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Efficient synthesis of ethyl 3-alkyl-4-oxo-2-thioxo-1,3-thiazolane-5-carboxylates from the reaction of carbon disulfide and primary amines in the presence of diethyl 2-chloromalonate

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Abstract An efficient synthesis of ethyl 3-alkyl-4-oxo-2-thioxo-1,3-thiazolane-5-carboxylates *via* reaction of primary amines with CS_2 in the presence of diethyl 2-chloromalonate is described.

Keywords Dithiocarbamates; 1,3-Thiazolane; Alkylamines; Carbon disulfide; Three-component reaction.

Introduction

Dithiocarbamates are bifunctional ligands which have received attention due to their wide use as agrochemicals [1], pharmaceuticals [2], protecting group in peptide synthesis [3], and chelatores in material chemistry [4]. Organic dithiocarbamates are valuable synthesis intermediates [5–8], which are ubiquitously found in a variety of biologically active compounds [9, 10]. Functionalization of the carbamate moiety offers an attractive method for the generation of derivatives, which may constitute interesting medicinal and biological properties [9, 10]. In fact, few methods for the synthesis of dithiocarbamates have been employed, and among them, reaction of amines with costly and toxic reagents, such as thiophosgene and isothiocyanates have been reported [11, 12]. As part of our current studies, on the development of new routes in hetrocyclic synthesis, we report the synthesis of 4-oxo-2-thioxo-1,3-thiazolane-5-carboxylates.

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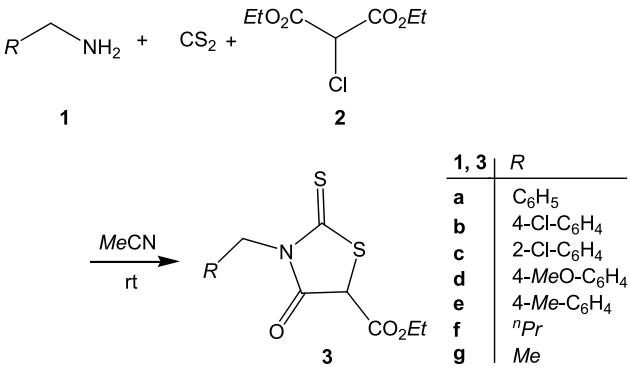
Results and discussion

The above three-component reaction of CS_2 and alkylamines **1** in the presence of diethyl 2-chloromalonate (**2**) proceeds smoothly in *Me*CN at room temperature to produce ethyl 3-alkyl-4-oxo-2-thioxo-1,3-thiazolane-5-carboxylates **3**, in good yields (Scheme 1).

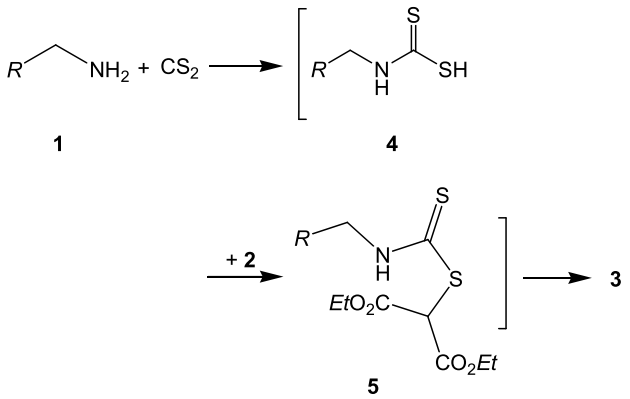
The products were characterized based on their IR, ^{1}H NMR, and ^{13}C NMR. The mass spectra of compounds **3a**–**3g** displayed molecular ion peaks at appropriate m/z values. The ^{1}H NMR spectra of **3a**–**3g** exhibited characteristic *AB* and $(AB)X_3$ spin systems for the NCH_2 and OCH_2 groups. The proton-decoupled ^{13}C NMR spectra of **3a**–**3g** showed the thiocarbonyl resonances at about $\delta = 187$ ppm.

