A Study of the Conjugate Addition of Thionucleophiles to 2(5*H*)-Furanones

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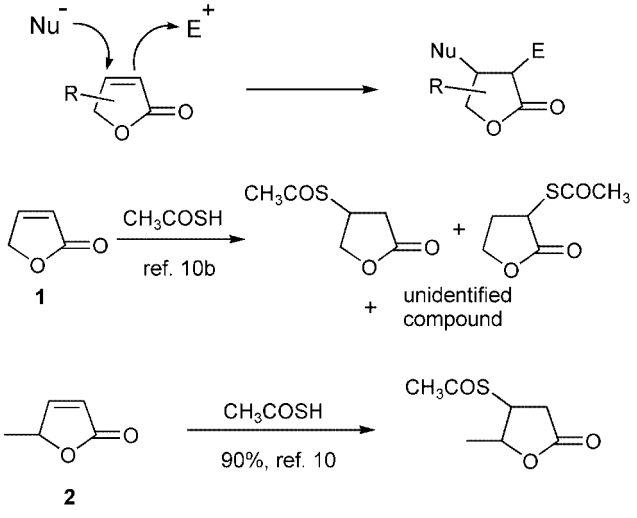
Several new 4-thio-4,5-dihydro-2(3*H*)-furanones were prepared by the conjugate addition reactions of different thioacids, dithioacids, xanthates and dithiocarbamates to 2(5*H*)-furanones. When 5-methyl-2(5*H*)-furanone was used as the electrophilic substrate, the reaction was diastereoselective affording exclusively the *cis*-α,β-disubstituted butanolides. Some adducts were selectively hydrolysed to deliver a free thiol functionality.

Introduction

Butenolides and butanolides are ubiquitous in nature as structural subunits in a wide variety of natural products, many of which are bioactive.[1] There are also a wide variety of pharmacologically active non-natural products bearing these heterocycles as the active site.[2] Furthermore, these lactones have been extensively used as building blocks in synthesis.[3] On the other hand, the conjugate addition of nucleophiles to α,β-unsaturated carbonyl groups is a very versatile synthetic reaction that successfully yields new carbon−carbon or carbon−heteroatom bonds.[4] Consequently, it is not surprising that α,β-unsaturated butyrolactones have been frequently used as Michael acceptors, and other butyrolactones as Michael donors. In particular, the strategy of a sequential Michael addition of different nucleophiles to an α,β-butenolide, followed by trapping of the resulting lactone enolate with various electrophiles, has been widely employed in the synthesis of both racemic and non-racemic compounds (Scheme 1). Most of these examples involve the use of a carbanion as the nucleophile[5] and a proton or an alkyl halide as the electrophile. This tandem addition has been extensively utilized for the preparation of a large number of lignans.[5a,5e−5g,5o,5r,5t−5w] Nevertheless, the number of cases dealing with nitrogen[5n,6] or oxygen[5d,5j,5n,7] nucleophiles is very scarce and there is only one example using a phosphorous[8] or a silicon[9] ion.

The nucleophilic addition of the thiol group has a prominent role in several biological reactions. To the best of our knowledge, the first example of the conjugate addition of a sulfur nucleophile to an α,β-unsaturated butyrolactone was reported by Fuchs[10] in the late 1960s. This author studied



Scheme 1

the addition of thioacetic acid to 2(5*H*)-furanone (**1**) and 5-methyl-2(5*H*)-furanone, (**2**; Scheme 1). While the latter reaction afforded a 90% yield of the expected Michael adducts, the former led to a mixture of 4- and 3-acetylthio-substituted furanones, along with an unidentified compound. The other described examples of sulfur nucleophile additions to α,β-butenolides deal with aliphatic or aromatic thiols.[5n,11] Considering these precedents, we decided to investigate the conjugate addition of various sulfur nucleophiles derived from carboxylic and carbonic acids to the α,β-unsaturated lactones **1** and **2** (Scheme 2).

The use of such thionucleophiles could provide the possibility of selective hydrolysis of the sulfur function to deliver a free thiol functionality at the β-position of the lactone. Herein, we report the successful isolation of several new 4,5-dihydro-2(3*H*)-furanones bearing a sulfur atom at the 4-position.

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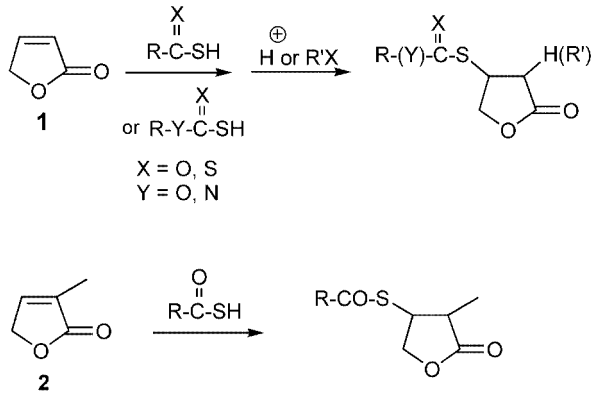
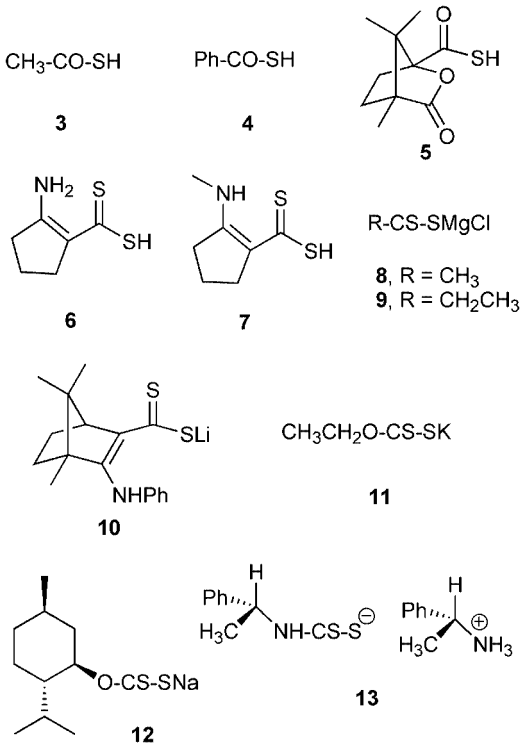


