Heterocycl. Commun., Vol. 16(4-6), pp. 275–278, 2010 • Copyright © by Walter de Gruyter • Berlin • New York. DOI 10.1515/HC.2010.015

Reaction of 2-thiazolidinethione with halohydrocarbon: synthesis of novel *N*-alkylated 2-thiazolidinethione and *S*-alkylated thiazoline derivatives

Yufa Liu*, Junwei Liu and Xiuming Liu

College of Chemistry, Chemical Engineering and Materials Science, Engineering Research Center of Pesticide and Medicine Intermediate Clean Production, Ministry of Education, Shandong Normal University, Jinan 250014, China

*Corresponding author
e-mail: yufaliu@yahoo.cn

Abstract

Reaction of 2-thiazolidinethione with halohydrocarbon in ethanol gave a series of *N*-alkylated 2-thiazolidinethione and *S*-alkylated thiazoline derivatives in excellent yields. The reaction was carried out under mild conditions using NaOH as a base and it did not require protection from air.

Keywords: halohydrocarbon; isomers; 2-thiazolidinethione; thiazole derivatives.

Introduction

2-Thiazolidinethione (Rachinskii et al., 1958) is the derivative of thiazole (Ingo et al., 2001) that belongs to an important group of heterocyclic compounds, many of which are widely used in medicinal and pesticidal fields (Kazuo et al., 1999). Some derivatives of thiazolidine have diverse biological activities, such as bactericidal, pesticidal, antiphlogistic, anticonvulsant, tuberculostatic, anti-inflammatory, analgesic, antiparasitic, and herbicidal agents (Tsymbal et al., 1968; Jean et al., 1990; Moulard et al., 1993; Masae et al., 2003; Tenorio et al., 2005; Kucukguzel et al., 2006; Li et al., 2006). Also, some thiazole derivatives are potent anti-HIV (Jan et al., 2002) and anticancer (Chandrappa et al., 2008) agents. Therefore, the synthesis and biological activity of thiazole derivatives have received much attention recently. Accordingly, we report here results from the reaction of 2-thiazolidinethione with 14 halohydrocarbon reagents using conventional heating.

Results and discussion

The strategy for the synthesis of 2-thiazolidinethione and its derivatives is outlined in Scheme 1. The halohydrocarbons (**1–14**) reacted efficiently with 2-thiazolidinethione to afford the desired *N*- and *S*-alkylated products in yields that were good to excellent. The results are summarized in Table 1.

The reaction of 2-thiazolidinethione with low-molecular-weight halohydrocarbons (**1–9**) in refluxing ethanol gave the corresponding *N*-alkylated 2-thiazolidinethione derivatives $\mathbf{I_{1a}}$-$\mathbf{I_{9a}}$ in high yields of 64–75%. The alternative *S*-alkylated isomers of $\mathbf{I_{1b}}$-$\mathbf{I_{9b}}$ were not isolated. The reaction of 2-thiazolidinethione was extended to include alkylation with higher-molecular-weight halohydrocarbon, such as bromododecane (**10**), bromohexadecane (**11**) and aryl halides (**12–14**). For these reactions, as depicted in Table 1, both the *N*- and *S*-alkylated derivatives $\mathbf{I_{10a–14a}}$ and $\mathbf{I_{10b–14b}}$ were isolated. The structures of the products were confirmed by hydrogen nuclear magnetic resonance (^{1}H NMR), carbon magnetic resonance (^{13}C NMR), infrared spectrometry (IR), and mass spectrometry (MS).

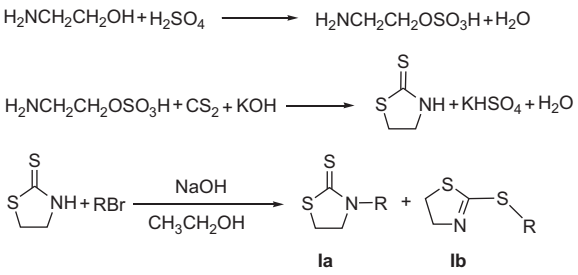
Conclusion

A method for efficient synthesis of a novel thiazole system by reaction of 2-thiazolidinethione with various halohydrocarbons at appropriate temperature is reported. The reaction could be carried out in ethanol or in other alcohols, without the need for protection from air. Ethanol proved to be a good solvent in the reactions, and it was convenient for product isolation.

