950 s, 2910 m, 2730 w, 1580 vs, 1470 m, 1455 m, 1380 s, 1348 m, 1330 s, 1300 s, 1250 s, 1200 vs, 1130 s, 1108 s, 1060 m, 1044 m, 1020 w, 1002 m, 962 s, 913 w, 878 m, 787 s and 717 m cm^{-1} (vs very strong, s strong, m medium and w weak). In chloroform solution, the spectrum of cleomin was considerably changed, exhibiting, *e.g.*, two bands at 1530 m and 1500 s cm^{-1}, instead of the 1580 cm^{-1} peak, but indistinguishable from the spectrum of (±)-5-ethyl-5-methyl-2-oxazolidinethione [6] in chloroform solution. In the solid state, however, the enantiomer and the racemic modification possessed markedly different spectra.

On paper chromatography with the upper layer of the solvent system benzene:heptane:water (9:2:9) as the mobile phase, cleomin migrated at an R_{Ph}-value* of 0.83 and was indistinguishable from (±)-5-ethyl-5-methyl-2-oxazolidinethione [6], whereas (±)-5-propyl- and (±)-5-isopropyl-2-oxazolidinethione migrated at rates corresponding to R_{Ph}-values of 0.95 and 0.93, respectively.

Syntheses

Resolution of 1-amino-2-methyl-2-butanol (III). An attempt was made to resolve the racemic amino alcohol by means of (−)-2-(2-naphthoxy)-propionic acid [7]**, which was

* *i.e.* the ratio between the distances travelled by the compound and (+)-5-phenyl-2-oxazolidinethione [16] as a reference.

** This acid was conveniently obtained by resolution of the racemic acid with (+)-1-phenyl-2-aminopropane, liberated from the commercially available sulphate ('Dextroamphetamine sulphate'), according to a suggestion by Matell [8]. The salt produced from equivalent amounts of the acid and amine was recrystallized four times from 85 % ethanol (yield 70 %), m.p. 197—198°, $[\alpha]_D^{23}$ −47.0° (*c* 1.0, CH_3OH). (Found: C 75.05; H 7.23; N 4.02. Calc. for $C_{22}H_{25}NO_3$: C 75.18; H 7.17; N 3.99). (−)-2-(2-Naphthoxy)-propionic acid was liberated from the salt, extracted with ether and recrystallized from benzene, m.p. 118°, $[\alpha]_D^{24}$ −93.5° (*c* 0.5, abs. C_2H_5OH). Lit. values [17]: m.p. 117°, $[\alpha]_D^{20}$ −93.33°.

successfully employed by Fourneau and Ribas [7] in a very similar case, but no fractionation into diastereoisomeric salts could be effected on recrystallization. The following procedure, however, proved useful in achieving the desired resolution:

A solution of the amino-alcohol (4.34 g) in a 3:1 mixture of ethyl acetate and anhydrous ethanol (475 ml) was mixed with another solution of L(+)-mandelic acid (6.40 g) in the same solvent mixture (200 ml), heated to 50° and cooled. The salt (10.6 g), m.p. 115–119°, separated on scratching and was recrystallized seven times from the above solvent system to give one of the diastereoisomeric salts in pure form (2.95 g), m.p. 131°, $[\alpha]_D^{24}$ + 69.0° (*c* 4, H_2O). (Found: C 61.02; H 8.20; N 5.43. Calc. for $C_{13}H_{21}O_4N$: C 61.15; H 8.29; N 5.49). The amino-alcohol was liberated with conc. NaOH and continuously extracted into ether. The dried solution was mixed with an ethereal solution of the calculated amount of oxalic acid dihydrate to form the *neutral oxalate*, which separated from 96 % ethanol in thin colourless plates, m.p. 192°, $[\alpha]_D^{25}$—4.2° (*c* 2.5, H_2O). (Found: C 48.43; H 9.61; N 9.34. Calc. for $C_{13}H_{28}N_2O_6$: C 48.63; H 9.52; N 9.46). On admixture with the racemic oxalate [6], the melting point was depressed to 187–188°. The two preparations gave nearly identical infra-red spectra (in KBr).