Scheme 2



Scheme 3

Results and Discussion

The nucleophiles selected for this study included achiral and enantiopure thioacids, dithioacids, xanthates, and dithiocarbamic acids (Scheme 3). Thioacetic acid (**3**) and thiobenzoic acid (**4**) are commercially available, and enantiopure thioacid **5** has already been described by our group.[12] Dithioacids **6** and **7** were synthesized following previously described procedures,[13] while salts **8** and **9** were prepared in situ by reaction of the Grignard reagent precursors with carbon disulfide.[14] The unknown salt **10** was obtained by reaction of the imine derived from camphor and aniline[15] with LDA and carbon disulfide and it was also allowed to react in situ due to its instability. Ethyl xanthate (**11**),[16] menthyl xanthate (**12**),[17] and dithiocarbamate salt **13**[18] were prepared following literature methods. Table 1 summarises the results of the reactions between these nucleophiles and lactones **1** and **2**.

The initial reactions, performed with thioacids **3** and **4** and lactone **1**, were run in dichloromethane solution at room temperature in the presence of a catalytic amount of triethylamine (TEA). These experiments furnished excellent yields of the expected adducts **14**,[10] as a colourless oil, and **15**, isolated as a white solid (Scheme 4; Table 1, Entries 1 and 2). All the proton absorptions of compound **15** could be assigned by NOE experiments, which allowed us to identify the signals of all the other products by comparison.

Attempts to trap the enolate formed by β-addition of the thiocarboxylates to **1** with methyl iodide were unsuccessful, but the α-methyl derivatives could be prepared by conjugate addition of **3** and **4** to butenolide **2**, although more rigorous experimental conditions were required, namely 50 °C without solvent (Table 1, Entries 3 and 4). Both compounds **16**, an oil, and **17**, a solid, were isolated in 95% and 90% yield, respectively, as a unique diastereoisomer. Their *cis* relative stereochemistry was secured by an NOE experiment on **17**: presaturation of the signal at δ = 3.04 ppm (3-H) caused a 6.5% NOE on the methyl group and an 8% NOE on 4-H (δ = 4.59 ppm), while irradiation of the methyl group had no effect on 4-H. This completely diastereoselective protonation process discloses a new access to *cis* α,β-disubstituted butanolides, since most previous syntheses by conjugate additions to α,β-butenolides afforded exclusively the *trans*-isomers.[5a,5e,5g,5h,5k,5o–5r]

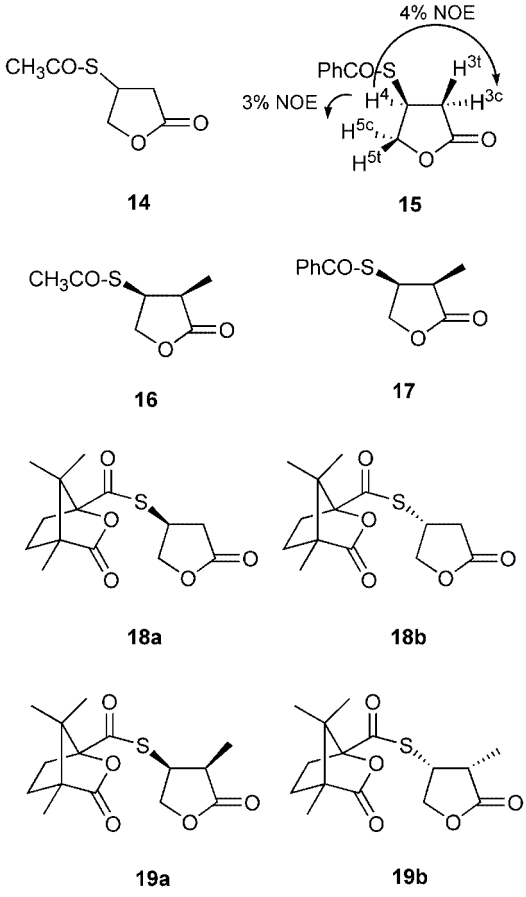
The reactions between the enantiopure thioacid **5** and the lactones **1** and **2** furnished the new solid compounds **18** and **19** in 92% and 72% yield, respectively (Table 1, Entries 5 and 6). Unfortunately, in both cases a roughly 1:1 mixture of two diastereoisomers was formed, product **19** consisting only of both *cis*-disubstituted stereoisomers. Repeated crystallization from ethyl acetate/hexane afforded enriched fractions (ca. 19:1) of each stereoisomer of **18**, albeit in small quantities. In the case of **19** all our efforts to obtain a pure stereoisomer were unsuccessful.

Next, we focused our attention on the dithioacids. The reactions of nucleophiles **6** and **7** with butenolide **1** afforded 80% and 87% yield of the new compounds **20** and **21** as yellow solids (Scheme 5; Table 1, Entries 7 and 8), while the addition of salts **8** and **9** to lactone **1** in THF solution at 0 °C led to the isolation of the new crystalline compounds **22** and **23** in 64% and 50% yield, respectively (Table 1, Entries 9 and 10). Due to its instability, salt **10** was allowed to react in situ with the butenolide **1** in THF at room temperature in the presence of acetic acid, providing compound **24**, a yellow solid, in 57% yield, once again without any diastereoselectivity (Table 1, Entry 11). The yields of the reactions with dithioacids are somewhat lower than those previously reported for the reactions with thioacids.

