New Synthesis of Chalcogenolactones. 1*H*,3*H*-Benzo[*c*]selenophen-1-one, 1*H*,3*H*-Benzo[*c*]tellurophen-1-one and the Related 3,4-Dihydro-1*H*-2-benzoselenin-1-one and 3,4-Dihydro-1*H*-2-benzotellurin-1-one

M. Loth-Compère (a), A. Luxen (a), Ph. Thibaut (a),
L. Christiaens (a), M. Guillaume (b) and M. Renson* (a)

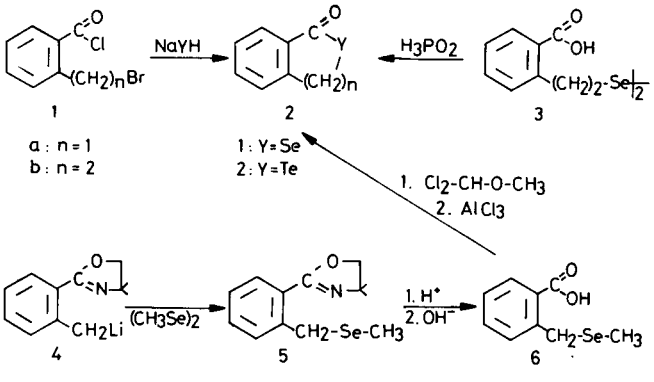
(a) Institute of Organic Chemistry, B 6, University of Liège, Sart-Tilman, 4000 Liège, Belgium
(b) Centre de Recherches du Cyclotron, B 20, University of Liège, Sart-Tilman, 4000 Liège, Belgium

Recieved July 18, 1980

The synthesis of three new basic heterocyclic systems namely, 1*H*,3*H*-benzo[*c*]tellurophen-1-one (2-tellurophthalide), 3,4-dihydro-1*H*-2-benzoselenin-1-one (3,4-dihydro-2-isoselenocoumarin) and 3,4-dihydro-1*H*-2-benzotellurin-1-one (3,4-dihydro-2-isotellurocoumarin), is reported through the cyclisation of *o*-(bromoalkyl)benzoyl chlorides.

J. Heterocyclic Chem., **18**, 343 (1981).

1*H*,3*H*-benzo[*c*]furan-1-one (phthalide) as well as its 2-suflur and 2-selenium analogs were synthesized by different chemical pathways and their structure firmly established (1-5). Nevertheless, 1*H*,3*H*-benzo[*c*]tellurophen-1-one (2-tellurophthalide) **2a2**, last system of this series, is still unknown. The recent synthesis of seleno and tellurophthalic anhydrides (6) prompted us to investigate this reaction in point of view of its application to the synthesis of chalcogenolactones. In fact, this reaction turns out to be ideal for the elaboration of such functions. Indeed the two phases tetrabutylammonium hydrogensulfate catalysed condensation of *o*-(bromomethyl)benzoyl chloride **1a** (7) with sodium hydrogenochalcogenate allowed the isolation of 2-selenophthalide and its telluro analog (Table I). We were also able to extend this one pot reaction to the elaboration of the hitherto unknown 3,4-dihydro-1*H*-2-benzoselenin-1-one **2b1** (3,4-dihydro-2-isoselenocoumarin) and its telluro analog **2b2** (3,4-dihydro-2-isotellurocoumarin) from acid chloride **1b** (8) (Table I). In addition, selenolactones **2a1** and **2b1** are also available by another pathway from selenide **6** or diselenide **3**. The diselenide **3**, prepared from 3,4-dihydro-1*H*-2-benzopyran, undergoes quantitatively the phosphinic acid induced ring closure (2b) leading to **2b1**. The selenide **6** was obtained by the following way: the α-lithio-Δ2-4,4-dimethyl-2-(*o*-tolyl)oxazoline **4** (9a) reacts with dimethyldiselenide affording the new oxazoline **5**. Hydrolysis of the oxazoline **5** gives the corresponding acid **6** which is also directly available from *o*-toluic acid by lithiumdiisopropylamide metallation (9b) followed by reaction with dimethyldiselenide. Cyclisation of its chloride affords selenolactone **2b1**. The ^{75}Se selenophthalide has been obtained through the one pot cyclisation procedure and the results will be published elsewhere.



