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Selenenylation–acylation of ketones with 2-chloroselenobenzoyl chloride. A novel route to benzo[*b*]selenophenes

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Abstract—It has been found that enolizable ketones and 1,3-diones react in neutral or basic medium with biselectrophiles such as 2-chloroselenobenzoyl chloride. The reaction takes place on the active α-methylene group. Selenenylation and subsequent acylation of the α-carbon atom take place and, depending on the ketone used, 3-hydroxybenzo[*b*]selenophenes or benzo[*b*]selenophen-3(2*H*)-ones are produced in moderate to high yields. © 2001 Published by Elsevier Science Ltd.

Selenenylation of carbon nucleophiles such as alkenes and carbanions, resulting in the formation of unsymmetrical selenides, is well known and commonly used as an intermediate step for the generation of new carbon–carbon double bonds.[1] The carboanions are usually generated from enols, unsaturated esters, lactones, lactams, aliphatic nitriles, β-ketosulfoxides, β-ketoselenoxides, alkyl malonates and other C–H acids by treatment with a base such as LDA and then selenenylated with commercially available reagents such as benzeneselenenyl chloride or bromide[2] and 2-pyridineselenenyl bromide.[3] When 2-pyridineselenenyl bromide is a selenenylating agent the reaction also proceeds in acidic medium. In this way α-ketoselenides, important intermediates for the synthesis of α,β-unsaturated ketones are obtained. Benzeneselenenyl chloride substituted in the *ortho* position with a chlorocarbonyl group (2-chloroselenobenzoyl chloride **1**) is a particular biselectrophile which can act as an acylation–selenenylation reagent. Primary amines, or other compounds having a primary amino group, upon treatment with 2-chloroselenobenzoyl chloride, are selenenylated and acylated on the nitrogen atom with ring closure and formation of benzisoselenazolon-3(2*H*)-ones.[4] To our knowledge, no study of the reactions of 2-chloroselenobenzoyl chloride with enolizable ketones and other C–H acids have been carried out. It begs a question: do both of these reactions, selenenylation and carbonylation, proceed on the active methylene carbon atom with formation of the benzo[*b*]selenophene ring system?

Our investigations, presented in this work, indicate that although selenenylation of a methylene group proceeds faster than acylation, both of these reactions take place and result in ring closure. It was found that the reaction is general for ketones having active α-methylene groups and that this is a new way for the selenophene ring formation, which might be useful for the synthesis of benzo[*b*]selenophen-3(2*H*)-ones (**3**) and 3-hydroxybenzo[*b*]selenophenes (**4**). Although a few of these compounds have been prepared previously, they were obtained in a more complex way.[5,6] In this paper we report a novel, simple and general approach for the synthesis of compounds **3** and **4** as exemplified by the preparation of **3a**–**c**,**f** and **4d**,**e**.

2-Chloroselenobenzoyl chloride (**1**) refluxed in acetone for a short period of time (15 min) gave 2-(acetylmethylseleno)benzoyl chloride (**2**) showing that selenenylation proceeded faster than acylation. Compound **2** was subsequently acylated and after a longer period (20 h) **4a** was formed, most probably via the unstable intermediate, 2-acetylbenzo[*b*]selenophen-3(2*H*)-one (**3a**). Under the same reaction conditions compound **2** was converted directly into **4a** (Scheme 1).[7]

It should be noted that although unsubstituted benzo[*b*]selenophen-3(2*H*)-one exists in the keto form (similar to **3a**), introduction of a 2-acetyl group promotes enolization, presumably by virtue of the extra stability conferred by intramolecular hydrogen bonding.[6a] The broad IR absorption band $\nu_{OH\cdots O} = 3005–1930\ cm^{-1}$ and

