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SYNTHESIS AND SPECTRAL PROPERTIES OF DIETHYL ORGANYLCHALCOGENOALKYL(ALKYL)MALONATES, $RX(CH_2)_nCR'(COOC_2H_5)_2$, AND 5-ALKYL-5-(ORGANYLCHALCOGENOALKYL)BARBITURATES, $RX(CH_2)_nC(R')CONHC(Y)NHCO$ (X = Se, Te)

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Summary

Barbiturates substituted at the 5-position with organyltelluroalkyl or organylselenoalkyl groups were prepared by ring annulation of appropriately substituted diethyl malonates with urea or thiourea. The substituted diethyl malonates [phenyltellurobutyl(ethyl), i-propyltelluropropyl(ethyl), i-propyltelluropropyl(allyl), i-propylselenopropyl(ethyl), and phenylselenohexyl(methyl)] were prepared in 55–91% yield by reaction of diethyl ω-bromoalkyl(alkyl)malonates with organyltellurolates or -selenolates (RXNa; X = Se, Te) in ethanol/benzene. The RXNa species were prepared by $NaBH_4$ reduction of the ditellurides (R_2Te_2) or diselenides (R_2Se_2) in ethanol/benzene. The ω-bromoalkyl(alkyl)malonates were obtained by reacting the sodio(alkyl)malonates, with α,ω-dibromoalkanes. Condensation of the diethyl organylchalcogenoalkyl(alkyl)malonates with an excess of urea or thiourea in dimethyl sulfoxide in the presence of potassium t-butoxide gave 5-organylchalcogenoalkyl-5-alkylbarbiturates or -thiobarbiturates. The following barbiturates were obtained in 28–84% yield: phenyltellurobutyl(ethyl), m.p. 100°C; i-propyltelluropropyl(ethyl), m.p. 119°C; i-propylselenopropyl(ethyl), m.p. 137°C; phenylselenohexyl(methyl), m.p. 124°C. The 5-substituted thiobarbiturates i-propyltelluropropyl(ethyl)- (m.p. 75°C) and i-propylselenopropyl(ethyl)thiobarbiturate (m.p. 83°C) were isolated in 32 and 20% yield, respectively. The barbiturates and thiobarbiturates were purified by chromatography and recrystallization and characterized by elemental analyses, mass spectrometry, ^1H, ^{125}Te and ^{77}Se NMR spectroscopy and UV-VIS spectrometry. The chalcogenobarbiturates radiolabeled with ^{123m}Te or ^{77}Se may be useful as brain imaging agents.

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Introduction

In 1863 Baeyer [1] obtained barbituric acid (1,3-diaza-2,4,6-trioxocyclohexane) through condensation of urea and malonic acid. Since that time a large number of barbituric acid derivatives have been prepared by ring annulation of appropriately substituted malonic esters with ureas or thioureas. In 1903, barbiturates were used clinically for the first time. 5,5-Diethylbarbiturate was employed as a depressant of the nervous system [2]. Several thousand barbiturates have been prepared and evaluated, and approximately a dozen are now employed for clinical purposes. These compounds can be classified according to the persistence of their depressant action. Barbiturates are more persistent than thiobarbiturates. As an example, thiopental [5-ethyl-5-(2′-pentyl)-1,3-diaza-3-thia-2,4,6-trioxocyclohexane] is a short-acting thiobarbiturate, which leaves the brain within a few minutes after administration [3]. In contrast, the *N*-methyl-substituted barbiturates and barbiturates substituted at the 5-position with alkyl groups containing more than seven carbon atoms are convulsants [4]. Several ^{14}C labeled barbiturates have been shown to be non-uniformly distributed in the brain tissue of experimental animals after intravenous administration, and the distribution pattern appears to reflect regional blood perfusion [5,6]. These studies suggested that barbiturates labeled with gamma-emitting radionuclides may be useful agents to evaluate regional blood flow in various diseased states by nuclear medicine procedures. Radioiodinated iodovinyl- and iodophenyl-substituted barbiturates have been prepared and studied in rats and show rapid loss from the brain [7,8]. The iodovinyl barbiturates are also rapidly deiodinated in-vivo [7].