The reaction of 2-thiazolidinethione with low-molecular-weight halohydrocarbon (chain hydrocarbon, C≤10, **1–9**) afforded *N*-alkylated 2-thiazolidinethione derivatives ($\mathbf{I_{1a–9a}}$). The yields dropped from 75 to 64% with increasing molecular weight of the halohydrocarbon. On the other hand, the reaction of 2-thiazolidinethione with bromododecane (**10**), bromohexadecane (**11**) or other aryl halides (**12–14**) gave isomeric mixtures of *N*-alkylated 2-thiazolidinethione ($\mathbf{I_{10a–14a}}$) and *S*-alkylated thiazoline ($\mathbf{I_{10b–14b}}$). In each case, the *N*-alkylated 2-thiazolidinethione derivatives were obtained as the main products, and the yields ranged from 48 to 64%. The isolated yields for the *S*-alkylated isomers ranged from 9 to 26%.

Experimental

Melting points were determined in soft-glass capillaries on the Electrothermal Melting Point apparatus and were uncorrected. Qualitative and quantitative thin-layer chromatography (TLC) was conducted on TLC silica gel sheets. ^{1}H NMR and ^{13}C NMR spectra



Scheme 1 Synthesis of 2-thiazolidinethione and its derivatives.

were recorded at 300 MHz and 75 MHz, respectively, on a Bruker DRX 300 instrument using $CDCl_3$ as solvent. The chemical shifts are reported in ppm. IR spectra were recorded on the Bruker Tensor 27 FTIR spectrometer with KBr pellet. Mass spectra were obtained on an AGILENT 5973N MSD mass spectrometer with EI. All compounds were homogeneous on TLC plates in various solvent systems, such as petroleum ether-acetic ether (20:1-10:3) and normal hexane-dichloromethane (20:1-5:1). 2-Aminoethylsulfuric acid and 2-thiazolidinethione were synthesized using published procedures (Owen, 1967; Taguchi et al., 1969; Kazuo et al., 1983; Kenso and Miyuki, 1984; Sugita, 1984).

General procedure for the preparation of the derivatives of 2-thiazolidinethione ($I_{1–14b}$)

A mixture of 2-thiazolidinethione (0.30 g, 2.50 mmol), NaOH (0.10 g, 2.50 mmol) and the appropriate halohydrocarbon (Table 1) in ethanol (10 ml) was stirred at refluxing temperature and the time indicated in Table 1. The progress of the reaction was monitored by TLC. The by-product NaX was removed by filtration and the residue was washed with ethanol (3×10 ml). The filtrate was washed with hydrochloric acid (1%, 3×10 ml) and dried with anhydrous $MgSO_4$. Derivatives $\mathbf{I_{1a–9a}}$ were purified with the silica gel column chromatography. Derivatives $\mathbf{I_{10a–14a}}$ and $\mathbf{I_{10b–14ab}}$ were purified with the silica gel column chromatography. The products were obtained in good purity indicated by ^{1}H NMR, ^{13}C NMR, IR and MS.

Characterization of products

2-Thiazolidinethione: White solid; 5.67 g (68%); mp 105–106°C. ^{1}H NMR: δ 3.56 (t, 2H, J=8.8 Hz, -S-CH_2), 3.99 (t, 2H, J=8.8 Hz, -S-CH_2-CH_2), 8.14 (s, 1H, NH); ^{13}C δ NMR: 35.12, 58.95, 201.63.

$\mathbf{I_{1a}}$: Yellow oil; 0.28 g (75%); ^{1}H NMR: δ 1.29 (t, 3H, J=6.7 Hz, CH_3), 3.02 (t, 2H, J=7.4 Hz, -S-CH_2), 3.32 (m, 2H, -$\underline{CH_2}CH_3$), 4.15 (t, 2H, J=7.4 Hz, -S-CH_2-$\underline{CH_2}$); ^{13}C NMR: δ 23.2, 34.9, 38.1, 64.4, 165.1; IR: 2929, 2850, 1715, 1571, 1448, 1372, 1305, 1266, 1218, 1058, 1017, 994, 964, 921, 756, 639 cm^{-1}; EI-MS: m/z 148.26 (M^++1).