Synthesis of (—)-5-ethyl-5-methyl-2-oxazolidinethione (cleomin). The above *levo*rotatory oxalate (675 mg) was suspended in chloroform (15 ml) and cooled in ice. Thiocarbonyl chloride (0.5 ml) was added to the stirred suspension, followed by triethylamine (1.4 g) dissolved in chloroform (5 ml). The reaction mixture was kept at 0° for several hours and then allowed to come to room temperature. The organic phase was extracted with three 5 ml-portions of 0.1 N HCl, washed with water and dried. On evaporation to dryness, a polymeric solid embedded in a yellow oil remained. The latter was thoroughly extracted with hot water until the extracts gave negative Grote-reaction. After concentration to 10 ml, the aqueous solution on cooling and seeding with cleomin slowly deposited colourless, rhombic plates (110 mg), which were recrystallized twice from water to give an analytical specimen, m.p. 50–51°, alone or in admixture with naturally derived cleomin, $[\alpha]_D^{24}$ —25.9° (*c* 1.0, H_2O). (Found: C 49.78; H 7.70; N 9.44). The synthetic specimen was indistinguishable from cleomin on basis of paper chromatography as well as ultra-violet, infra-red and n.m.r. spectra.

5-Propyl-2-oxazolidinethione. (i) *2-Hydroxyvaleronitrile.* Butyraldehyde was converted into the cyanohydrin in 70 % yield on treatment with liquid hydrocyanic acid and a few drops of piperidine, following the general procedure of Linstead and Whalley [18], b.p. 97–98°/11 mm, n_D^{15} 1.4224 (Lit. values: b.p. 110.5–111°/20.5 mm [19], 73–74°/3 mm [20]; $n_D^{15.5}$ 1.42285 [19], n_D^{20} 1.4220 [20]). (ii) *1-Amino-2-pentanol.* The cyanohydrin was reduced in ether solution with a five-fold excess of lithium aluminium hydride, and the reaction mixture was worked up as previously described for analogous cases [9]. The amino-alcohol was obtained in 60 % yield and distilled as a colourless oil, b.p. 83°/10 mm, n_D^{25} 1.4490 (supercooled), which solidified in the receiver, m.p. 29°. (Found: C 58.13; H 12.63; N 13.40. Calc. for $C_5H_{13}NO$: C 58.21; H 12.70; N 13.58). An incorrectly analyzing sample was previously recorded with the b.p. 75–80°/3.5–4 mm [21]. For comparison, the benzamide was prepared as described elsewhere [21], m.p. 112.5° (reported [21] 112–113.5°). The *normal oxalate*, m.p. 212° (decomp.), separated from water (Found: C 48.61; H 9.36; N 9.47). (iii) *(+)-5-Propyl-2-oxazolidinethione.* Upon reaction of 1-amino-2-pentanol with thiocarbonyl chloride in chloroform and addition of triethylamine, a method previously utilized in this laboratory [12], 5-propyl-2-oxazolidinethione was obtained in a 25 % yield. The substance separated from ethyl acetate: pentane mixtures in flat colourless needles, m.p. 51° (Found: C 49.53; H 7.47; N 9.59. Calc. for $C_6H_{11}NOS$: C 49.62; H 7.64; N 9.65). The ultra-violet spectrum (in ethanol) possessed the following characteristics: λ_{max} 243 mμ (ε 18 250), λ_{max} 204 mμ (ε 5100), and λ_{min} 217 mμ (ε 1540). The infra-red spectrum exhibited the expected bands.

5-Isopropyl-2-oxazolidinethione. (i) *2-Hydroxyisovaleronitrile.* Prepared from isobutyraldehyde by the same procedure as employed above for butyraldehyde, b.p. 90°/10 mm, $n_D^{15.5}$ 1.4215 (Lit. values: b.p. 106–106.5°/22 mm [19], n_D^{16} 1.42215 [19]). (ii) *1-Amino-3-methyl-2-butanol.* The reduction of the cyanohydrin proceeded in 80 % yield as described in the above straight-chain series. The amino-alcohol distilled at 76–77°/9 mm as a colour-