We have observed that various ^{123m}Te labeled telluraalkanoic acids [$RTe(CH_2)_nCOOH$] are preferentially extracted by the heart and retained much longer than the alkanoic acids [$R(CH_2)_nCOOH$] [9–13]. This prolonged retention, which freezes the initial distribution pattern, would allow an accurate determination of regional blood flow. In the heart, the prolonged retention appears to result from the unique intracellular oxidation of the telluraalkanoic acids to an insoluble product of unknown structure [14].

The goals of the present study were the synthesis and characterization of several new telluraalkyl-substituted barbiturates. These agents appropriately radiolabeled may be useful as imaging agents for the brain [15].

Experimental

Materials. Tellurium and selenium powder (99.9%), Noranda Brand, were obtained as a gift from Canadian Copper Refiners, Limited. Diphenyl diselenide was supplied by Strem Chemicals, Inc. Diphenyl ditelluride was synthesized from phenylmagnesium bromide and tellurium powder [16]. Diisopropyl ditelluride and diisopropyl diselenide were obtained from disodium ditelluride or disodium diselenide and 2-bromopropane in dimethylformamide (DMF) solution [17]. Sodium metal, urea (J.T. Baker Chem. Co.), 2-bromopropane (Eastman Organic Chemicals), diethyl ethylmalonate, diethyl allylmalonate, diethyl methylmalonate, 1,3-dibromopropane, 1,4-dibromobutane, 1,6-dibromohexane, potassium t-butoxide (Aldrich) and sodium borohydride (Fisher Scientific) were used as received. Sodium hydride dispersed in mineral oil (1:1 by weight) was obtained from Alfa Products.

Thiourea (Matheson, Coleman and Bell) was dried in a vacuum dessicator over calcium chloride for at least one week prior to use. *N,N*-Dimethylformamide (Fisher Scientific) and dimethyl sulfoxide (gold-label, Aldrich Chemical Co.) were distilled from calcium oxide at atmospheric pressure before use. All other solvents were ACS reagent grade. Silicic acid, Sil-A-200 and Sil-B-200, was supplied by Sigma Chemical Co. MN-Silica-Gel P/UV-254 with $CaSO_4$ used for preparative TLC was purchased from Brinckman Instruments, Inc.

Instrumentation and analysis. Proton nuclear magnetic resonance (NMR) spectra were recorded on a Varian T-60 spectrometer. ^{125}Te and ^{77}Se resonances were determined on a Varian FT-80 spectrometer. Mass spectral measurements were performed on a CEC21-110B mass spectrometer at 70 eV electron energy. The ultraviolet spectra were recorded on Cary-14 or Cary-219 spectrophotometers. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn., or by Chemalytics, Inc., of Tempe, Arizona.

Diethyl 6-bromohexyl(methyl)malonate

An oven-dried 250-ml, two-necked flask equipped with a magnetic stirring bar, an addition funnel and a nitrogen inlet was flushed with nitrogen and charged with DMF (50 ml) and sodium hydride/mineral oil (1:1 by weight) (5.10 g, 0.10 mol NaH). Diethyl methylmalonate (17.42 g, 0.10 mol) was added dropwise to the stirred solution over a 30 min period. The mixture was stirred for an additional 90 min, then transferred to a nitrogen-flushed 250-ml dropping funnel and added (30 min) with stirring to 1,6-dibromohexane (36.60 g, 0.15 mol) contained in an oven-dried, nitrogen flushed, 500-ml, two-necked flask equipped with a nitrogen inlet and a magnetic stirring bar. The mixture was stirred for an additional hour, then poured into distilled water (150 ml) and extracted with two 50-ml portions of chloroform. The combined chloroform extracts were dried over anhydrous calcium chloride. Chloroform was removed from the filtered extract under a water aspirator vacuum. The residual liquid was distilled at reduced pressure using a 30-cm Vigreux column. Diethyl 6-bromohexyl(methyl)malonate (13.88 g, 41% yield) was collected at 134–138°C/3.0 Torr.