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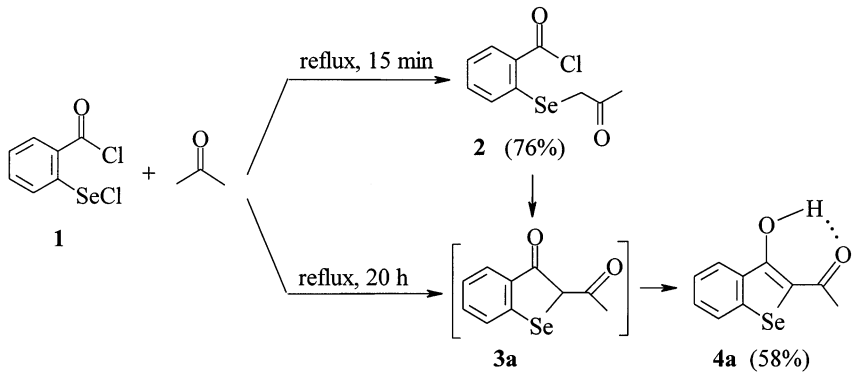
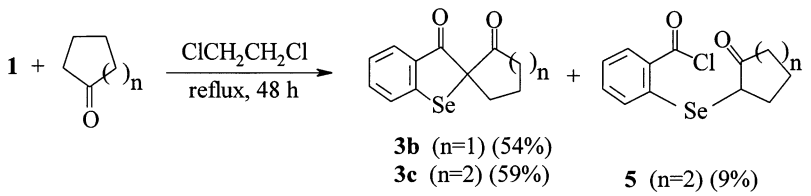
band $\nu_{C=O}=1583\ cm^{-1}$ are shifted to lower frequencies[8] as well as the signal for the acid proton ($\delta=12.86$ ppm) in the ^1H NMR spectrum both provide the evidence for structure **4a**. The same effects were observed for other 2-acetyl-3-hydroxy-benzo[*b*]selenophenes (**4d** and **4e**).

Both cyclopentanone and cyclohexanone react in a similar way to acetone but the reaction proceeds more slowly. The final products are unenolizable 2,2-spirobenzo[*b*]selenophen-3(2*H*)-ones **3b** and **3c**. Identification of selenide **5** as a by-product provides evidence that selenenylation of the ketone is the initial step of the reaction (Scheme 2).[9] Reaction of 2-chloroselenobenzoyl chloride with acetone and cycloalkanones was also carried out in the presence of bases such as NEt_3, $NEt(i\text{-}Pr)_2$, NaH, LDA and K_2CO_3, but in all of these cases a complex mixture of products were formed.

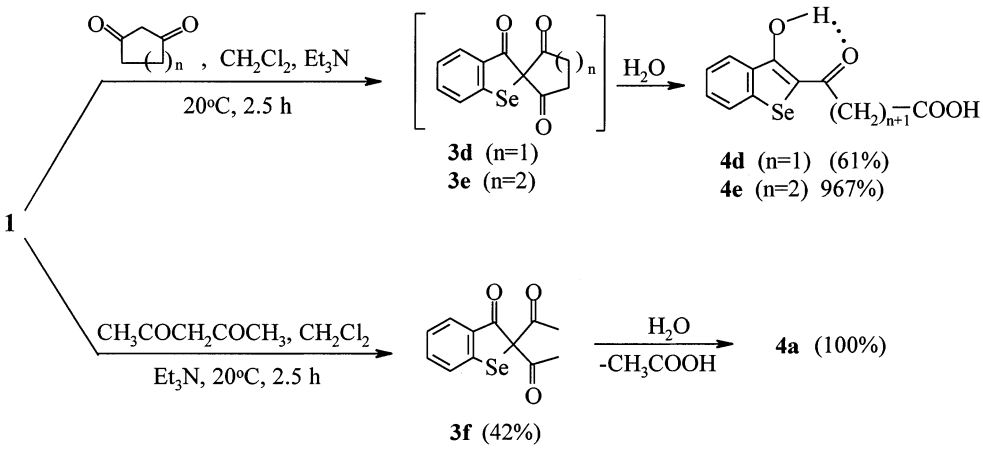
1,3-Diketones reacted with chloroselenobenzoyl chloride **1** more smoothly than monoketones and the side reaction was limited, particularly when the reaction proceeded in the presence of triethylamine. Unstable by-products such as **3d** and **3e**, which could not be isolated, spontaneously underwent deacylation in the presence of moisture absorbed on silica gel during their separation by column chromatography. Consequently, the enol **4d** or **4e** was the final product. In a similar reaction, acetylacetone produced relatively stable compound **3f**, which was isolated and characterized although during storage it also underwent decomposition to 2-acetylbenzo[*b*]selenophen-3(2*H*)-one (**4a**) and acetic acid (Scheme 3).[10]



Scheme 1.