$\mathbf{I_{2a}}$: Yellow oil; 0.30 g (74%); ^{1}H NMR: δ 0.98 (t, 3H, J=7.3 Hz, CH_3), 1.64–1.77 (m, 2H, -$\underline{CH_2}CH_3$), 3.06 (t, 2H, J=7.9 Hz, -SCH_2), 3.36 (t, 3H, J=7.3 Hz, -N-$\underline{CH_2}CH_2CH_3$), 4.19 (t, 2H, J=7.9 Hz, -NCH_2); ^{13}C NMR: δ 13.5, 22.7, 34.7, 35.3, 64.2, 165.9; IR: 3445, 2963, 2931, 2360, 1570, 1456, 1303, 1017, 994, 921, 783, 732, 639, 530 cm^{-1}; EI-MS: m/z 162.29 (M^++1).

$\mathbf{I_{3a}}$: Yellow oil; 0.27 g (66%); ^{1}H NMR: δ 1.34 [d, 6H, J=6.8 Hz, -CH($\underline{CH_3}$)$_2$], 3.32 (t, 2H, J=8.0 Hz, -S-CH_2), 3.74–3.83 (m, 1H, -N-CH), 4.19 (t, 2H, J=8.0 Hz, -S-CH_2-$\underline{CH_2}$); ^{13}C NMR: δ 14.5, 30.8, 30.8, 35.1, 64.1, 206.6; IR: 2962, 2927, 2864, 1567, 1448, 1383, 1365, 1304, 1240, 1191, 1157, 1057, 1013, 994, 963, 920, 882, 703, 650 cm^{-1}; EI-MS: m/z 162.30 (M^++1).

Table 1 Reaction of 2-thiazolidinethione with halohydrocarbons in the presence of NaOH in ethanol under reflux conditions (see Experimental for additional details).

Starting material	mmol	Product	Time (h)	Yield (%)
CH_3CH_2Br (**1**)	3.00	$\mathbf{I_{1a}}$	2.5	75
$CH_3CH_2CH_2Br$ (**2**)	3.00	$\mathbf{I_{2a}}$	2.5	74
$(CH_3)_2CHBr$ (**3**)	3.50	$\mathbf{I_{3a}}$	3.0	66
$CH_3CH_2CH_2CH_2Br$ (**4**)	3.00	$\mathbf{I_{4a}}$	3.0	70
$(CH_3)_2CHCH_2Br$ (**5**)	3.50	$\mathbf{I_{5a}}$	3.0	68
$CH_3CH_2CH(CH_3)Br$ (**6**)	3.50	$\mathbf{I_{6a}}$	3.5	66
$CH_3(CH_2CH_2)_2Br$ (**7**)	3.50	$\mathbf{I_{7a}}$	4.0	65
$CH_3(CH_2CH_2)_3CH_2Br$ (**8**)	3.50	$\mathbf{I_{8a}}$	4.0	65
$CH_3(CH_2CH_2)_4CH_2Br$ (**9**)	4.00	$\mathbf{I_{9a}}$	4.5	64
$CH_3(CH_2CH_2)_5CH_2Br$ (**10**)	4.00	$\mathbf{I_{10a}}$+$\mathbf{I_{10b}}$	5.0	56+11
$CH_3(CH_2CH_2)_7CH_2Br$ (**11**)	4.00	$\mathbf{I_{11a}}$+$\mathbf{I_{11b}}$	5.0	48+9
$PhCH_2Cl$ (**12**)	3.00	$\mathbf{I_{12a}}$+$\mathbf{I_{12b}}$	1.5	64+26
p-NO_2PhCH_2Cl (**13**)	3.00	$\mathbf{I_{13a}}$+$\mathbf{I_{13b}}$	2.0	61+22
$PhCH_2CH_2Cl$ (**14**)	3.00	$\mathbf{I_{14a}}$ +$\mathbf{I_{14b}}$	2.5	57+18