The following mechanism (Scheme 2) may be invoked for the formation of compounds **3**. Conceivably, the starting point of the reaction is the formation of a 1:1 adduct **4** between amine **1** and CS_2, which undergoes substitution reaction with **2** to produce **5**. Intermediate **5** is converted to **3** by elimination of *Et*OH.

In conclusion, we report a novel transformation involving carbon disulfide and alkyl amines in the



Scheme 1



Scheme 2

presence of diethyl 2-chloromalonate, which affords ethyl 3-alkyl-4-oxo-2-thioxo-1,3-thiazolane-5-carboxylates. The advantage of the present procedure is that the reaction is performed under neutral conditions by simple mixing of the starting materials. The procedure described here provides an acceptable one-pot method for the preparation of 4-oxo-2-thioxo-1,3-thiazolanes.

Experimental

Carbon disulfide, **1**, and **2** were obtained from Fluka and were used without further purification. M.p.: Electrothermal-9100 apparatus. IR Spectra: Shimadzu IR-460 spectrometer. ^{1}H and ^{13}CNMR spectra: Bruker DRX-300 AVANCE instrument; in $CDCl_3$ at 300 and 75 MHz. EI-MS (70 eV): Finnigan-MAT-8430 mass spectrometer. Elemental analyses (C, H, and N) were performed with a Heraeus CHN-O-Rapid analyzer. The results agreed favorably with the calculated values.

General procedure for the preparation of compounds 3

To a stirred solution of 0.15 g CS_2 (2 mmol) and 0.39 g **2** (2 mmol) in 10 cm^3 *Me*CN was added 2 mmol **1** at room temperature. The reaction mixture was then stirred for 12 h. The solvent was removed under reduced pressure and the residue was purified by column chromatography (SiO_2; *n*-hexan:*Et*OAc = 3:1) to afford the pure title compounds.

Ethyl 3-benzyl-4-oxo-2-thioxo-1,3-thiazolane-5-carboxylate (**3a**, $C_{13}H_{13}NO_3S_2$)

Dark yellow oil; yield: 0.47 g (80%); IR (KBr): $\bar{\nu} = 1745$, 1665, 1571, 1504, 1428 cm^{-1}; EI-MS: m/z (%) = 295 (M^+, 8), 222 (22), 219 (65), 91 (100); ^{1}H NMR: $\delta = 1.26$ (t, $^3J =$ 7.1 Hz, *Me*), 4.27–4.31 (m, OCH_2), 5.22 (AB q, $\Delta\nu_{AB} =$ 22 Hz, $J_{AB} = 13.2$ Hz, NCH_2), 5.40 (s, CH), 7.34–7.36 (m, 5CH) ppm; ^{13}C NMR: $\delta = 13.7$ (*Me*), 47.9 (NCH_2), 52.8 (CH), 63.3 (OCH_2), 128.1 (CH), 128.2 (CH), 128.8 (CH), 135.3 (C), 165.2 (C=O), 171.3 (C=O), 186.9 (C=S) ppm.

Ethyl 3-(4-chlorobenzyl)-4-oxo-2-thioxo-1,3-thiazolane-5-carboxylate (**3b**, $C_{13}H_{12}ClNO_3S_2$)

Dark yellow oil; yield: 0.53 g (80%); IR (KBr): $\bar{\nu} = 1739$, 1636, 1575, 1545, 1461 cm^{-1}; EI-MS: m/z (%) = 329 (M^+, 5), 256 (22), 253 (67), 126 (100), 91 (39); ^{1}H NMR: $\delta = 1.18$ (t, $^3J = 7.2$ Hz, *Me*), 4.12–4.17 (m, OCH_2), 5.22 (AB q, $\Delta\nu_{AB} = 15$ Hz, $J_{AB} = 13.0$ Hz, NCH_2), 5.36 (s, CH), 7.23 (d, $^3J = 8.8$ Hz, 2CH), 7.42 (d, $^3J = 8.8$ Hz, 2CH) ppm; ^{13}C NMR: $\delta = 14.5$ (*Me*), 46.3 (NCH_2), 54.9 (CH), 59.98 (OCH_2), 128.3 (CH), 130.8 (CH), 132.8 (C), 136.3 (C), 164.9 (C=O), 165.5 (C=O), 187.0 (C=S) ppm.

