SYNTHESIS OF 2-OXAZOLIDINESELONES[a]

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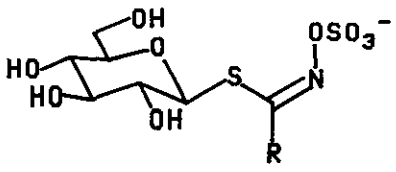
Abstract - A series of 2-oxazolidineselones are synthesized by mercuric chloride assisted reactions of 1,2-aminoalcohols and carbon diselenide.

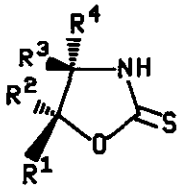
A characteristic, conspicuous, and important property of about one hundred glucosinolates (1) thus far identified in higher plants is their ability to undergo enzymic hydrolysis, resulting in the formation of isothiocyanates (mustard oils) (2). When the side-chains of (1) contain a β-positioned hydroxy group, as obtain for about a tenth of all known glucosinolates, the derived isothiocyanates undergo spontaneous cyclization to 2-oxazolidinethiones (3), some of which possess interesting and important biological properties.[1]



1

R-N=C=S

2

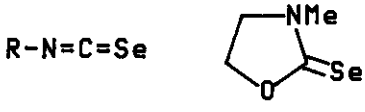


3

As an overture to our search in Nature for the selenoglucoside equivalents of 1 we recently synthesized a few representatives of this new class of compounds and noticed that their enzymic hydrolysis gave isoselenocyanates (4).[2] In a subsequent study the major glucosinolates in the selenium-accumulating crucifer Stanleya pinnata were identified as 3-butenylglucosinolate (1, R = CH_2:CH[CH_2]$_2$),

[a]Dedicated to Professor D.H.R. Barton on the occasion of his 70th birthday.

(R)-2-hydroxy-3-butenylglucosinolate (1, R = (R)-CH_2:CHCH(OH)CH_2), and (S)-2-hydroxy-3-butenylglucosinolate (1, R = (S)-CH_2:CHCH(OH)CH_2), which on enzymic hydrolysis afforded 3-butenyl isothiocyanate (2, R = CH_2:CH[CH_2]$_2$), (S)-5-vinyl-2-oxazolidinethione (3, R^1 = CH_2:CH; R^2 = R^3 = R^4 = H), and (R)-5-vinyl-2-oxazolidinethione (3, R^1 = R^3 = R^4 = H; R^2 = CH_2:CH), respectively.[3] In connexion herewith we synthesized racemic 5-vinyl-2-oxazolidineselone (6c)[3] by a method which proved of general utility for the production of 2-oxazolidineselones. We report the synthesis of additional members of this virtually unknown class of compounds.



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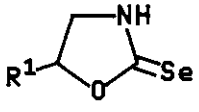
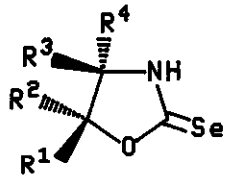


6a, R^1 = H
6b, R^1 = Me
6c, R^1 = H_2C:CH



6d, R^1 = R^2 = R^3 = H; R^4 = Me
6e, R^1 = Ph; R^2 = R^3 = R^4 = H
6f, R^1 = R^2 = Me; R^3 = R^4 = H

Prior to this study, N-methyl-2-oxazolidineselone (5), produced by Devillanova and Verani,[4a] in unstated yield, from N-methylethanolamine and carbon diselenide was the only known, monocyclic 2-oxazolidineselone and all attempts at preparation of the non-methylated parent compound (6a) by the same authors were unsuccessful.[4] In 1976, Henriksen and Ehrbar[5] found that 1:1 complexes of primary amines with mercuric chloride react with carbon diselenide and triethylamine in acetonitrile to give moderate to good yields of isoselenocyanates (4). When we applied this procedure to primary 1,2-aminoalcohols a smooth conversion into 2-oxazolidineselones took place.

By this approach, both the parent ring compound (6a) and a series of C-substituted derivatives, (6b)-(6f), were produced as crystalline, colourless, light-sensitive compounds which can be stored indefinitely at -25°C in the dark. Of the four chiral 2-oxazolidineselones, two, (6d) and (6e), were produced in supposedly enantiomerically homogeneous form. The ^{1}H nmr spectra of the six 2-oxazolidineselones are almost identical with those of the corresponding, known 2-oxazolidinethiones (3), save for the NH-signals appearing at δ 8.8-9.2, compared to δ-values of about 8.1 for the sulfur isologues. Again, the solid-state infrared spectra, within the wave-length range 600-4000 cm^{-1}, are virtually superimposable on those

of the corresponding 2-oxazolidinethiones, previously proven to exist exclusively in the thione form;[6] hence, we conclude that also the 2-oxazolidineselones exist exclusively in their selone forms. The EI mass spectra of 6a-6d and 6f exhibit base peak molecular ions, whereas in the spectrum of 6e the molecular ion only ranks second in intensity.

Our search in Nature for selenoglucosinolates affording 2-oxazolidineselones on enzymic hydrolysis has not thus far been rewarding, but a useful collection of reference specimens are now in hand. Other potential properties of the 2-oxazolidineselones, such as their ability to coordinate metal ions, deserve attention.

EXPERIMENTAL

Mps are uncorrected. ^{1}H Nmr spectra are measured on a Bruker HX-90E instrument in deuteriochloroform. Mass spectra are recorded on a VG Micromass 7070 instrument; the m/z values quoted for selenium-containing fragments are based on ^{80}Se.