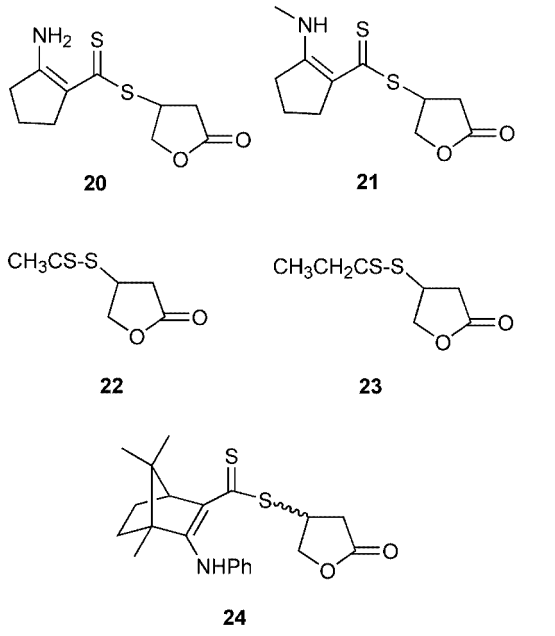
When the butenolide **1** was treated with the xanthate **11** in chloroform at room temperature in the presence of two equivalents of acetic acid, compound **25** was isolated as an oil in 35% yield (Scheme 6; Table 1, Entry 12). The modest

Table 1. Conjugate addition reactions of different thioacids, dithioacids, xanthates, and dithiocarbamates to 2(5*H*)-furanones

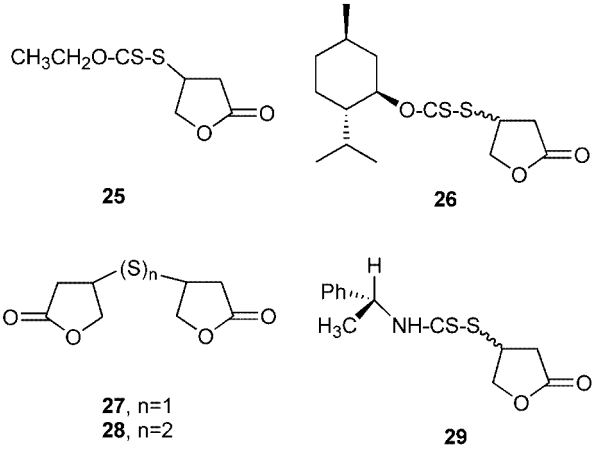
Entry	Electrophile	Nucleophile	Conditions	Product (yield, %)
1	**1**	**3**	CH_2Cl_2, room temp., TEA	**14** (91)
2	**1**	**4**	CH_2Cl_2, room temp., TEA	**15** (90)
3	**2**	**3**	neat, 50 °C, TEA	**16** (95)
4	**2**	**4**	neat, 50 °C, TEA	**17** (90)
5	**1**	**5**	CH_2Cl_2, room temp., TEA	**18** (92)
6	**2**	**5**	neat, 50 °C, TEA	**19** (72)
7	**1**	**6**	CH_2Cl_2, room temp., TEA	**20** (80)
8	**1**	**7**	CH_2Cl_2, room temp., TEA	**21** (87)
9	**1**	**8**	THF, 0 °C	**22** (64)
10	**1**	**9**	THF, 0 °C	**23** (50)
11	**1**	**10**	THF, room temp., AcOH	**24** (57)
12	**1**	**11**	$CHCl_3$, room temp., AcOH	**25** (35)
13	**1**	**12**	$CHCl_3$, room temp., AcOH	**26** (18)
14	**1**	**13**	$CHCl_3$, room temp., AcOH	**29** (50)



Scheme 4



Scheme 5



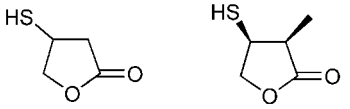
Scheme 6

yield of this addition reaction was attributed to the low stability of the starting xanthate. From the reaction of **1** with the enantiopure xanthate **12**, the conjugate addition product **26** was isolated in 18% yield (Table 1, Entry 13), once again as a roughly 1:1 diastereoisomeric mixture, along with several decomposition by-products such as menthol, the thioether **27**[19] and the disulfide **28**.[20]

In view of the lack of diastereoselectivity observed for all the above chiral sulfur donors, a last attempt was carried

out using the known enantiopure dithiocarbamate **13**[18] as the nucleophile. The addition reaction of **13** to **1** did not proceed in the absence of a proton source and various trials in different solvents furnished thiourea as the only isolable product. However, when the reaction was performed in the presence of one equivalent of acetic acid in chloroform solution at room temperature, a roughly 1:1 diastereoisomeric mixture of the new compound **29** was isolated as a solid in 50% yield (Table 1, Entry 14). Thiourea and the dimeric compounds **27** and **28** were also identified as by-products. All attempts to separate the diastereoisomers of **29** failed.

Having prepared thioesters **14** and **16** with excellent yields, we explored the selective hydrolysis of this function. Treatment of **14** with methanol, in either an acidic or basic medium, produced the hydrolysis of both the thioester and the lactone functional groups. Reaction of **14** with *p*-toluidine[10b] gave the known thiol **30**[10b] in 78% yield, while **16** afforded the new compound **31** in 75% yield (Scheme 7).