EXPERIMENTAL

Physical constants, yields and analytical values are reported in Table I. Melting points are uncorrected. The infrared spectra were obtained on a Beckman IR 20A apparatus in chloroform (**2b2**) or carbon tetrachloride (**2a2, 2b1**) solutions. The pmr spectra were recorded on a Varian T-60 in deuteriochloroform with hexamethyldisiloxane as internal standard. ^{13}C nmr values (Table II) were obtained on a Bruker HFX-90 from solutions containing 500 mg. of compound in 1 ml. of deuteriochloroform with hexamethyldisiloxane as internal standard. The values in Table II (δ in ppm) were converted with respect to tetramethylsilane.

Excellent linear correlations can be calculated between the δ values of the $^{13}CH_2$ adjacent to the chalcogen atom in these molecules and of the methyl group in methyl chalcogenobenzoates, confirming the shielding effect of selenium and tellurium recently described by our group (11).

Tables I and II

Mass spectra were determined on a Varian MAT 112 apparatus, at 70 eV, with vpc introduction on a 3% SE 30 column at 240°.

The molecular ion gave a correct isotopic ratio for one selenium or one tellurium per molecule: Table III shows the main fragmentation of 2-tellurophthalide **2a2** and a comparison of the fragmentation of the S, Se and Te analogs **2b**. The mass spectra of the thio and selenophthalides were already recorded (4).

1. Seleno and Telluro Lactones (**2**).

To a well-stirred suspension of 3.15 g. (39 mmoles) of powdered selenium (or 5 g. of tellurium) in 50 ml. of water, 3 g. (79 mmole) of sodium borohydride was added in an argon atmosphere. Vigourous reaction and considerable foaming occur. The mixture was then warmed and stirred for 30 minutes at 40° until dissolution of the chalcogen. Tetrabutylammonium hydrogen sulfate (0.5 g.) was then added, followed by 39 mmoles of acid chloride **1** in 160 ml. of toluene. Stirring was continued during 3 hours at room temperature and the reaction mixture was left overnight. After washing with sodium carbonate (5%), the organic layer was dried and evaporated. The residue was recrystallized in light

0022-152X/81/020343-03$02.25

Table I

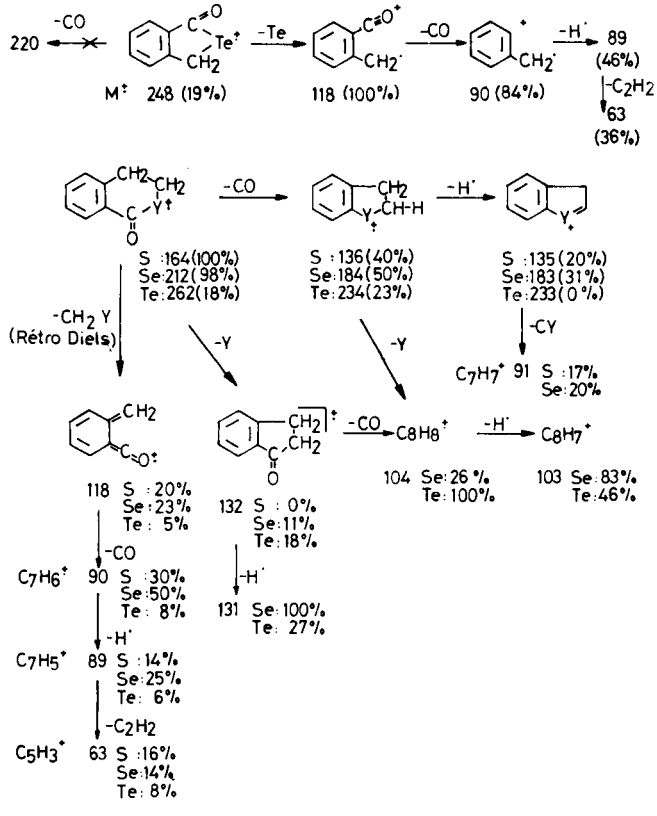
Product	M.p. °C	Yield %	Empirical Formula	Calcd. C	Calcd. H	Found C	Found H
2a2	58	72	C_8H_6OTe	39.18	2.45	40.1	2.5
2b1	62	49	C_9H_8OSe	51.18	3.79	51.2	3.9
2b2	52	52	C_9H_8OTe	41.60	3.08	41.4	3.1
3	134	7	$C_{18}H_{18}O_4Se_2$	47.36	3.94	47.2	3.9
5	liquid (b.p.) 150-154°/1 mm	39	$C_{13}H_{17}NOSe$	55.32	6.03 4.96 (N)	55.1	6 4.8 (N)
6	164	65	$C_9H_{10}O_2Se$	47.16	4.37	46.9	4.3