Ethyl 3-(2-chlorobenzyl-4-oxo-2-thioxo-1,3-thiazolane-5-carboxylate (**3c**, $C_{13}H_{12}ClNO_3S_2$)

Dark yellow oil; yield: 0.53 g (80%); IR (KBr): $\bar{\nu} = 1747$, 1630, 1587, 1521, 1453 cm^{-1}; EI-MS: m/z (%) = 329 (M^+, 7), 256 (22), 253 (72), 126 (100), 91 (61); ^{1}H NMR: $\delta = 1.21$ (t, $^3J = 7.2$ Hz, *Me*), 4.02–4.07 (m, OCH_2), 5.28 (AB q, $\Delta\nu_{AB} = 23$ Hz, $J_{AB} = 12.1$ Hz, NCH_2), 6.75 (d, $^3J = 6.9$ Hz, CH), 7.22 (m, 2CH), 7.41 (d, $^3J = 7.6$ Hz, CH) ppm; ^{13}C NMR: $\delta = 14.5$ (*Me*), 44.7 (CH), 55.0 (NCH_2), 56.1 (OCH_2), 127.1 (CH), 127.3 (CH), 128.4 (CH), 129.4 (CH), 130.1 (C), 132.4 (C), 164.7 (C=O), 165.0 (C=O), 186.4 (C=S) ppm.

Ethyl 3-(4-methoxybenzyl)-4-oxo-2-thioxo-1,3-thiazolane-5-carboxylate (**3d**, $C_{14}H_{15}NO_4S_2$)

Dark yellow oil; yield: 0.48 g (75%); IR (KBr): $\bar{\nu} = 1738$, 1655, 1587, 1532, 1441 cm^{-1}; EI-MS: m/z (%) = 325 (M^+, 11), 252 (22), 249 (69), 122 (100), 91 (36); ^{1}H NMR: $\delta = 1.19$ (t, $^3J = 7.2$ Hz, *Me*), 3.52 (s, *Me*O), 4.12–4.18 (m, OCH_2), 5.14 (AB q, $\Delta\nu_{AB} = 16$ Hz, $J_{AB} = 14.2$ Hz, NCH_2), 5.2 (s, CH), 6.73 (d, $^3J = 8.3$ Hz, 2CH), 7.39 (d, $^3J = 8.3$ Hz, 2CH) ppm; ^{13}C NMR: $\delta = 14.4$ (*Me*), 46.0 (NCH_2), 54.0 (CH), 54.9 (*Me*O), 60.0 (OCH_2), 113.6 (2CH), 129.4 (C), 130.5 (2CH), 159.4(C), 165.1 (C=O), 165.7 (C=O), 186.6 (C=S) ppm.

Ethyl 3-(4-methylbenzyl)-4-oxo-2-thioxo-1,3-thiazolane-5-carboxylate (**3e**, $C_{14}H_{15}NO_3S_2$)

Dark yellow oil; yield: 0.48 g (75%); IR (KBr): $\bar{\nu} = 1742$, 1632, 1574, 1511, 1434 cm^{-1}; EI-MS: m/z (%) = 309 (M^+, 8), 236 (22), 233 (78), 106 (100), 91 (45); ^{1}H NMR: $\delta = 1.19$ (t, $^3J = 7.2$ Hz, *Me*), 2.15 (s, *Me*), 4.10–4.16 (m, OCH_2), 5.20

(AB q, $\Delta\nu_{AB} = 18$ Hz, $J_{AB} = 13.9$ Hz, NCH_2), 5.20 (s, CH), 6.90 (d, $^3J = 7.6$ Hz, 2CH), 7.37 (d, $^3J = 7.6$ Hz, 2CH) ppm; ^{13}C NMR: $\delta = 14.5$ (*Me*), 21.1 (*Me*), 46.7 (NCH_2), 53.5 (CH), 60.5 (OCH_2), 129.3 (CH), 129.4 (CH), 134.9 (C), 137.4 (C), 165.1 (C=O), 165.7 (C=O), 187.3 (C=S) ppm.