I_{4a}: Yellow oil; 0.31 g (70%); ^{1}H NMR: δ 0.90 (t, 3H, J=7.8 Hz, -CH_3), 1.34–1.46 (m, 2H, -$\underline{CH_2}CH_3$), 1.60–1.69 (m, 2H, -$\underline{CH_2}$-CH_2CH_3), 3.10 (t, 2H, J=7.9 Hz, -SCH_2), 3.37 (t, 2H, J=7.3 Hz, -N-$\underline{CH_2}CH_2CH_2CH_3$), 4.18 (t, 2H, J=7.9 Hz, -NCH_2); ^{13}C NMR: δ 13.5, 22.1, 29.3, 31.3, 35.3, 64.3, 165.7; IR: 2957, 2930, 2854, 1571, 1463, 1378, 1303, 1273, 1228, 1191, 1017, 995, 964, 921, 745, 639 cm^{-1}; EI-MS: m/z 176.31 (M^++1).

I_{5a}: Yellow oil; 0.29 g (68%); ^{1}H NMR: δ 0.84 (d, 3H, J=3.7 Hz, -CH_3), 1.00 (d, 3H, J=3.7 Hz, CH_3), 1.34 (m, 1H, -CH), 3.09 (m, 2H, -CH_2CH), 3.66 (t, 2H, J=7.8 Hz, -SCH_2), 4.20 (t, 2H, J=7.8 Hz, -NCH_2); ^{13}C NMR: δ 14.3, 20.0, 27.0, 35.1, 44.5, 64.2, 165.8; IR: 2964, 2930, 2852, 1567, 1455, 1379, 1303, 1225, 1190, 1150, 1060, 994, 963, 920, 646 cm^{-1}; EI-MS: m/z 176.32 (M^++1).

I_{6a}: Yellow oil; 0.30 g (66%); ^{1}H NMR: δ 0.99 (t, 3H, J=7.3 Hz, -$CH_2\underline{CH_3}$), 1.36 (m, 3H, -CH$\underline{CH_3}$), 1.60 (m, 2H, -$\underline{CH_2}CH_3$), 3.32 (t, 2H, J=7.9 Hz, -SCH_2), 3.66 (m, 1H, J=7.0 Hz, -$\underline{CH}CH_3$), 4.20 (t, 2H, J=7.9 Hz, -NCH_2); ^{13}C NMR: δ 8.2, 21.1, 29.6, 34.9, 44.7, 64.3, 165.83; IR: 2964, 2930, 2852, 1567, 1455, 1379, 1303, 1225, 1190, 1150, 1060, 994, 963, 920, 646 cm^{-1}; EI-MS: m/z 176.31 (M^++1).

I_{7a}: Yellow oil; 0.31 g (65%); ^{1}H NMR: δ 0.87 (t, 3H, J=6.9 Hz, -CH_3), 1.34–1.69 [m, 6H, -$(\underline{CH_2})_3CH_3$], 3.08 [t, 2H, J=7.3 Hz, -$\underline{CH_2}(CH_2)_3CH_3$], 3.35 (t, 2H, J=7.9 Hz, -SCH_2), 4.18 (t, 2H, J=7.9 Hz, -NCH_2); ^{13}C NMR: δ 13.9, 28.9, 31.8, 32.7, 35.3, 38.9, 64.3, 165.7; IR: 2956, 2929, 2854, 1571, 1464, 1378, 1303, 1260, 1190, 1061, 1017, 996, 965, 920, 730, 639 cm^{-1}; EI-MS: m/z 190.34 (M^++1).

I_{8a}: Yellow oil; 0.31 g (65%); ^{1}H NMR: δ 0.85 (t, 3H, J=6.9 Hz, -CH_3), 1.26–1.39 [m, 10H, -$(\underline{CH_2})_5CH_3$], 1.68 [t, 2H, J=7.3 Hz, -$\underline{CH_2}(CH_2)_5CH_3$], 3.09 [t, 2H, J=5.4 Hz, -$\underline{CH_2}(CH_2)_6CH_3$], 3.37 (t, 2H, J=7.9 Hz, -SCH_2), 4.21 (t, 2H, J=7.9 Hz, -NCH_2); ^{13}C NMR: δ 14.0, 22.6, 28.7, 29.1, 29.2, 29.7, 31.8, 34.1, 38.9, 64.3, 165.7; IR: 2925, 2853, 2361, 1649, 1570, 1460, 1302, 1190, 1017, 994, 965, 919, 722 cm^{-1}; EI-MS: m/z 232.42 (M^++1).