less oil, n_D^{26} 1.4501 (supercooled), crystallizing in the receiver, m.p. 27°. (Found: C 58.15; H 12.70; N 13.42). (Lit.values [22]: b,p. 174°/754 mm, m.p. 26–27°). The *benzamide* was prepared for comparison as described above, m.p. 116° (Found: C 70.09; H 8.19; N 6.79. Calc. for $C_{11}H_{17}NO_2$: C 69.52; H 8.26; N 6.76). The *normal oxalate* separated from water, m.p. 229° (decomp.). (Found: C 48.62; H 9.37; N 9.57). (iii) (±)-*5-Isopropyl-2-oxazolidinethione*. The above described procedure was adopted unchanged for the conversion of 1-amino-3-methyl-2-butanol into 5-isopropyl-2-oxazolidinethione, which separated from a mixture of ethyl acetate and pentane in flat, colourless needles, m.p. 99.5°, possessing an ultra-violet spectrum coinciding with that of the 5-propyl derivative. (Found: C 49.62; H 7.72; N 9.44). The infra-red spectrum, however, was markedly different from that of the 5-propyl-substituted compound.

Microanalyses were performed by Mr. G. Cornali.

The authors acknowledge the assistance of Miss E. Vesterager in part of the synthetic work. Thanks are due to Dr. O. Rosenlund, *Ferrosan Ltd.*, for a generous gift of 'Dextro-amphetamine sulphate' and to *The Botanical Garden of the University of Copenhagen* for numerous seed and plant specimens.

The work is part of investigations supported by *The Danish State Research Foundation (Statens Almindelige Videnskabsfond), The Carlsberg Foundation (Carlsbergfondet)* and *Kai Hansen's Fond.*

REFERENCES

1. Kjær, A., Gmelin, R. and Larsen, I. *Acta Chem. Scand.* **9** (1955) 857.
2. Kjær, A. and Gmelin, R. *Acta Chem. Scand.* **10** (1956) 335.
3. Kjær, A. *Fortschr. Chem. Org. Naturstoffe* **18** (1960) 122.
4. Ettlinger, M. G. and Lundeen, A. J. *J. Am. Chem. Soc.* **78** (1958) 4172.
5. Kjær, A. and Christensen, B. W. *Acta Chem. Scand.* **16** (1962) 71.
6. Kjær, A. and Boe Jensen, R. *Acta Chem. Scand.* **12** (1958) 1746.
7. Fourneau, E. and Ribas, I. *Anales soc. españ. fis. y quim.* **25** (1927) 401.
8. Matell, M. *Acta Chem. Scand.* **7** (1953) 698.
9. Kjær, A., Gmelin, R. and Boe Jensen, R. *Acta Chem. Scand.* **10** (1956) 432.
10. Schultz, O.-E. and Wagner, W. *Arch. Pharm.* **289/61** (1956) 597.
11. Gmelin, R. and Virtanen, A. I. *Acta Chem. Scand.* **13** (1959) 1718.
12. Kjær, A. and Christensen, B. W. *Acta Chem. Scand.* **13** (1959) 1575.
13. Kjær, A. and Friis, P. *Acta Chem. Scand.* **16** (1962.) *In press.*
14. Schultz, O.-E. and Wagner, W. *Z. Naturforsch.* **11b** (1956) 73.
15. Schwimmer, S. *Acta Chem. Scand.* **15** (1961) 535.
16. Kjær, A. and Gmelin, R. *Acta Chem. Scand.* **11** (1957) 906.
17. Fourneau, E. and Balaceano *Bull. soc. chim. France* [4] **37** (1925) 1602.
18. Linstead, R. P. and Whalley, M. *J. Chem. Soc.* **1954** 3722.
19. Ultée, A. J. *Rec. trav. chim.* **28** (1909) 248.
20. Nazarov, I. N., Akhrem, A. A. and Kamernitskiĭ, A. V. *Zhur. Obshcheĭ Khim.* **25** (1955) 1345; *Chem. Abstr.* **50** (1956) 4950.
21. Fort, G. and McLean, A. *J. Chem. Soc.* **1948** 1907.
22. Krassuski, K. and Kriwonoss, F. *Ukrain. Khim. Zhur.* **4** (1929) 79; *Chem. Zentr.* **1929 II** 2174.
23. Ettlinger, M.G. and Dateo, Jr.,G.P. *Final Report, Contract DA 19-129-QM-1059.* Departm. of Chemistry, Rice Institute, Houston, Texas (1961) p.12.

Received September 9, 1961.