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Convenient route to dialkyl diselenides from alkyl tosylates. Synthesis of di(*cis*-myrtanyl) diselenide

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Abstract—A one-step method for the synthesis of dialkyl diselenides, by reaction of alkyl tosylates with sodium diselenide is described. Three variants of the synthesis, using as an example the preparation of optically active di(*cis*-myrtanyl) diselenide, are compared.

Recently the chemistry of organoselenium compounds has played an important role in organic synthesis. The use of reagents containing the selenium function makes it possible to introduce new functional groups into molecules.[1] The oxidation of phenyl selenides, widely employed in the formation of carbon–carbon double bonds, serves as a classical example.[1] The biological and medicinal role of selenium and organoselenium compounds is also increasingly appreciated, mainly due to their antioxidant, antitumour, antimicrobial, and antiviral properties.[2]

Diselenides are of especial significance in organic synthesis. These compounds can act as electrophilic reagents, for example, in additions to double bonds,[3] as well as nucleophilic reagents for the syntheses of allylic alcohols and amines.[4] Since the early nineties, diselenides have been employed in asymmetric syntheses, for example, in the asymmetric opening of epoxides,[5] in hydroxy and methoxyselenylation,[6] azidoselenylation,[7] and others.[1]

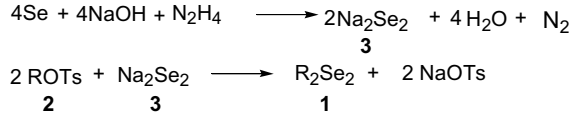
Diselenides have been synthesised by (a) oxidation of the products of reacting Grignard or organolithium reagents with selenium,[8] (b) oxidation of selenols,[9] (c) the reaction of sodium or lithium diselenide with alkyl halides,[10] (d) the reaction of selenourea with alkyl halides,[11] (e) reduction of selenocyanates,[12] or (f) the reaction of selenocyanates with samarium iodide.[13]

Efficient methods are available for the syntheses of diaryl diselenides, but convenient routes to dialkyl diselenides are still under investigation. Recently the methods currently known were modified[14] and new reagents to introduce a diselenide function, for example, $[Et_4N]_2WSe_4$ were described.[15]

Here we present a new and convenient method to make dialkyl diselenides **1** based on the reaction of alkyl tosylates **2** with sodium diselenide **3**. Sodium diselenide was obtained according to the modified method described earlier[16] (Scheme 1).

The dialkyl diselenides were prepared in a one-step reaction from tosylates, obtained using the pyridine method.[17] As a result of the reactions of methyl **4**, isopropyl **5**, *n*-butyl **6**, 2-pentyl **7**, isoamyl **8**, 2-octyl **9** and cyclohexyl **10** tosylates with sodium diselenide **3**, the corresponding dialkyl diselenides **11**–**17** were obtained (Table 1).

The reactions were conducted under argon, dropping hydrazine monohydrate (0.3 mL) into a mixture of



Scheme 1. Synthesis of dialkyl diselenides.

Keywords: Dialkyl diselenides; Sodium diselenide; Di(*cis*-myrtanyl) diselenide.
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Table 1. Synthesis of dialkyl diselenides **11–17** from alkyl tosylates **4–10**

Entry	Tosylate	Diselenide	Yield (%)	^{77}Se NMR δ ($CDCl_3$)
1	—OTs **4**	—Se)$_2$ **11**	87[a,b]	269.0
2	OTs **5**	Se)$_2$ **12**	90[b,c]	402.5
3	OTs **6**	Se)$_2$ **13**	98[c]	308.3
4	OTs **7**	Se)$_2$ **14**	96	373.6, 373.9[g]
5	OTs **8**	Se)$_2$ **15**	86[d]	311.8
6	OTs **9**	Se)$_2$ **16**	90[e]	374.7, 375.1[g]
7	OTs **10**	Se)$_2$ **17**	69[c,f]	364.2

[a–f] Literature data.[18]

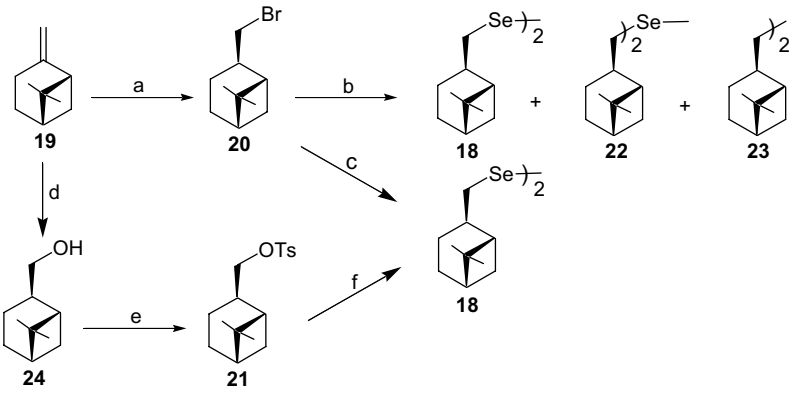
[g] Signals for diastereomers.

selenium (22 mmol) and sodium hydroxide (33 mmol) in DMF (20 mL). After 15 min the respective tosylate (22 mmol) dissolved in DMF (20 mL) was added and the reaction mixture was heated for 1 h at 100 °C. The mixture was cooled, poured into water (100 mL) and extracted with petroleum ether (3×100 mL). The combined ethereal solutions were washed with water (100 mL) and dried over anhydrous $MgSO_4$. The extracts were evaporated and the crude product was purified by column chromatography (petroleum ether, silica gel 70–230 mesh).