30 **31**

Scheme 7

Conclusion

In summary, several new 4-thio-4,5-dihydro-2(3*H*)-furanones derived from the nucleophilic addition of different sulfur functionalities to α,β-butenolide **1** have been prepared. The reactions with thioacids proceed with excellent yields and some thioesters have been selectively hydrolysed to the corresponding thiols. In general, dithioacids, xanthates and dithiocarbamates give lower yields and less-stable addition products. The addition of thioacids to the α,β-unsaturated lactone **2** provides a new access to *cis*-α,β-disubstituted butanolides. None of the chiral analogues of the sulfur nucleophiles under study provided significant diastereoselectivity in the formation of the new stereogenic centre at C-4.

Experimental Section

General Remarks: The reaction mixtures were stirred magnetically. The organic extracts were dried with anhydrous sodium sulfate. Reaction solutions were concentrated using a rotary evaporator at 5−10 Torr. Flash chromatography was performed using Merck silica gel (230−400 mesh). Infrared spectra were recorded with a Nicolet 5 ZDX spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded with Bruker AC-250-WB or AM-400-WB instruments at 250 or 400 MHz and 62.5 or 100 MHz, respectively, in $CDCl_3$ solutions. Mass spectra were performed with a Hewlett−Packard 5985B instrument at 70 eV; only peaks with intensities higher than 20% are reported, unless they belong to the molecular ions or to other significant fragments. The butenolide **1** is commercially available or can be easily prepared following the procedure described by Price.[21] Lactone **2** was obtained by isomerization of 4,5-dihydro-3-methylene-2(3*H*)-furanone using $RhCl_3 \cdot 3\ H_2O$.[22]

4-Acetylthio-4,5-dihydro-2(3*H*)-furanone (14): A solution of **1** (765 μL, 10.8 mmol) in CH_2Cl_2 (9 mL) was treated with thioacetic acid (767 μL, 10.8 mmol) and two drops of a dilute solution of triethylamine in CH_2Cl_2. The mixture was stirred at room temperature for 21 h, washed with water (3 × 5 mL) and concentrated to yield an oil (1.7 g), which was purified by flash chromatography (hexane/ethyl acetate, 2:1) to afford 1.60 g (9.9 mmol, 91% yield) of **14**. An analytical sample was obtained by distillation, b.p. 124−126 °C/0.07 Torr. IR (film): $\tilde{\nu}$ = 2966, 1785, 1693, 1166, 1131, 1018 cm^{-1}. ^{1}H NMR (400 MHz): δ = 4.67 (dd, $J_{5,5}$ = 9.8, $J_{5,4}$ = 6.7 Hz, 1 H, 5-H), 4.22 (m, 1 H, 4-H), 4.15 (dd, $J_{5,5}$ = 9.8, $J_{5,4}$ = 5.5 Hz, 1 H, 5-H), 2.95 (dd, $J_{3,3}$ = 17.7, $J_{3,4}$ = 8.5 Hz, 1 H, 3-H), 2.47 (dd, $J_{3,3}$ = 17.7, $J_{3,4}$ = 6.4 Hz, 1 H, 3-H), 2.34 (s, 3 H, CH_3) ppm. ^{13}C NMR (62.5 MHz): δ = 194.1 (COS), 174.3 (CO), 72.7 (C-5), 37.2 (C-4), 33.7 (C-3), 30.2 (CH_3) ppm. MS: *m*/*z* (%) = 160 (1) [M$^+$], 43 (100). $C_6H_8O_3S$ (160.19): calcd. C 44.99, H 5.03, S 20.02; found C 44.91, H 5.12, S 19.94.

4-Benzoylthio-4,5-dihydro-2(3*H*)-furanone (15): A solution of **1** (765 μL, 10.8 mmol) in CH_2Cl_2 (9 mL) was treated with thiobenzoic acid (1.2 mL, 10.8 mmol) and two drops of a dilute solution of triethylamine in CH_2Cl_2. The mixture was stirred at room temperature for 21 h, washed with water (3 × 5 mL) and concentrated to yield an oil (2.6 g), which was purified by flash chromatography (hexane/ethyl acetate, 2:1) to afford 2.20 g (9.8 mmol, 90% yield) of **15** as a solid, m.p. 67−69 °C (ethyl acetate/pentane). IR (KBr): $\tilde{\nu}$ = 2994, 2931, 1778, 1658, 1215, 1166, 913, 688 cm^{-1}. ^{1}H NMR (400 MHz): δ = 7.88 (d, *J* = 7.3 Hz, 2 H, 2 Ph), 7.60 (t, *J* = 7.3 Hz, 1 H, Ph), 7.45 (t, *J* = 7.3 Hz, 2 H, 2 Ph), 4.77 (dd, $J_{5,5}$ = 9.8, $J_{5,4}$ = 6.7 Hz, 1 H, 5-H), 4.40 (m, 1 H, 4-H), 4.26 (dd, $J_{5,5}$ = 9.8, $J_{5,4}$ = 5.2 Hz, 1 H, 5-H), 3.05 (dd, $J_{3,3}$ = 18.0, $J_{3,4}$ = 8.8 Hz, 1 H, 3-H), 2.59 (dd, $J_{3,3}$ = 18.0, $J_{3,4}$ = 6.4 Hz, 1 H, 3-H) ppm. ^{13}C NMR (62.5 MHz): δ = 190.1 (COS), 174.3 (CO), 135.8/133.8/128.6/127.0 (Ph), 72.9 (C-5), 37.2 (C-4), 33.7 (C-3) ppm. MS: *m*/*z* (%) = 222 (1) [M$^+$], 105 (100), 77 (35). $C_{11}H_{10}O_3S$ (222.26): calcd. C 59.44, H 4.53, S 14.43; found C 59.49, H 4.51, S 14.36.