Synthesis of 2-Oxazolidineselones. The 2-aminoalcohol (5 mmol) is added to a well-stirred, argon-covered solution of mercuric chloride (1.36 g, 5 mmol) in acetonitrile (20 ml), resulting in the immediate separation of a colourless solid. Carbon diselenide (0.32 ml, 5 mmole) is added, followed by triethylamine (1.39 ml, 10 mmol), causing a change in colour of the precipitate from colourless to black within a few secs. The mixture is stirred for 20 mins and filtered through a pad of Celite into a half-saturated salt solution (200 ml). Three extractions with dichloromethane (100 ml, plus 2 x 50 ml), drying ($MgSO_4$), and evaporation to dryness give the crude 2-oxazolidineselones, which are purified by column chromatography ('Kieselgel 40', ethyl acetate), followed by recrystallization from appropriate solvents as specified below.

2-Oxazolidineselone (6a). Prepared from ethanolamine; recrystallized from ethyl acetate:hexane (31% yield), mp 194-196°C (decomp). (Found: C, 24.36; H, 3.37; N, 9.31. C_3H_5NOSe requires: C, 24.02; H, 3.36; N, 9.34). ^{1}H Nmr δ 3.81 (2H, dd, J = 10 Hz, J = 10 Hz, CH_2N), 4.78 (2H, dd, J = 10 Hz, J = 10 Hz, CH_2O), and 8.90 ppm (1H, br s, HN). Ms, m/z (% rel. int.): 151 [M^+] (100), 80 (10), 43 (23), and 42 (35).

(±)-5-Methyl-2-oxazolidineselone (6b). Prepared from (±)-1-amino-2-propanol; recrystallized from ethyl acetate (42% yield), mp 83-85°C. (Found: C, 29.54; H, 4.41; N, 8.57. C_4H_7NOSe requires: C, 29.28; H, 4.30; N, 8.54). ^{1}H Nmr δ 1.56 (3H, d, J = 6 Hz, Me), 3.36 (1H, dd, J = 8 Hz, J = 10 Hz, CHN), 3.88 (1H, dd, J = 10 Hz, J = 10 Hz, CHN), 4.9-5.4 (1H, m, HCO), and 8.90 ppm(1H, br s, HN). Ms, m/z (% rel. int.): 165 [M^+] (100), 84 (12), 57 (16), 56 (50), 42 (29), 41 (50), and 39 (13).

(S)-4-Methyl-2-oxazolidineselone (6d). Prepared from (S)-alaninol; recrystallized from ethyl acetate:hexane (57% yield), mp 78-80°C; $[\alpha]_D^{20}$ + 9.8° (c 1.3, dichloromethane). (Found: C, 29.44; H, 4.27; N, 8.52. C_4H_7NOSe requires: C, 29.28; H, 4.30; N, 8.54). ^{1}H Nmr δ 1.41 (3H, d, J = 6 Hz, Me), 4.0-4.5 (2H, m, CH_2O), 4.6-5.0 (1H, m, HCN), and 9.20 ppm (1H, br.s, HN). Ms, m/z (% rel. int.): 165 [M^+] (100), 107 (10), 57 (14), 56 (30), 42 (100), 41 (33), and 39 (12).

(±)-5-Vinyl-2-oxazolidineselone (6c). Prepared as previously described.[3] Ms, m/z (% rel. int.): 177 [M^+] (100), 134 (14), 96 (10), 69 (15), 68 (70), 57 (12), 55 (11), 54 (33), 52 (28), 43 (20), 42 (34), 41 (58), and 39 (46).

(S)-5-Phenyl-2-oxazolidineselone (6e). Prepared from (S)-2-amino-1-phenylethanol[7]; recrystallized from benzene:hexane (34% yield), mp 118°C (decomp). The product was not sufficiently stable to allow for combustion analysis and determination of reliable optical rotation values. ^{1}H Nmr δ 3.71 (1H, dd, J = 10 Hz, J = 8 Hz, CHN), 4.14 (1H, dd, J = 10 Hz, J = 9 Hz, CHN), 5.93 (1H, dd, J = 9 Hz, J = 8 Hz, CHPh), 7.31-7.47 (5H, m, Ph), and 8.80 ppm(1H, s, HN). Ms, m/z (% rel. int.): 227 (M^+) (82), 184 (41), 146 (100), 128 (69), 119 (34), 118 (56), 107 (20), 104 (59), 103 (46), 92 (52), 91 (88), 78 (86), 77 (48), 65 (17), 63 (17), 52 (24), 51 (46), 50 (20), and 39 (27).

5,5-Dimethyl-2-oxazolidineselone (6f). Prepared from 1-amino-2-methyl-2-propanol; recrystallized from benzene:hexane (53% yield), mp 124-126°C. (Found: C, 33.91; H, 5.07; N, 7.84. C_5H_9NOSe requires: C, 33.72; H, 5.09; N, 7.86). ^{1}H Nmr δ 1.58 (6H, s, Me), 3.49 (2H, s, CH_2), and 8.80 ppm (1H, br.s, HN). Ms, m/z (% rel. int.): 179 (M^+) (100), 98 (32), 71 (10), 70 (27), 59 (11), 56 (66), 55 (93), 43 (28), 42 (11), 41 (35), and 39 (22).

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