The structures of the obtained diselenides **11–17** were confirmed on the basis of the ^{1}H, ^{13}C and ^{77}Se NMR spectra[19] and by comparison to the literature data.[18]

The methodology was employed for the synthesis of optically active di(*cis*-myrtanyl) diselenide **18**. Previously, only camphor derived dialkyl diselenides had been investigated.[20] In order to compare our method with other routes to dialkyl diselenides, three other syntheses of diselenide **18** from (−)-β-pinene **19** were examined (Scheme 2).

Myrtanyl bromide[21] **20** or myrtanyl tosylate **21** were alternatively employed for the synthesis of **18**. Reaction of bromide **20** with magnesium and selenium then air, gave di(*cis*-myrtanyl) diselenide **18** (32%), myrtanyl selenide **22** (4%) and dimyrtanyl **23** (15%). Using sodium diselenide prepared under the reaction conditions previously described by Syper and Młochowski,[16] myrtanyl



Scheme 2. Synthesis of di(*cis*-myrtanyl) diselenide. Reagents and conditions: (a) BH_3/THF, Br_2/CH_3ONa, 60%; (b) Mg/Et_2O, Se/O_2; (c) Se, NaOH, $N_2H_4{\cdot}xH_2O$, 6 h, rt, 78%; (d) BH_3/THF, H_2O_2/NaOH, 86%; (e) TsCl, pyridine, 87%; (f) Se NaOH, $N_2H_4{\cdot}xH_2O$, 1 h, 100 °C, 91%.

bromide **20** gave diselenide **18** in 78% yield. Conducting the same reaction in our one-step version from tosylate **21**, the diselenide **18** was formed in 91% yield. The myrtanyl tosylate **21** was synthesised via hydroboration–oxidation of (−)-β-pinene **19**,[22] and then further reaction of the *cis*-myrtanol **24** obtained with tosyl chloride in pyridine.[17] The structures of the resulting products **18**, **22** and **23** were established from their ^{1}H, ^{13}C and ^{77}Se NMR spectra.[23]

In conclusion, a new rapid and efficient method for the synthesis of other dialkyl diselenides from alkyl tosylates has been established. This methodology was successfully applied for the synthesis of optically active di(*cis*-myrtanyl) diselenide, not previously described in the literature. The applications of this method for the synthesis of another dialkyl diselenides from the terpene group are being investigated.

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19. Spectral data; dimethyl diselenide **11**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.54 (s, 6H, $2\times CH_3$); ^{13}C NMR (200 MHz, $CDCl_3$): δ 10.5 ($2\times CH_3$); diisopropyl diselenide **12**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.39 (d, 12H, $4\times CH_3$ $J = 7.0$ Hz), 3.19 (m, 2H, $2\times CH$); ^{13}C NMR (200 MHz, $CDCl_3$): δ 24.6 ($4\times CH_3$), 33.5 ($2\times CH$); di(*n*-butyl) diselenide **13**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.92 (t, 6H, $2\times CH_3$, $J = 7.2$ Hz), 1.45 (m, 4H, $2\times CH_2$), 1.74 (m, 4H, $2\times CH_2$), 2.91 (t, 4H, $2\times CH_2$, $J = 7.4$ Hz); ^{13}C NMR (200 MHz, $CDCl_3$): δ 13.5 ($2\times CH_3$), 22.5 ($2\times CH_2$), 29.8 ($2\times CH_2$), 33.0 ($2\times CH_2$); di(2-pentyl) diselenide **14**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.92 (t, 6H, $2\times CH_3$, $J = 6.4$ Hz), 1.43 (d, 6H, $2\times CH_3$, $J = 7.0$ Hz), 1.57 (m, 8H, $4\times CH_2$), 3.09 (m, 2H, $2\times CH$); ^{13}C NMR (200 MHz, $CDCl_3$): signals for diastereomers δ 13.80, 13.80 ($2\times CH_3$), 21.14, 21.16 ($2\times CH_2$), 22.62, 22.72 ($2\times CH_3$), 39.47, 39.49 ($2\times CH$), 40.01, 40.06 ($2\times CH_2$); diisoamyl diselenide **15**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.91 (d, 12H, $4\times CH_3$, $J = 6.2$ Hz), 1.63 (m, 6H, $2\times CH$, $2\times CH_2$), 2.93 (m, 4H, $2\times CH_2$); ^{13}C NMR (200 MHz, $CDCl_3$): δ 22.1 ($4\times CH_3$), 28.0 ($2\times CH$), 28.1 ($2\times CH_2$), 40.0