Diethyl 3-bromopropyl(ethyl)malonate

Diethyl ethylmalonate (40.00 g, 0.21 mol) was reacted with sodium hydride/mineral oil (1:1 by weight) (10.2 g, 0.21 mol NaH) in DMF (125 ml). This mixture was added to 1,3-dibromopropane (83.62 g, 0.41 mol) to produce diethyl 3-bromopropyl(ethyl) malonate (27.41 g, 42% yield) with a boiling point of 97°C/0.01 Torr (lit. 169–174°C/20 Torr [18]).

Diethyl 4-bromobutyl(ethyl)malonate

Diethyl ethylmalonate (27.26 g, 0.15 mol) and sodium (3.34 g, 0.15 mol) were reacted in refluxing absolute ethanol (150 ml) for 12 h. The solution was then added to 1,4-dibromobutane (33.26 g, 0.15 mol) to produce diethyl 4-bromobutyl-(ethyl)malonate (16.03 g, 34% yield), which boiled at 80–82°C/2.0 Torr.

Diethyl phenyltellurobutyl(ethyl)malonate

Diphenyl ditelluride (2.56 g, 0.006 mol) was dissolved in a mixture of ethanol (20 ml) and benzene (20 ml) and placed in a nitrogen-purged 100-ml flask equipped with

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TABLE 1

DIETHYL ORGANYLCHALCOGENOALKYL(ORGANYL)MALONATES, $RX(CH_2)_nC(R')(COOC_2H_5)_2$

R	X	n	R′	Prepared from (g, mol)	Analyses (Found (calcd.) (%))		Yield [b] (%)
					C	H	
C_6H_5	Te	4	C_2H_5	$(C_6H_5)_2Te_2$ (2.56, 0.006) $Br(CH_2)_4C(C_2H_5)(COOC_2H_5)_2$ (1.00, 0.003)	50.48 (50.94) 450.1031 [a]	6.20 (6.30) (450.1056) [a]	60
i-C_3H_7	Te	3	C_2H_5	$(i\text{-}C_3H_7)_2Te_2$ (2.73, 0.004) $Br(CH_2)_3C(C_2H_5)(COOC_2H_5)_2$ (2.00, 0.0065)	44.87 (45.04) 402.1057 [a]	7.20 (7.06) (402.1056) [a]	77
i-C_3H_7	Te	3	CH_2=$CHCH_2$	$(i\text{-}C_3H_7)_2Te_2$(5.11, 0.015) $Br(CH_2)_3C(CH_2CH$=$CH_2)(COOC_2H_5)_2$ (8.00, 0.025)	44.27 (46.65) 414.1070 [a]	7.02 (6.85) (414.1056) [a]	55
i-C_3H_7	Se	3	C_2H_5	$(i\text{-}C_3H_7)_2Se_2$(2.73, 0.013) $Br(CH_2)_3C(C_2H_5)(COOC_2H_5)_2$ (4.00, 0.013)	51.94 (51.28) 352.1151 [a]	7.85 (8.03) (352.1152) [a]	91
C_6H_5	Se	6	CH_3	$(C_6H_5)_2Se_2$(0.60, 0.002) $Br(CH_2)_6C(CH_3)(COOC_2H_5)_2$ (1.00, 0.003)	57.49 (58.11) 414.1320 [a]	6.45 (7.31) (414.1308) [a]	85

[a] Molecular mass by mass spectrometry based on ^1H, ^{12}C, ^{16}O, ^{80}Se, ^{130}Te. [b] Purified product based on diethyl ω-bromoalkyl(organyl)malonate.