Table II

Comparison of the ^{13}C nmr Values of the Heterocycles **2a** and **2b**

Y		O	S	Se	Te
2a	C=O	171	197.8	199.9	200.3
	CH_2	69.6	34.6	29.5	13.9
2b	C=O	165	190.3 (10)	192.5	193.6
	C_3	67.3	28.6	20.7	5.2
	C_4	27.7	30.2	32	34.3

Table III : Main mass fragmentations



petroleum ether. The telluroesters were light sensitive.

Compound **2a2**.

This compound had ir: 1725, 1685, 1655 (C=O) (12); ^1H nmr: δ 4.78 (s, CH_2), 6.84-7.74 (m, ArH), $J_{^{125}Te\text{-}CH_2}$ = 22.8 Hz.

Compound **2b1**.

This compound had ir: 1663 (C=O); ^1H nmr: 3.25-3.35 (m, H_3-H_4), 7.1-7.4 (m, ArH); 7.8-8 (m, H_8).

Compound **2b2**.

This compound had ir: 1720, 1635 (12) C=O); ^1H nmr: 3.1-3.8 (m, H_3-H_4), 7-7.5 (m, ArH), 7.5-7.8 (m, H_8).

2. Δ-2-4,4-Dimethyl-(*o*-methylselenomethylphenyl)oxazoline (**5**).

To a stirred solution of 29.8 g. (0.15 mole) of Δ-2-4,4-dimethyl-2-(*o*-tolyloxazoline) in 100 ml. of dry ether, 94 ml. of *n*-butyllithium (1.6*M* in hexane) were slowly added at 0°. After one hour, 17.6 ml. (0.15 mole) of dimethyldiselenide was introduced through a dropping funnel. The reaction mixture was then stirred for one hour at the same temperature and poured on ice. After extraction with 200 ml. of ether the organic layer was dried on potassium carbonate, filtered and concentrated. The oily residue was then fractionated in vacuum to give a mixture 9:1 of oxazoline **5** and its isomeric Δ-2-4,4-dimethyl-2-(methyl-2'- methylseleno-6')-phenyloxazoline as shown by mass and ^1H nmr spectra; ^1H nmr: δ 1.3 [s, $(CH_3)_2C$], 1.8 (s, Se-CH_3), 3.1 (s, CH_2-Se), 4.1 (s, CH_2-O), 7.0-7.3 (m, 3H), 7.5-7.9 (m, 1H).

3. *o*-Methylselenomethylbenzoic Acid (**6**).

A solution of 8.5 g. of oxazoline **5**, 75 ml. of water and 5 ml. of concentrated hydrochloric acid was refluxed during 2 hours. After cooling, the reaction mixture was brought to *p*H 14 with concentrated sodium hydroxide. After refluxing for 2 additional hours and cooling, concentrated hydrochloric acid was added and the precipitated acid was collected, dried and recrystallized in benzene-ethanol (Table I); ^1H nmr: δ 1.8 (s, Se-CH_3), 4.1 (s, CH_2-Se), 7.0-7.4 (m, 5H), 7.7-8.0 (m, 1H).