Scheme 2.



Scheme 3.

Acknowledgements

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7. The solution of dichloride **1** (2.54 g, 10 mmol) in dry acetone (20 ml, 270 mmol) was refluxed under moisture-free conditions for 15 min. Acetone was evaporated in vacuo, and crude **2** was recrystallized from hexane. Under the same conditions, when the reaction time was prolonged to 20 h compound **4a** was obtained. Compound **2**: yield 76%, mp 65–67°C, pale yellow needles from hexane (found: C, 43.41; H, 3.14; Cl, 15.59. $C_{10}H_9ClO_2Se$ requires: C, 43.58; H, 3.29; Cl, 12.86%). ν_{max} (KBr) 3091, 3054, 2963, 1668, 1583, 1233, 1129; δ_H ($CDCl_3$, 300 MHz) 2.36 (s, 3H, CH_3), 3.68 (s, 2H, CH_2), 7.35–7.38 (m, 1H, ArH), 7.52–7.58 (m, 1H, ArH), 7.63 (d, 1H, $J=7.5$ Hz, ArH), 8.36 (d, 1H, $J=7.5$ Hz, ArH). Compound **4a**: yield 58%, mp 76–78°C, orange-red prisms from hexane (found: C, 50.09; H, 3.23. $C_{10}H_8O_2Se$ requires: C, 50.23; H, 3.37%). ν_{max} (KBr) 3059, 3005–1930, 1593, 1566, 1522, 1298; δ_H ($CDCl_3$, 300 MHz) 2.48 (s, 3H, CH_3), 7.41–7.53 (m, 2H, ArH), 7.80 (d, 1H, $J=7.5$ Hz, ArH), 8.01 (d, 1H, $J=7.5$ Hz, ArH), 12.86 (s, 1H, OH).
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9. The solution of dichloride **1** (2.54 g, 10 mmol) and cycloalkanone (20 mmol) in dry 1,2-dichloroethane (60 ml) was refluxed for 48 h under moisture-free conditions. The solvent was evaporated in vacuo and the residue was triturated with hot hexane (4×15 ml). Hexane was removed in vacuo and crude product (**3b**, **3c**) was purified by recrystallization from hexane. The mother liquid from recrystallization of **3c** was evaporated to dryness and crude **5** thus obtained was recrystallized from hexane. Compound **3b**: yield 54%, mp 91–92°C, pale yellow prisms from hexane (found: C, 54.20; H, 3.72. $C_{12}H_{10}O_2Se$ requires: C, 54.35; H, 3.80%). ν_{max} (KBr) 3064, 2901, 1730, 1677, 1584, 1281; δ_H ($CDCl_3$, 300 MHz) 1.88–1.97 (m, 1H, -CH_2-), 2.31–2.39 (m, 2H, -CH_2-), 2.42–2.54 (m, 2H, -CH_2-), 2.93–3.04 (m, 1H, -CH_2-), 7.28–7.33 (m, 1H, ArH), 7.49–7.58 (m, 2H, ArH), 7.76 (d, 1H, $J=7.5$ Hz, ArH). Compound **3c**: yield 59%, mp 162–164°C, pale yellow prisms from hexane (found: C, 55.66; H, 4.21. $C_{13}H_{12}O_2Se$ requires: C, 55.92; H, 4.33%). ν_{max} (KBr) 2950, 2853, 1702, 1672, 1586, 1277; δ_H ($CDCl_3$, 300 MHz) 1.65–1.86 (m, 2H, -CH_2-), 