***cis*-4-Acetylthio-3-methyl-4,5-dihydro-2(3*H*)-furanone (16):** The butenolide **2** (200 mg, 2.04 mmol) was treated with thioacetic acid (217 μL, 3.06 mmol) and two drops of a dilute solution of triethylamine in CH_2Cl_2. The mixture was stirred at 50 °C for 3 days, dissolved in CH_2Cl_2 (4 mL), washed with water (4 mL) and concentrated to yield an oil (420 mg), which was purified by flash chromatography (hexane/ethyl acetate, 3:1) to afford 368 mg (2.12 mmol, 95% yield) of **16**. An analytical sample was obtained by distillation, b.p. 99−101 °C/0.01 Torr. IR (film): $\tilde{\nu}$ = 2980, 2924, 2860, 1778, 1693, 1166, 1131, 1039 cm^{-1}. ^{1}H NMR (250 MHz): δ = 4.55 (dd, $J_{5,5}$ = 10.2, $J_{5,4}$ = 5.8 Hz, 1 H, 5-H), 4.36 (m, 1 H, 4-H), 4.15 (dd, $J_{5,5}$ = 10.2, $J_{5,4}$ = 3.3 Hz, 1 H, 5-H), 2.93 (quint, $J_{3,Me}$ = $J_{3,4}$ = 7.3 Hz, 1 H, 3-H), 2.34 (s, 3 H, CH_3CO), 1.18 (d, $J_{Me,3}$ = 7.3 Hz, 3 H, CH_3) ppm. ^{13}C NMR (62.5 MHz): δ = 193.9 (COS), 177.2 (COO), 71.7 (C-5), 44.2 (C-4), 37.2 (C-3), 30.7 (*C*H$_3$CO), 11.3 (CH_3) ppm. MS: *m*/*z* (%) = 174 (0.4) [M$^+$], 132 (7), 114 (9), 43 (100). $C_7H_{10}O_3S$ (174.22): calcd. C 48.26; H 5.78, S 18.41; found C 48.01, H 5.79, S 18.20.

***cis*-4-Benzoylthio-3-methyl-4,5-dihydro-2(3*H*)-furanone (17):** The butenolide **2** (200 mg, 2.04 mmol) was treated with thiobenzoic acid

(330 μL, 3.06 mmol) and two drops of a dilute solution of triethylamine in CH_2Cl_2. The mixture was stirred at 50 °C for 2 days, dissolved in CH_2Cl_2 (4 mL), washed with water (4 mL) and concentrated to yield a solid material (530 mg), which was purified by flash chromatography (hexane/diethyl ether, 1:1) to afford 432 mg (1.83 mmol, 90% yield) of **17** as a solid, m.p. 54−55 °C (ethyl acetate/hexane). IR (KBr): $\tilde{\nu}$ = 3140, 3026, 2994, 2868, 1764, 1679, 1208, 1173, 997, 899, 688 cm^{-1}. ^1H NMR (400 MHz): δ = 7.92 (d, J = 7.3 Hz, 2 H, 2 Ph), 7.58 (t, J = 7.3 Hz, 1 H, Ph), 7.44 (t, J = 7.3 Hz, 2 H, 2 Ph), 4.66 (dd, $J_{5,5}$ = 9.8, $J_{5,4}$ = 5.5 Hz, 1 H, 5-H), 4.59 (m, 1 H, 4-H), 4.28 (dd, $J_{5,5}$ = 9.8, $J_{5,4}$ = 3.0 Hz, 1 H, 5-H), 3.04 (quint, $J_{3,Me}$ = $J_{3,4}$ = 7.3 Hz, 1 H, 3-H), 1.28 (d, $J_{Me,3}$ = 7.3 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz): δ = 190.0 (COS), 177.3 (COO), 136.1/134.0/128.7/127.3 (Ph), 72.0 (C-5), 44.3 (C-4), 37.5 (C-3), 11.5 (CH_3) ppm. MS: m/z (%) = 236 (1) [M^+], 105 (100), 77 (41). $C_{12}H_{12}O_3S$ (236.29): calcd. C 61.00, H 5.12, S 13.57; found C 61.11, H 5.10, S 13.50.