($2 \times CH_2$); di(2-octyl) diselenide **16**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.88, (t,6H, $2 \times CH_3$, J = 6.8 Hz), 1.27 (m, 20H, $5 \times CH_3$), 1.41 (d, 6H, CH_3, J = 7.0 Hz), 3.05 (m, 2H, CH); ^{13}C NMR (200 MHz, $CDCl_3$): δ 14.0 ($2 \times CH_3$), 22.5 ($2 \times CH_3$), 22.6 ($2 \times CH_2$), 27.9 ($2 \times CH_2$), 29.0 ($2 \times CH_2$), 31.7 ($2 \times CH_2$), 37.8 ($2 \times CH_2$), 39.8 ($2 \times CH$); dicyclohexyl diselenide **17**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.55 (m, 20H, $10 \times CH_2$), 3.05 (m, 2H, CH); ^{13}C NMR (200 MHz, $CDCl_3$): δ 25.6 ($2 \times CH_2$), 26.9 ($4 \times CH_2$), 34.5 ($4 \times CH_2$), 43.3 ($2 \times CH$).

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23. Spectral data; diselenide **18**: ^{1}H NMR (200 MHz, $CDCl_3$): 0.92 (d, 2H, J = 8.4 Hz, $2 \times CH$), 0.99 (s, 6H, $2 \times CH_3$), 1.19 (s, 6H, $2 \times CH_3$), 1.51 (m, 2H, $2 \times CH$), 2.00 (m, 10H), 2.36 (m, 4H), 3.01 (m, 4H, $2 \times CH_2$); ^{13}C NMR (200 MHz, $CDCl_3$): δ 22.6 ($2 \times CH_2$), 23.2 ($2 \times CH_3$), 26.0 ($2 \times CH_2$), 27.9 ($2 \times CH_3$), 33.2 ($2 \times CH_2$), 38.0 ($2 \times CH_2$), 38.6 ($2 \times C$), 41.2 ($2 \times CH$), 41.9 ($2 \times CH$), 46.0 ($2 \times CH$); ^{77}Se NMR (200 MHz, $CDCl_3$): δ 291.5; $[\alpha]_D^{20}$ −87.4 (c 10.43, $CHCl_3$); Anal. Calcd for $C_{20}H_{34}Se_2$: C, 55.55; H, 7.93%. Found: C, 55.57; H, 8.06%; selenide **22**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.88 (d, 2H, J = 9.4 Hz, $2 \times CH$), 0.99 (s, 6H, $2 \times CH_3$), 1.19 (s, 6H, $2 \times CH_3$), 1.50 (m, 2H, $2 \times CH$), 1.98 (m, 10H), 2.66 (m, 4H), 2.62 (m, 2H, $2 \times CH_2$); ^{13}C NMR (200 MHz, $CDCl_3$): δ 23.0 ($2 \times CH_2$), 23.3 ($2 \times CH_3$), 26.2 ($2 \times CH_2$), 28.0 ($2 \times CH_3$), 32.2 ($2 \times CH_2$), 33.4 ($2 \times CH_2$), 38.6 ($2 \times C$), 41.3 ($2 \times CH$), 42.1 ($2 \times CH$), 46.4 ($2 \times CH$); ^{77}Se NMR (200 MHz, $CDCl_3$): δ 129.1; $[\alpha]_D^{20}$ −44.7 (c 9.84, $CHCl_3$); Anal. Calcd for $C_{20}H_{34}Se$: C, 67.96; H, 9.70%. Found: C, 67.95; H, 9.84%; dimyrtanyl **23**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.85 (d, 2H, J = 9.3 Hz, $2 \times CH$), 0.99 (s, 6H, $2 \times CH_3$), 1.17 (s, 6H, $2 \times CH_3$), 1.51 (m, 6H), 1.88 (m, 12H), 2.30 (m, 2H); ^{13}C NMR (200 MHz, $CDCl_3$): δ 22.7($2 \times CH_2$), 23.4 ($2 \times CH_3$), 26.6 ($2 \times CH_2$), 28.3 ($2 \times CH_3$), 33.8 ($2 \times CH_2$), 36.11 ($2 \times CH_2$), 38.7 ($2 \times C$), 41.6 ($2 \times CH$), 41.7 ($2 \times CH$), 46.4 ($2 \times CH$); $[\alpha]_D^{20}$ −45.3 (c 11.49, $CHCl_3$); Anal. Calcd for $C_{20}H_{34}$: C, 87.52; H, 12.48%. Found: C, 87.60; H, 12.56%.