I_{9a}: Yellow oil; 0.39 g (64%); ^{1}H NMR: δ 0.83 (t, 3H, J=3.4 Hz, -CH_3), 1.23–1.37 [m, 14H, -$(\underline{CH_2})_7CH_3$], 1.64 [m, 2H, -$\underline{CH_2}(CH_2)_7CH_3$], 3.07 [t, 2H, J=7.3 Hz, -$\underline{CH_2}(CH_2)_8CH_3$], 3.35 (t, 2H, J=7.9 Hz, -SCH_2), 4.19 (t, 2H, J=7.9 Hz, -NCH_2); ^{13}C NMR: δ 14.0, 22.6, 28.7, 29.1, 29.2, 29.4, 29.5, 31.8, 32.6, 35.0, 64.0, 166.1; IR: 2925, 2853, 2361, 1649, 1570, 1460, 1302, 1190, 1017, 994, 965, 919, 722 cm^{-1}; EI-MS: m/z 260.47 (M^++1).

I_{10a}: White solid; Mp 44–46°C; 0.40 g (56%); ^{1}H NMR: δ 0.87 (t, 3H, J=3.4 Hz, -CH_3), 1.24 [m, 18H, -$(\underline{CH_2})_9CH_3$], 1.67 [m, 2H, -$\underline{CH_2}(CH_2)_9CH_3$], 3.08 [m, 2H, J=7.3 Hz, -$\underline{CH_2}(CH_2)_{10}CH_3$], 3.36 (t, 2H, J=7.9 Hz, -SCH_2), 4.20 (t, 2H, J=7.9 Hz, -NCH_2); ^{13}C NMR: δ 14.1, 22.6, 28.7, 29.0, 29.3, 29.4, 29.5, 29.6 (two signals), 31.9, 32.8, 33.9, 35.2, 64.2, 167.0; EI-MS: m/z 288.53 (M^++1).

I_{10b}: White solid; Mp 65–67°C; 0.08 g (11%); ^{1}H NMR: δ 0.87 (t, 3H, J=3.4 Hz, -CH_3), 1.25 [m, 18H, -$(\underline{CH_2})_9CH_3$], 1.65 [m, 2H, -$\underline{CH_2}(CH_2)_9CH_3$], 3.26 [t, 2H, J=7.7 Hz, -$\underline{CH_2}(CH_2)_{10}CH_3$], 3.74 (t, 2H, J=7.7 Hz, -SCH_2), 4.06 (t, 2H, J=7.7 Hz, -NCH_2); ^{13}C NMR: δ 14.1, 22.7, 28.7, 29.1, 29.3, 29. 5, 29.5, 29.6 (two signals), 31.9, 32.9, 33.9, 35.2, 64.2, 166.3; EI-MS: m/z 288.53 (M^++1).

I_{11a}: White solid; Mp 40–41°C; 0.42 g (48%); ^{1}H NMR: δ 0.89 (t, 3H, J=6.0 Hz, -CH_3), 1.25 [m, 26H, -$(\underline{CH_2})_{13}CH_3$], 1.68 [m, 2H, -$\underline{CH_2}(CH_2)_{13}CH_3$], 3.09 [t, 2H, J=7.3 Hz, -$\underline{CH_2}(CH_2)_{14}CH_3$], 3.37 (t, 2H, J=7.9 Hz, -SCH_2), 4.20 (t, 2H, J=7.9 Hz, -NCH_2); ^{13}C NMR: δ 14.1, 22.7, 26.8, 24.2, 29.1 (two signals), 29.2 (three signals), 29.3 (two signals), 29.4, 29.5, 29.6, 31.8, 31.9, 49.3, 59.6, 196.1; IR: 3443, 2919, 2848, 1637, 1572, 1469, 1302, 996, 914, 719, 645, 582, 526 cm^{-1}; EI-MS: m/z 344.63 (M^++1).