TABLE 2

5-ALKYL-5-(ORGANYLCHALCOGENOALKYL)BARBITURATES AND THIOBARBITURATES

R	X	*n*	R′	Y [e]	Prepared from (g, mol)		Analyses (Found (calcd.) (%))			M.p. (°C)	Yield [b] (%)
							C	H	N		
C_6H_5	Te	4	C_2H_5	O	R [c]OK	(0.40, 0.004)	46.05	4.85	6.76	100	84
					Urea	(1.00, 0.017)	(46.20)	(4.85)	(6.73)		
					Mal [c]	(0.90, 0.002)	418.0540 [a]	(418.0543) [a]			
i-C_3H_7	Te	3	C_2H_5	O	R [c]OK	(1.40 g, 0.013)	38.99	5.52	7.61	119	61
					Urea	(2.38, 0.040)	(39.18)	(5.48)	(7.61)		
					Mal [c]	(2.40, 0.006)	370.0548 [a]	(370.0543) [a]			
i-C_3H_7	Te	3	C_2H_5	S	R [c]OK	(1.12, 0.010)	34.46	4.89	7.26	75	32
					Thiourea	(2.66, 0.035)	(37.54)	(5.25)	(7.30)		
					Mal [c]	(2.00, 0.005)	386.0301 [a]	(386.0314) [a]			
i-C_3H_7	Se	3	C_2H_5	O [d]	R [c]OK	(1.27, 0.011)	44.93	6.48	8.68	137	28
					Urea	(1.70, 0.028)	(45.19)	(6.31)	(8.77)		
					Mal [c]	(2.00, 0.006)	320.0643 [a]	(320.0638) [a]			
i-C_3H_7	Se	3	C_2H_5	S [d]	R [c]OK	(1.27, 0.011)	44.12	6.52	8.06	20	
					Thiourea	(2.16, 0.028)	(42.98)	(6.01)	(8.35)		
					Mal [c]	(2.00, 0.006)	336.0403 [a]	(336.0410) [a]			
C_6H_5	Se	6	CH_3	O	R [c]OK	(0.48, 0.004)	53.45	5.92	–	124	42
					Urea	(0.75, 0.011)	(53.55)	(5.82)	–		
					Mal [c]	(0.75, 0.002)	382.0805 [a]	(382.0795) [a]			

[a] Molecular mass by mass spectrometry based on ^{1}H, ^{12}C, ^{16}O, ^{80}Se, ^{130}Te. [b] Yields of purified product. [c] R = t-C_4H_9, Mal = R-X$(CH_2)_n$C(R′)$(COOC_2H_5)_2$. [d] Purified by recrystallization from cyclohexane. [e] R, X, *n*, R′ and Y are defined in Scheme 1, structure II.

a magnetic stirring bar and a nitrogen inlet. Sodium borohydride was added in small portions to the stirred, red solution until the red color had disappeared. Diethyl ethyl(4-bromobutyl)malonate (1.00 g, 0.003 mol) was then added dropwise from a pipette. The reaction mixture was stirred at room temperature for 30 min and then poured into a separatory funnel containing distilled water (40 ml). The product was extracted with diethyl ether (40 ml) and the extract dried with anhydrous calcium chloride. The ether was removed from the filtered solution under an aspirator vacuum. The residue was chromatographed on a silicic acid column (3 × 75 cm) containing Sil-A-200 (50 g). Excess diphenyl ditelluride was eluted with petroleum ether. Diethyl phenyltellurobutyl(ethyl)malonate was then removed from the column with a mixture of diethyl ether/petroleum ether (3/97 v/v). Evaporation of the combined fractions gave analytically pure diethyl phenyltellurobutyl(ethyl)malonate (0.80 g, 60% yield).

The other telluroalkylmalonates and selenoalkylmalonates were prepared similarly. Details are given in Table 1.

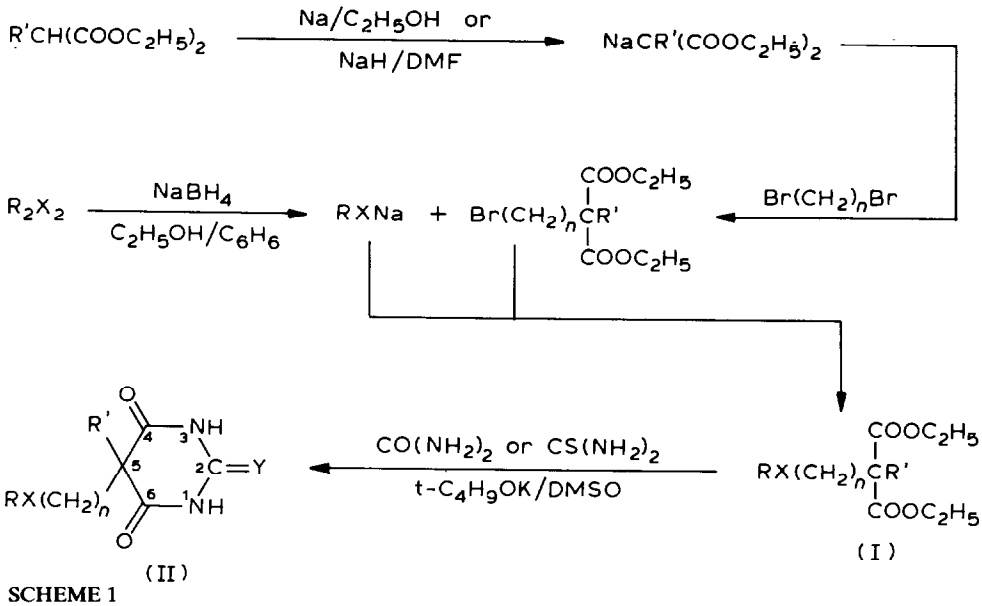
5-Ethyl-5-(phenyltellurobutyl)barbiturate