4. Selenophthalide (**2a1**) from **6**.

To a solution of 2.3 g. (10 mmoles) of acid **6** in 50 ml. of dichloromethane were successively added 100 mg. of dry zinc chloride and 5 ml. of α,α-dichloromethyl methyl ether. The mixture was left at 50° for two hours and then overnight. The solvent and the excess of reagent were eliminated under vacuum and the oily residue was dissolved in 100 ml. of dry dichloromethane. The stirred mixture was cooled to −78° and 1.33 g. (10 mmoles) of dry aluminium trichloride was added. After 30 minutes at −78° the reaction mixture is allowed to warm at room temperature for 30 minutes and hydrolysed on ice-cooled hydrochloric acid. The organic layer was washed with sodium carbonate (5%), dried on magnesium sulfate, filtered and concentrated under vacuum. The residue, recrystallized in light petroleum ether, affords 0.87 g. (44%) of selenophthalide identical to the product obtained above.

5. Di(*o*-carboxy-β-phenethyl)diselenide (**3**).

A solution of sodium diselenide, prepared from 2 g. (87 mmoles) of sodium, 6.7 g. (87 mmoles) of selenium and 100 ml. of liquid ammonia was dissolved in 100 ml. of dry dimethylformamide, 8.9 g. (60 mmoles) of 3,4-dihydroisocoumarin (8) was then added and the mixture was stirred at 100° during 20 hours. The solvent was evaporated and the residue was treated with concentrated hydrochloric acid. The precipitate was filtered and purified through sodium bicarbonate extraction. After recrystallisation from toluene-alcohol, 950 mg. (7%) of the acid **3** was obtained. This solid was refluxed for 5 hours with 50 ml. of acetic acid, 10 ml. of hypophosphorous acid and 2 ml. of concentrated hydrogen chloride. After dilution with 100 ml. of ice cooled water and extraction with 100 ml. of dichloromethane, the organic layer was washed with sodium carbonate (5%), dried and concentrated under vacuum. The solid residue, recrystallised from light petroleum ether, afforded 425 mg. (75%) of **2b1** identical to the product obtained above.

Acknowledgment.

We are very grateful to the Fonds de la Recherche Collective, for financial support in purchasing the MAT 112 mass spectrometer.

REFERENCES AND NOTES

(1) M. Renson and R. Collienne, *Bull. Soc. Chim. Belg.*, **73**, 491 (1964).

(2a) W. H. H. Gunther, *J. Org. Chem.*, **31**, 1202 (1966); (b) W. H. H. Gunther, *ibid.*, **32**, 3929 (1967).

(3) L. Christiaens and M. Renson, *Tetrahedron*, **28**, 5405 (1972).

(4) W. J. McMurray, S. R. Lipsky, R. J. Cashley and H. G. Mautner, *J. Heterocyclic Chem.*, **9**, 1093 (1972).

(5) I. Wallmark, M. H. Krackov, Shi-Hsi Chu and H. G. Mautner, *J. Am. Chem. Soc.*, **92**, 4447 (1970).

(6) J. Bergman and L. Engman, *Org. Prep. Proce Int.*, **10**, 289 (1978).

(7) S. Lepetit, Netherlands Patent Application 6,614,224, April 13, 1967; *Chem. Abstr.*, **68**, p-2905b (1968).

(8) P. Maitte, *Ann. Chim. (Paris)*, **9**, 431 (1954).

(9a) H. Gschwend and A. Hamdan, *J. Org. Chem.*, **40**, 2008 (1975); (b) F. M. Hauser and R. Rhec, *Synthesis*, **9**, 245 (1977).

(10) For the synthesis see, W. C. Lamma, G. A. Dutra and C. A. Voeker, *J. Org. Chem.*, **35**, 3442 (1970).

(11) L. Laitem, L. Christiaens and M. Renson, *Org. Magn. Reson.*, **13**, 319 (1980).

(12) M. Renson and J-L. Piette, *Spectrochim. Acta*, **29A**, 285 (1973).

(13) A. G. London, A. Maccoll and S. K. Wong, *J. Chem. Soc. B*, 1727 (1970).