I_{11b}: White solid; Mp 61–63°C; 0.08 g (9%); ^{1}H NMR: δ 0.86 (t, 3H, J=3.3 Hz, -CH_3), 1.25 [m, 26H, -$(\underline{CH_2})_{13}CH_3$], 1.66 [m, 2H, -$\underline{CH_2}(CH_2)_{13}CH_3$], 3.27 [t, 2H, J=7.8 Hz, -$\underline{CH_2}(CH_2)_{14}CH_3$], 3.75 (t, 2H, J=7.6 Hz, -SCH_2), 4.07 (t, 2H, J=7.9 Hz, -NCH_2); ^{13}C NMR: δ 14.1, 22.7, 26.8, 27.2, 29.3 (two signals), 29.5, 29.5, 29.6, 29.7, 31.9, 49.3, 56.6, 196.1; EI-MS: m/z 344.63 (M^++1).

I_{12a}: White solid; Mp 72–74°C; 0.34 g (64%); ^{1}H NMR: δ 3.40 (t, 2H, J=8.0 Hz, -SCH_2), 4.24 (t, 2H, J=8.0 Hz, -NCH_2), 4.38 (s, 2H, $\underline{CH_2}$-Ar), 7.26–7.38 (m, 5H, -Ar); ^{13}C NMR: δ 25.5, 48.0, 52.0, 126.1, 127.2, 128.1, 128.2, 128.4, 130.2, 172.1; IR: 3452, 3023, 2944, 1660, 1489, 1448, 1410, 1363, 1315, 1243, 1178, 1075, 1043, 982, 918, 730, 692, 587 cm^{-1}; EI-MS: m/z 210.33 (M^++1).

I_{12b}: White solid; Mp 94–96°C; 0.14 g (26%); ^{1}H NMR: δ 3.23 (t, 2H, J=7.9 Hz), 3.94 (t, 2H, J=7.9 Hz), 4.99 (s, 2H), 7.26–7.34 (m, 5H); ^{13}C NMR: δ 32.1, 38.1, 127.2, 127.9, 128.9, 139.6, 162.6; EI-MS: m/z 210.33 (M^++1).

I_{13a}: White solid; Mp 79–81°C; 0.39 g (61%); ^{1}H NMR: δ 3.43 (t, 2H, J=7.9 Hz), 4.22 (t, 2H, J=7.9 Hz), 4.42 (s, 2H), 7.53 (d, 2H, J=8.5 Hz), 8.15 (d, 2H, J=8.5 Hz); ^{13}C NMR: δ 35.8, 36.0, 63.6, 123.7, 129.9, 144.7, 147.2, 165.5; EI-MS: m/z 255.33 (M^++1).

I_{13b}: White solid; Mp 114–116°C; 0.14 g (22%); ^{1}H NMR: δ 3.46 (t, 2H, J=7.9 Hz), 4.31 (t, 2H, J=7.9 Hz), 4.57 (s, 2H), 7.55 (d, 2H, J=8.6 Hz), 8.19 (d, 2H, J=8.6 Hz); ^{13}C NMR: δ 35.9, 36.1, 64.3, 125.4, 130.7, 146.8, 149.0, 166.5; EI-MS: m/z 255.33 (M^++1).

I_{14a}: White solid; Mp 84–86°C; 0.32 g (57%); ^{1}H NMR: δ 3.02 (t, 2H, J=7.6 Hz), 3.34–3.42 (m, 4H), 4.23 (t, 2H, J=7.9 Hz), 7.23–7.39 (m, 5H); ^{13}C NMR: δ 35.2, 35.4, 35.7, 64.2, 126.6, 128.5, 128.6, 139.8, 165.7; EI-MS: m/z 224.35 (M^++1).

I_{14b}: White solid; Mp 107–109°C; 0.10 g (18%); ^{1}H NMR: δ 3.08 (t, 2H, J=7.7 Hz), 3.39–3.58 (m, 4H), 4.41 (t, 2H, J=7.9 Hz), 7.26–7.41 (m, 5H); ^{13}C NMR: δ 35.5, 35.6, 35.7, 64.8, 127.1, 129.0, 129.3, 139.9, 167.6; EI-MS: m/z 224.36 (M^++1).