A dry, 100-ml, nitrogen-purged, single-necked, round bottom flask fitted with a nitrogen-inlet and a magnetic stirring bar was charged with freshly distilled dimethyl sulfoxide (75 ml) and potassium t-butoxide (0.40 g, 0.004 mol). Urea (0.50 g, 0.008 mol) was added to the stirred solution. After the urea had dissolved diethyl phenyltellurobutyl(ethyl)malonate (0.90 g, 0.002 mol) was added to the solution. After 0.5 h, additional urea (0.50 g, 0.008 mol) was added. The reaction mixture was stirred for 2 h at room temperature and then poured into distilled water (100 ml). This mixture was acidified with 0.01 *N* sulfuric acid to pH 4 and then extracted with three portions (25 ml each) of chloroform. The combined extracts were evaporated under an aspirator vacuum. The residue was dissolved in a minimal volume of chloroform/methanol (1/1, v/v) and the solution transferred to a silicic acid (Sil-B-200) column (25 mm × 55 cm). Methanol was passed through the column. The effluent was collected in 25-ml fractions. Each fraction was tested for the presence of a tellurium compound by spotting a drop of the solution on a TLC strip and placing the strip into a chamber containing iodine. An orange-reddish spot indicated the presence of a tellurium compound. The fractions giving a positive test were combined and evaporated under vacuum. A portion of the residue was dissolved in $CDCl_3$ and a proton NMR spectrum taken to confirm the presence of the barbiturate. The residue was then chromatographed in two portions on 2 mm-thick TLC plates using chloroform/methanol (4/1, v/v) as the mobile phase. The bands containing the barbiturate were marked under UV-light and scraped from the plate. The barbiturate was extracted with methanol. Evaporation gave crystalline 5-ethyl-5-(phenyltellurobutyl)barbiturate (0.70 g, 84% yield, m.p. 99–100°C).

The other tellurium- and selenium-containing barbiturates were prepared similarly. Details are given in Table 2.

Results and discussion

5-Alkyl-5-(organylchalcogenoalkyl)barbiturates (II) were obtained by condensation of urea or thiourea with diethyl organylchalcogenoalkyl(alkyl)malonates (I), which in turn were prepared from diorganyl ditellurides and diethyl ω-



SCHEME 1

bromoalkyl(alkyl)malonates (Scheme 1). The sodiomalonates were generated from the malonic esters and sodium in absolute ethanol [19] or sodium hydride in DMF [20–22]. Reactions of the sodiomalonates with equimolar quantities or an excess of $Br(CH_2)_nBr$ ($n = 3$, 4, 6) produced bromoalkyl(alkyl)malonates in yields of approximately 40%. These compounds were isolated and purified by vacuum distillation.

The organyl sodium chalcogenides, RXNa (R = C_6H_5, i-C_3H_7, X = Se, Te), were generated from crude diorganyl dichalcogenides by reduction with sodium borohydride in ethanol/benzene and coupled at room temperature with the bromoalkylmalonates to produce organylchalcogenoalkyl(alkyl)malonates in yields ranging from 55–91%. The light-yellow tellurium compounds and the colorless selenium derivatives were purified by column chromatography on silicic acid. With the exception of the isopropyltelluropropyl(alkyl)malonate the substituted malonates gave acceptable C/H analyses (Table 1), had the expected NMR spectra (Table 3) and produced molecular ions in the mass spectrometer. The compositions of the molecular ions were confirmed by exact mass measurements (Table 1).