Ethyl 3-butyl-4-oxo-2-thioxo-1,3-thiazolane-5-carboxylate (**3f**, $C_{10}H_{15}NO_3S_2$)
Yellow oil; yield: 0.48 g (75%); IR (KBr): $\bar{\nu} = 1737$, 1630, 1598, 1556, 1434 cm^{-1}; EI-MS: m/z (%) = 261 (M^+, 6), 188 (22), 185 (48), 204 (24), 57 (100); ^{1}H NMR: $\delta = 0.93$ (t, $^3J =$ 7.0 Hz, *Me*), 1.27 (t, $^3J = 7.2$ Hz, *Me*), 1.35–1.39 (m, CH_2), 1.62–1.66 (m, CH_2), 4.07–4.12 (m, N-CH_2), 4.24–4.29 (m, OCH_2), 5.29 (s, CH), ppm; ^{13}C NMR: $\delta = 13.5$ (*Me*), 14.5 (*Me*), 20.0 ($2CH_2$), 43.9 (NCH_2), 47.5 (CH), 59.9 (OCH_2), 165.0 (C=O), 165.8 (C=O), 186.4 (C=S) ppm.

Ethyl 3-ethyl-4-oxo-2-thioxo-1,3-thiazolane-5-carboxylate (**3g**, $C_8H_{11}NO_3S_2$)
Yellow oil; yield: 0.37 g (80%); IR (KBr): $\bar{\nu} = 1743$, 1625, 1570, 1524, 1444 cm^{-1}; EI-MS: m/z (%) = 233 (M^+, 6), 160 (22), 157 (76), 204 (24), 29 (100); ^{1}H NMR: $\delta =$ 1.13 (t, $^3J = 7.2$ Hz, *Me*), 1.19 (t, $^3J = 7.2$ Hz, *Me*), 4.02–4.07 (m, NCH_2), 4.13–4.18 (m, OCH_2), 5.2 (s, CH), ppm; ^{13}C NMR: $\delta = 12.5$ (*Me*), 14.9 (*Me*), 47.0 (NCH_2), 52.0 (CH), 60.5 (OCH_2), 165.5 (C=O), 165.7 (C=O), 186.7 (C=S) ppm.

References

1. Rafin C, Veignie E, Sanchelle M, Postal D, Len C, Villa P, Ronco G (2000) J Agric Food Chem 48:5283
2. Cao SL, Feng YP, Jiang YY, Liu SY, Dind GY, Li RT (2005) Bioorg Med Chem Lett 15:1915
3. Greene TW, Wuts PGM (1999) Protecting Groups in Organic Synthesis, 3rd edn. Wiley Interscience, New York p 484
4. Zhao Y, Perez-Segarra W, Shi Q, Wei A (2005) J Am Chem Soc 127:7328
5. Gautier N, Gallego-planas N, Mercier N, Levillain E, Hudhomme P (2002) Org Lett 4:961
6. Elgemeie GH, Sayed SH (2001) Synthesis:1747
7. Boas U, Gertz H, Christensen JB, Heegaard PMH (2004) Tetrahedron Lett 45:269
8. Azizi N, Aryanasab F, Torkiyan L, Ziyaei A, Saidi MR (2006) J Org Chem 71:3634
9. Dhooghe M, De Kime N (2006) Tetrahedron 62:513
10. Fernandez JMG, Mellet CO, Blanco JLJ, Mota JF, Gadelle A, Coste-Sargute A, Defaye J (1995) Carbohydr Res 268:57
11. Chin-Hsien W (1981) Synthesis:622
12. Mizuno T, Iwai T, Ishino Y (2005) Tetrahedron 61:9157
13. Li Q, Yang C, Ge Z, Li R, Cui Y (2006) Magn Reson Chem 44:720
14. Goubert-Renaudin S, Schneider R, Walcarius A (2007) Tetrahedron Lett 48:2113