References

Chandrappa, S.; Benaka Prasad, S. B.; Vinaya, K.; Ananda Kumar, C. S.; Thimmegowda, N. R.; Rangappa, K. S. Synthesis and in vitro antiproliferative activity against human cancer cell lines of novel 5-(4-methyl-benzylidene)-thiazolidine-2,4-diones. *Invest. New. Drugs.* **2008**, *26*, 437–444.

Ingo, S.; Olaf, M.; Michael, R. WO, 1*87863*, **2001,** 11–22.

Jan, B.; Barbara, O. K.; Maurin, J. K.; Andrzej, O. Synthesis and anti-HIV studies of 2- and 3-adamantyl-substituted thiazolidin-4-ones. *J. Med. Chem.* **2002**, *44*, 303–311.

Jean, L. B.; Laurent, T.; Jean, T. EP376819, 07-04. **1990**.

Kazuo, O.; Hideo, N.; Kouzo, I.; Hideo, N.; Hiromi, I.; Kunio, W. JP58041873, 03-11. **1983**.

Kazuo, S.; Hiromi, S.; Hiroyuki, K. N.; Oriaki, K.; Soji, M.; Junji, K.; Kiyoshi, K. JP11180966, 07-06. **1999**.

Kenso, S.; Miyuki, I. Synthesis of 1,3-thiazolidine-2-thione and (4R)-methoxyca-rbonyl-1,3-thiazolidine-2-thione using N, N'-thiocarbonyldiimida zole. *Heterocycles* **1984**, *22*, 2827–2828.

Kucukguzel, G.; Kocatepe, A.; Clercq, E. D.; Sahin, F.; Gulluce, M. Synthesis and biological activity of 4-thiazolidinones,

thiosemicarbazides derived from diflunisal hydrazide. *Eur. J. Med. Chem.* **2006**, *41*, 353–359.

Li, Y. X.; Wang, S. H.; Li, Z. M.; Su, N.; Zhao, W. G. Synthesis of novel 2-phenylsulfonylhydrazono-3-(2',3',4',6'-tetra-O-acetyl-beta-d-glucopyranosyl)thiazolidine-4-ones from thiosemicarbazide precursors. *Carbohyd. Res.* **2006**, *341*, 2867.

Masae, T.; Keiichi, I.; Nishibe, T. WO03031414, 04-17. **2003**.

Moulard, T.; Lagorce, J. F.; Thomas, J. C.; Raby, C. Biological evaluation of compounds with -NCS- group or derived from thiazole and imidazole. Activity on prostaglandin synthetase complex. *J. Pharmacy. Pharmacol.* **1993**, *45*, 731–735.

Owen, T. C. Amino-alkanethiols from amino-alcohols via aminoalkyl sulphates and thiazolidinethiones. *J. Chem. Soc.* **1967**, *15*, 1373–1376.

Rachinskii, F. Y.; Slavacheskaya, N. M.; Ioffe, D. V. 2-Mercaptoethylamine and its N-substituted derivatives. *Zhurnal Obshchei Khimii.* **1958**, *28*, 2998–3004.

Sugita, S. JP59001473, 01-06. **1984**.

Taguchi, T.; Kiyoshima, Y.; Komori, O.; Mori, M. Improvement in syntheses of mercaptans via thiol esters. *Tetrahedron Lett.* **1969**, *41*, 3631–3634.

Tenorio, R.P.; Carvalho, C. S.; Pessanha, C. S.; de Lima, J. G.; de Faria, A. R.; Alves, A. J.; de Melo, E. J. T.; Goes, A. J. S. Synthesis of thiosemicarbazone and 4-thiazolidinone derivatives and their in vitro anti-toxoplasma gondii activity. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2575.

Tsymbal, M. M.; Filippova, N. I.; Burmistrov, S. I.; Tito-, Ye. A.; Seraya, V. I. Antismut activity of some chemical compounds. *Khimiya v Sel'skom Khozyaystve*. **1968**, *6*, 350–351.