The classical method for preparation of barbiturates uses sodium ethoxide as the base and ethanol as the solvent for condensation of malonates with urea and its derivatives [23,24]. When the diethyl organylchalcogenoalkyl(alkyl)malonates were treated with urea under these conditions barbiturates were not formed. However, the procedure employed for the condensation of urea or thiourea with sterically hindered malonates [21] provided the desired compounds. Using this procedure, diethyl organylchalcogenoalkyl(alkyl)malonates were successfully condensed in DMSO at room temperature using an excess of urea or thiourea and potassium t-butoxide as the base. Addition of urea in two equal portions improved the yields. A reaction period of 2 h was used to avoid the decomposition of the malonates or barbiturates by strong base. The six barbiturates prepared in this manner were purified by recrystallization from cyclohexane or by column chromatography on silicic acid

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TABLE 3

^{1}H, ^{77}Se AND ^{125}Te NMR DATA [a] FOR DIETHYL ORGANYLCHALCOGENOALKYL(ALKYL)MALONATES AND 5-ORGANYL-CHALCOGENOALKYL(ALKYL)BARBITURATES (II)

Compound	R	X	*n*	R′	Y [d]	NH(s)	OCH_2(q)	OCH_2CH_3(t)	CH_2–X–CH_2(t)	CHX(sept)	$(CH_3)_2CH$(d)	CH_3(R′)	Other CH_2(m)	C_6H_5(m)	^{125}Te or ^{77}Se(s)
I	C_6H_5	Te	4	C_2H_5	–	–	4.13	1.16	2.83	–	–	0.75	1.1–2.2	7.0–7.9	479.5
II	C_6H_5	Te	4	C_2H_5	O	9.46	–	–	2.81	–	–	0.86	1.1–2.3	7.1–7.9	486.1
I	C_6H_5	Se	6	CH_3	–	–	4.15	1.25	2.88	–	–	0.85	1.1–2.3	7.2–7.5	295.1
II	C_6H_5	Se	6	CH_3	O	9.03	–	–	2.90	–	–	0.78	1.1–2.3	7.2–7.7	[b]
I	i-C_3H_7	Te	3	C_2H_5	–	–	3.97	1.08	2.45	3.15	1.42	0.88	1.5–2.3	–	466.2
II	i-C_3H_7	Te	3	C_2H_5	O	9.03	–	–	2.52	3.25	1.52	0.85	1.5–2.2	–	467.9
II	i-C_3H_7	Te	3	C_2H_5	S	9.92	–	–	2.46	3.20	1.43	0.78	1.5–2.2	–	[e]
I	i-C_3H_7	Te	3	C_3H_5	–	–	4.12	1.23	2.60	3.30	1.57	[c]	1.7–2.4	–	476.1
I	i-C_3H_7	Se	3	C_2H_5	–	–	4.10	1.25	2.48	3.00	1.37	0.92	1.7–2.4	–	289.2
II	i-C_3H_7	Se	3	C_2H_5	O	8.88	–	–	2.55	3.10	1.38	0.92	1.5–2.3	–	294.3
II	i-C_3H_7	Se	3	C_2H_5	S		–	–	2.47	3.05	1.37	0.90	2.4–2.2	–	294.1

[a] $CDCl_3$ solution, ~0.4 *M*; δ(H) relative to internal TMS; δ(Se) relative to external $(CH_3)_2Se$; δ(Te) relative to external $(CH_3)_2Te$. [b] Not determined. [c] $CH_2CH{=}CH_2$: 2.53(t), 4.77–5.17(m), 5.27–5.94(m). [d] R, X, *n*, R′ and Y are defined in Scheme 1, structures I and II. [e] Insufficiently soluble in $CDCl_3$ to obtain a spectrum.