(4*RS*)-{[(1*S*,4*R*)-4,7,7-Trimethyl-3-oxo-2-oxabicyclo[2.2.1]hept-1-yl)carbonylthio}-4,5-dihydro-2(3*H*)-furanone (18a and 18b): A solution of **1** (198 μL, 2.8 mmol) in CH_2Cl_2 (6 mL) was treated with thioacid **5** (600 mg, 2.8 mmol) and two drops of a dilute solution of triethylamine in CH_2Cl_2. The mixture was stirred at room temperature for 5 days, washed with water (6 mL) and concentrated to yield a solid (1.8 g), which was purified by flash chromatography (hexane/ethyl acetate, 2:1) to give 767 mg (2.6 mmol, 92% yield) of a 1:1 mixture of diastereoisomers **18a** and **18b** as a solid. Pure samples of each diastereoisomer were obtained by means of successive crystallizations in ethyl acetate/hexane. **18a/18b:** (less-soluble diastereoisomer). M.p. 185−187 °C. ^1H NMR (250 MHz): δ = 4.72 (dd, $J_{5,5}$ = 9.5, $J_{5,4}$ = 7.3 Hz, 1 H, 5-H), 4.20 (m, 2 H, 5-H, 4-H), 3.00 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 8.8 Hz, 1 H, 3-H), 2.48 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 6.6 Hz, 1 H, 3-H), 2.43−2.32 (m, 1 H, 6′-H), 2.01−1.82 (m, 2 H, 5′-H, 6′-H), 1.72−1.60 (m, 1 H, 5′-H), 1.06 (s, 3 H, CH_3), 0.98 (s, 3 H, CH_3), 0.89 (s, 3 H, CH_3) ppm. ^{13}C NMR (62.5 MHz): δ = 195.9 (COS), 177.1 (C-3′), 174.1 (C-2), 95.6 (C-1′), 72.4 (C-5), 55.4 (C-7′), 54.8 (C-4′), 36.4 (C-4), 33.7 (C-3), 31.0 (C-5′), 28.6 (C-6′), 16.6 (CH_3), 16.3 (CH_3), 9.5 (CH_3) ppm. $[\alpha]_D^{20}$ = −89 (c = 1.1, chloroform). **18a/18b:** (more-soluble diastereoisomer). M.p. 154−155 °C. ^1H NMR (250 MHz): δ = 4.71 (dd, $J_{5,5}$ = 9.5, $J_{5,4}$ = 7.3 Hz, 1 H, 5-H), 4.23 (m, 1 H, 4-H), 4.13 (dd, $J_{5,5}$ = 9.5, $J_{5,4}$ = 5.8 Hz, 1 H, 5-H), 3.00 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 8.8 Hz, 1 H, 3-H), 2.51 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 6.6 Hz, 1 H, 3-H), 2.43−2.32 (m, 1 H, 6′-H), 2.01−1.82 (m, 2 H, 5′-H, 6′-H), 1.72−1.60 (m, 1 H, 5′-H), 1.06 (s, 3 H, CH_3), 0.98 (s, 3 H, CH_3), 0.89 (s, 3 H, CH_3) ppm. ^{13}C NMR (62.5 MHz): δ = 195.9 (COS), 177.1 (C-3′), 174.1 (C-2), 95.6 (C-1′), 72.5 (C-5), 55.4 (C-7′), 54.8 (C-4′), 36.5 (C-4), 33.5 (C-3), 30.9 (C-5′), 28.6 (C-6′), 16.6 (CH_3), 16.3 (CH_3), 9.5 (CH_3) ppm. $[\alpha]_D^{20}$ = −22 (c = 0.9, chloroform). **Mixture of 18a and 18b:** IR (KBr): $\tilde{\nu}$ = 2973, 1785, 1764, 1665, 1187, 1018, 850 cm^{-1}. MS: m/z (%) = 298 (5) [M^+], 181 (21), 125 (77), 97 (53), 83 (100), 55 (33), 41 (27). $C_{14}H_{18}O_5S$ (298.35): calcd. C 56.36, H 6.08, S 10.75; found C 56.17, H 6.09, S 10.78.

***cis*-3-Methyl-4-{[(1*S*,4*R*)-4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]-hept-1-yl]carbonylthio}-4,5-dihydro-2(3*H*)-furanone (19a and 19b):** A mixture of the butenolide **2** (345 mg, 3.5 mmol), the thioacid **5** (899 mg, 4.2 mmol) and two drops of a dilute solution of triethylamine in CH_2Cl_2 was stirred at 50 °C for 6 days. The resultant mixture was dissolved in CH_2Cl_2 (5 mL), washed with water (5 mL) and concentrated to yield a solid residue (1.04 g), which was purified by flash chromatography (hexane/ethyl acetate, 2:1) to afford 787 mg (2.5 mmol, 72% yield) of a 1:1 mixture of diastereoisomers **19a** and **19b** as a solid, m.p. 150−151 °C. IR (KBr): $\tilde{\nu}$ = 2973, 2920, 2868, 1785, 1665, 1159, 1082, 1018, 842 cm^{-1}. ^1H NMR (250 MHz): δ = 4.63 (dd, $J_{5,5}$ = 10.2, $J_{5,4}$ = 6.1 Hz) and 4.62 (dd, $J_{5,5}$ = 10.2, $J_{5,4}$ = 6.1 Hz) (1 H, 5-H), 4.42 (m, 1 H, 4-H), 4.20 (dd, $J_{5,5}$ = 10.2, $J_{5,4}$ = 3.7 Hz) and 4.14 (dd, $J_{5,5}$ = 10.2, $J_{5,4}$ = 3.7 Hz) (1 H, 5-H), 3.00 (quint, $J_{3,Me}$ = $J_{3,4}$ = 7.3 Hz, 1 H, 3-H), 2.46−2.33 (m, 1 H, 6′-H), 2.03−1.86 (m, 2 H, 5′-H, 6′-H), 1.76−1.65 (m, 1 H, 5′-H), 1.25 (d, $J_{Me,3}$ = 7.3 Hz) and 1.24 (d, $J_{Me,3}$ = 7.3 Hz) (3 H, CH_3), 1.10 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 0.94 (d, J = 3.6 Hz, 3 H, CH_3) ppm. ^{13}C NMR (62.5 MHz): δ = 195.4 and 195.3 (COS), 177.1 (C-3′), 176.9 (C-2), 95.8 and 95.6 (C-1′), 71.6 and 71.1 (C-5), 55.4 and 55.3 (C-7′), 54.7 and 54.6 (C-4′), 43.3 and 43.2 (C-4), 37.1 and 36.9 (C-3), 31.03 and 30.96 (C-5′), 28.6 (C-6′), 16.6 (CH_3), 16.5 (CH_3), 11.4 and 11.3 (CH_3), 9.5 and 9.4 (CH_3) ppm. MS: m/z (%) = 312 (3) [M^+], 125 (63), 97 (55), 83 (100), 67 (21), 55 (61), 43 (26), 41 (60). $C_{15}H_{20}O_5S$ (312.38): calcd. C 57.67, H 6.45, S 10.26; found C 57.68, H 6.49, S 10.36.