2.06–2.15 (m, 2H, -CH_2-), 2.27–2.32 (m, 1H, -CH_2-), 2.54–2.61 (m, 1H, -CH_2-), 2.78–2.90 (m, 2H, -CH_2-), 7.27–7.32 (m, 1H, ArH), 7.44 (d, 1H, $J=7.6$ Hz, ArH), 7.50–7.55 (m, 1H, ArH), 7.81 (d, 1H, $J=7.6$ Hz, ArH). Compound **5**: yield 9%, mp 58–60°C, yellow needles from hexane (found: C, 49.69; H, 4.38, Cl, 11.48. $C_{13}H_{13}ClO_2Se$ requires: C, 49.46; H, 4.15; Cl, 11.23%). ν_{max} (KBr) 2929, 2901, 2864, 1756, 1699, 1583, 1522, 1202; δ_H ($CDCl_3$, 300 MHz) 1.76–2.06 (m, 4H, -CH_2-), 2.31–2.42 (m, 3H, -CH_2-), 3.06–3.17 (m, 1H, -CH_2-), 4.09–4.12 (m, 1H, >CH), 7.31–7.36 (m, 1H, ArH), 7.51–7.57 (m, 1H, ArH), 7.80 (d, 1H, $J=8.1$ Hz, ArH), 8.31 (d, 1H, $J=8.1$ Hz, ArH).
10. To a stirred solution of 1,3-dione (2.5 mmol) and triethylamine (0.556 g, 5.5 mmol) in dry dichloromethane (10 ml) the solution of dichloride **1** (0.635 g, 2.5 mmol) in dry dichloromethane (20 ml) was added dropwise at room temperature for 30 min and the reaction was continued for additional 2 h. The compounds **4d** and **4e** were isolated by column chromatography on silica gel using ethyl acetate as the eluent. The compound **3f** was isolated in the same way as **3b** and **3c**. Compound **4d**: yield 61%, mp 200°C, brownish-red prisms from ethyl acetate (found: C, 48.80; H, 3.62. $C_{12}H_{10}O_4Se$ requires: C, 48.50; H, 3.39%). ν_{max} (KBr), 3045, 2939, 2912–2198 (broad), 1709, 1599, 1528, 1234; δ_H (DMSO-d_6, 300 MHz), 2.59 (t, 2H, $J=6.3$ Hz, $\underline{CH_2}$COOH), 3.21 (t, 2H, $J=6.3$ Hz, CH_2CO), 7.44–7.54 (m, 2H, ArH), 8.00–8.10 (m, 2H, ArH), 11.92 (broad s, 2H, OH, COOH). Compound **4e**: yield 67%, mp 175–178°C, yellow prisms from ethyl acetate (found: C, 50.47; H, 3.94%. $C_{13}H_{12}O_4Se$ requires:

C, 50.17; H, 3.89%). ν_{max} (KBr) 3046–2220 (broad) 1708, 1604, 1569, 1523, 1298; δ_H (DMSO-d_6, 300 MHz) 1.86 (quintet, 2H, $J=7.2$ Hz, -$CH_2\underline{CH_2}CH_2$-), 3.31 (t, 2H, $J=7.2$ Hz, -$\underline{CH_2}$COOH), 3.98 (t, 2H, $J=7.2$ Hz, $COCH_2$-), 7.40–7.52 (m, 2H, ArH), 8.07–8.06 (m, 2H, ArH), 11.98 (broad s, 2H, OH and COOH). Compound **3f**: yield 42%, mp 109–111°C, yellow needles from hexane (found: C, 51.03; H, 3.42. $C_{12}H_{10}O_3Se$ requires: C, 51.26; H, 3.59%), ν_{max} (KBr), 3086, 3059, 3012, 2923, 1720, 1681, 1580, 1277, 1164; δ_H ($CDCl_3$, 300 MHz), 2.40 (s, 6H, CH_3), 7.34–7.39 (m, 1H, ArH), 7.53–7.64 (m, 2H, ArH), 7.82–7.85 (m, 1H, ArH).