TABLE 4

UV-VISIBLE ABSORPTION DATA FOR DIETHYL ORGANYLCHALCOGENOALKYL(ALKYL)MALONATES (I) AND 5-ORGANYLCHALCOGENOALKYL(ALKYL)BARBITURATES (II)

Compound	R	X	n	R′	Y [a]	UV-VIS (methanol)		
						λ_{max} (nm), log ϵ		
I	C_6H_5	Te	4	C_2H_5	–	223.0, 4.20	268.2, 3.64	323.7, 2.74
II	C_6H_5	Te	4	C_2H_5	O	222.9, 3.65	269.4, 3.65	326.2, 2.80
I	C_6H_5	Se	6	CH_3	–	246.0, 3.56	2.690, 3.51	–
II	C_6H_5	Se	6	CH_3	O	246.1, 3.63	268.3, 3.58	–
I	i-C_3H_7	Te	3	C_2H_5	–	232.8, 3.81	280.0, 2.29	355.0, 1.84
II	i-C_3H_7	Te	3	C_2H_5	O	212.2, 4.06	230.6, 3.57	[b]
II	i-C_3H_7	Te	3	C_2H_5	S	234.9, 4.21	287.2, 4.47	[b]
I	i-C_3H_7	Te	3	C_2H_5	–	233.2, 3.70	270.0, 2.48	355.0, 1.92
I	i-C_3H_7	Se	3	C_2H_5	–	218.7, 3.99	255.0, 2.07	–
II	i-C_3H_7	Se	3	C_2H_5	O	212.2, 3.31	279.0, 2.02	–
II	i-C_3H_7	Se	3	C_2H_5	S	236.4, 3.87	286.3, 4.29	–

[a] R, X, n, R′ and Y are defined in Scheme 1, structures I and II. [b] Not determined.

followed by preparative thin-layer chromatography. Difficulties were encountered in the purification of the isopropylchalcogenopropyl(ethyl)thiobarbiturates. Although the proton NMR spectra indicated that these compounds were homogeneous after chromatography or recrystallization, the carbon analyses deviated from the calculated values. Since tellurium was observed in samples which had been stored in closed vials for a few days at room temperature, the compounds might have decomposed during shipment for analysis. Mass spectral (Table 2) and NMR data (Table 3) confirmed, however, that these compounds had the expected structures. Attempts to condense diethyl isopropyltelluropropyl(allyl)malonate with urea or thiourea were unsuccessful.

Proton NMR data for the chalcogen-containing malonates and barbiturates are presented in Table 3. The carbethoxy protons, the protons of the alkyl groups and the methylene groups not bonded to the chalcogen atoms resonate at approximately the same frequencies as the protons in chalcogen-free malonates [25] and barbiturates. The protons of the CH_2Te and CH_2Se groups have chemical shifts in the 2.45 to 2.90 ppm range. The CHTe and CHSe resonances of the isopropylchalcogeno derivatives are in the 3.00 to 3.30 ppm range. The chemical shifts of these malonates and barbiturates are similar to those of diorganyl tellurides [26], diorganyl selenides [27] and chalcogenaalkanoates [28].

The ^{125}Te and ^{77}Se resonances of the malonates and barbiturates (Table 3) agree with those characteristic for phenyl butyl telluride (488 ppm), i-propyl butyl telluride (471 ppm) and the corresponding selenium compounds (287, 275 ppm) [29].

The UV absorption characteristics (Table 4) of the malonates and barbiturates are quite similar. The tellurium derivatives have a rather weak absorption maximum at approximately 325 or 355 nm, which causes their light-yellow color. The colorless selenium compounds do not have maxima above 286 nm. The UV spectra of the phenylchalcogenoalkyl-malonates and -barbiturates are very similar to those of phenyl ethyl telluride [30] and phenyl ethyl selenide [31].

Radiolabeled analogs of the compounds described above such as 5-ethyl-5-(4-phenyl[^{123m}Te]tellurobutyl)barbiturate and 5-ethyl-5-(4-phenyl[^{123m}Te]tellurobutyl)-barbiturate showed significant brain uptake in rats [15], although these reagents were not retained in the brain as long as telluraalkanoates in the heart. These results may indicate that the telluraalkylbarbiturates are not oxidized in the brain. These studies demonstrated, however, that structurally modified barbiturates freely cross the intact blood-brain barrier and may be useful in investigations of the pharmacologic properties and the metabolism of this important class of compounds.

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