4-[(2-Amino-1-cyclopenten-1-yl)(thiocarbonyl)thio]-4,5-dihydro-2(3*H*)-furanone (20): A solution of **1** (191 μL, 2.7 mmol) in CH_2Cl_2 (5 mL) was treated with dithioacid **6** (472 mg, 3.0 mmol) and two drops of a dilute solution of triethylamine in CH_2Cl_2. The mixture was stirred at room temperature for 2 days, then washed with water (3 × 5 mL) and concentrated to yield a solid residue (815 mg), which was purified by flash chromatography (hexane/ethyl acetate, 3:1) to afford 521 mg (2.1 mmol, 80% yield) of **20** as a yellow solid, m.p. 100−101 °C (ethyl acetate/hexane). IR (KBr): $\tilde{\nu}$ = 3400−3000, 2959, 2889, 2824, 1778, 1609, 1468, 1278, 1173, 1018, 955, 793 cm^{-1}. ^1H NMR (250 MHz): δ = 5.98 (br. s, 2 H, NH_2), 4.77 (dd, $J_{5,5}$ = 9.5, $J_{5,4}$ = 7.3 Hz, 1 H, 5-H), 4.67 (m, 1 H, 4-H), 4.27 (dd, $J_{5,5}$ = 9.5, $J_{5,4}$ = 5.1 Hz, 1 H, 5-H), 3.03 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 8.8 Hz, 1 H, 3-H), 2.71 (t, J = 7.3 Hz, 2 H, 2 × 3′-H/2 × 5′-H), 2.61 (t, J = 7.3 Hz, 2 H, 2 × 3′-H/2 × 5′-H), 2.55 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 5.8 Hz, 1 H, 3-H), 1.83 (m, 2 H, 2 × 4′-H) ppm. ^{13}C NMR (62.5 MHz): δ = 197.7 (CS), 175.5 (CO), 169.4 (C-2′), 118.1 (C-1′), 73.4 (C-5), 40.0 (C-4), 36.3/33.3/32.5 (C-3/C-3′/C-5′), 20.4 (C-4′) ppm. MS: m/z (%) = 243 (8) [M^+], 159 (32), 126 (100). $C_{10}H_{13}NO_2S_2$ (243.35): calcd. C 49.36, H 5.38, N 5.76, S 26.35; found C 49.40, H 5.40, N 5.70, S 26.33.

4-{[2-(*N*-Methylamino)-1-cyclopenten-1-yl](thiocarbonyl)thio}-4,5-dihydro-2(3*H*)-furanone (21): A solution of **1** (82 μL, 1.2 mmol) in CH_2Cl_2 (3 mL) was treated with dithioacid **7** (200 mg, 1.2 mmol) and two drops of a dilute solution of triethylamine in CH_2Cl_2. The mixture was stirred at room temperature for 7 h, washed with water (3 × 2 mL) and concentrated to yield a solid (369 mg), which was purified by flash chromatography (hexane/ethyl acetate, 2:1) to afford 260 mg (1.0 mmol, 87% yield) of **21** as a yellow solid, m.p. 122−124 °C (ethyl acetate/pentane). IR (KBr): $\tilde{\nu}$ = 2945, 2896, 1778, 1609, 1489, 1343, 1278, 1159 cm^{-1}. ^1H NMR (400 MHz): δ = 4.80 (dd, $J_{5,5}$ = 9.4, $J_{5,4}$ = 7.0 Hz, 1 H, 5-H), 4.72 (m, 1 H, 4-H), 4.29 (dd, $J_{5,5}$ = 9.4, $J_{5,4}$ = 4.6 Hz, 1 H, 5-H), 3.07 (d, $J_{Me,NH}$ = 3.7 Hz, 3 H, CH_3), 3.04 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 8.5 Hz, 1 H, 3-H), 2.72 (t, J = 7.9 Hz, 2 H, 2 × 3′-H/2 × 5′-H), 2.68 (t, J = 7.9 Hz, 2 H, 2 × 3′-H/2 × 5′-H), 2.58 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 6.1 Hz, 1 H, 3-H), 1.87 (quint, $J_{4',5'}$ = $J_{4',3'}$ = 7.9 Hz, 2 H, 2 × 4′-H) ppm. ^{13}C NMR (100 MHz): δ = 190.7 (CS), 175.3 (CO), 172.2 (C-2′), 118.6 (C-1′), 73.5 (C-5), 39.7 (C-4), 33.4/33.2/32.7/31.4 (C-3/C-3′/C-5′/CH_3), 20.3 (C-4′) ppm. MS: m/z (%) = 257 (20) [M^+], 242 (1), 173 (33), 171 (25), 140 (100). $C_{11}H_{15}NO_2S_2$ (257.37): calcd. C 51.33, H 5.87, N 5.44, S 24.92; found C 51.26, H 5.99, N 5.35, S 24.86.

4-Methyl(thiocarbonyl)thio-4,5-dihydro-2(3*H*)-furanone (22): A solution of carbon disulfide (123 mg, 1.62 mmol) was added to a solution of methylmagnesium chloride (0.81 mmol) in dry THF (2 mL) at 0 °C, and the mixture was warmed to room temperature.

After 4 h at room temperature, the red solution was treated with the butenolide **1** (68 mg, 0.81 mmol) and glacial acetic acid (46 μL, 0.81 mmol). The mixture was stirred at room temperature for 16 h, acidified with 1 M HCl solution to pH 2 and extracted with diethyl ether (3 × 5 mL). The organic phases were combined and concentrated to yield an oil (150 mg), which was purified by flash chromatography (hexane/ethyl acetate, 9:1) to afford 92 mg (0.52 mmol, 64% yield) of **22** as a solid, m.p. 30−31 °C (ethyl acetate/pentane). IR (KBr): $\tilde{\nu}$ = 2987, 2924, 2865, 1778, 1370, 1194, 1166, 1025, 864 cm^{-1}. ^1H NMR (400 MHz): δ = 4.75 (dd, $J_{5,5}$ = 9.8, $J_{5,4}$ = 7.0 Hz, 1 H, 5-H), 4.51 (m, 1 H, 4-H), 4.27 (dd, $J_{5,5}$ = 9.8, $J_{5,4}$ = 4.5 Hz, 1 H, 5-H), 3.09 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 9.2 Hz, 1 H, 3-H), 2.81 (s, 3 H, CH_3), 2.55 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 5.5 Hz, 1 H, 3-H) ppm. ^{13}C NMR (100 MHz): δ = 223.6 (CS), 174.2 (CO), 71.9 (C-5), 43.9 (C-4), 38.8 (CH_3), 32.8 (C-3) ppm. MS: *m*/*z* (%) = 176 (19) [M^+], 92 (31), 85 (54), 59 (100). $C_6H_8O_2S_2$ (176.26): calcd. C 40.89, H 4.57, S 36.38; found C 40.90, H 4.53, S 36.37.

4-Ethyl(thiocarbonyl)thio-4,5-dihydro-2(3*H*)-furanone (23): A solution of carbon disulfide (344 μL, 5.71 mmol) was added to a 25% solution of ethylmagnesium chloride in THF (1.64 mL, 4.76 mmol) in dry THF (5 mL) at 0 °C, and the mixture was stirred for 10 min at the same temperature. The resulting red solution was then treated with a solution of butenolide **1** (337 μg, 4.76 mmol) in THF (1 mL). The mixture was stirred at 0 °C for 45 min, quenched with saturated NH_4Cl solution and extracted with diethyl ether (3 × 5 mL). The organic phases were combined and concentrated to yield an oil (716 mg), which was purified by flash chromatography (hexane/diethyl ether, 7:3) to afford 452 mg (2.38 mmol, 50% yield) of **23** as a red solid, m.p. 24−25 °C (ethyl acetate/pentane). IR (KBr): $\tilde{\nu}$ = 2973, 2931, 1778, 1159, 1025 cm^{-1}. ^1H NMR (400 MHz): δ = 4.67 (dd, $J_{5,5}$ = 10.4, $J_{5,4}$ = 6.7 Hz, 1 H, 5-H), 4.46 (m, 1 H, 4-H), 4.16 (dd, $J_{5,5}$ = 10.4, $J_{5,4}$ = 4.3 Hz, 1 H, 5-H), 3.02 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 9.1 Hz, 1 H, 3-H), 2.89 (q, J = 7.3 Hz, 2 H, CH_2), 2.47 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 5.2 Hz, 1 H, 3-H) 1.25 (t, J = 7.3 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz): δ = 216.8 (CS), 174.2 (CO), 71.7 (C-5), 44.4/43.0 (C-4/CH_2), 32.5 (C-3), 14.9 (CH_3) ppm. MS: *m*/*z* (%) = 190 (14) [M^+], 106 (42), 85 (59), 73 (100), 45 (31). $C_7H_{10}O_2S_2$ (190.28): calcd. C 44.18, H 5.30, S 33.70; found C 44.01, H 5.28, S 33.75.

(4*RS*)-4-{[(1*R*,4*S*)-2-*N*-Phenylamino-1,7,7-trimethylbicyclo-[2.2.1]hept-2-en-3-yl](thiocarbonyl)thio}-4,5-dihydro-2(3*H*)-furanone (24a and 24b): A solution of freshly prepared (1*R*,4*R*)-*N*-(1,7,7-trimethylbicyclo[2.2.1]hept-2-ylidene)phenylamine[15] (0.50 g, 2.20 mmol) in dry THF (2 mL) was added to a solution of LDA at 0 °C, prepared from a solution of diisopropylamine (370 μL, 2.64 mmol) in dry THF (5 mL) and 1.6 M *n*BuLi in hexane (1.65 mL, 2.64 mmol). The solution was stirred at 0 °C for 2 h and was then treated with carbon disulfide (265 μL, 4.40 mmol). The red mixture was warmed to room temperature, stirred for 4 h and treated with the butenolide **1** (156 μL, 2.20 mmol) and glacial acetic acid (126 μL, 2.20 mmol). The mixture was stirred at room temperature for 16 h, acidified with 1 M HCl solution to pH 2 and extracted with diethyl ether (3 × 5 mL). The organic phases were combined and concentrated to yield a red oil (614 mg), which was purified by flash chromatography (hexane/ethyl acetate, 9:1) to afford 486 mg (1.25 mmol, 57% yield) of a 1:1 mixture of both diastereoisomers of **24** as a yellow solid, m.p. 144−145 °C (ethyl acetate/pentane). IR (KBr): $\tilde{\nu}$ = 3124, 3087, 2959, 2898, 2765, 1778, 1581, 1496, 1342, 1270, 1173 cm^{-1}. ^1H NMR (400 MHz): δ = 7.35 (m, 3 H, 3 Ph), 7.22 (m, 2 H, 2 Ph), 4.85 (dd, $J_{5,5}$ = 9.5, $J_{5,4}$ = 7.0 Hz, 1 H, 5-H), 4.71 (m, 1 H, 4-H), 4.33 (dd, $J_{5,5}$ = 9.5, $J_{5,4}$ = 5.2 Hz) and 4.31 (dd, $J_{5,5}$ = 9.5, $J_{5,4}$ = 5.2 Hz) (1 H, 5-H), 3.05 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 9.1 Hz, 1 H, 3-H), 2.95 (d, $J_{4',5'}$ = 3.1 Hz, 1 H, 4′-H), 2.60 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 6.4 Hz) and 2.59 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 6.4 Hz) (1 H, 3-H), 1.95 (m, 1 H), 1.80−1.55 (m, 2 H), 1.50−1.30 (m, 2 H), 0.80 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 0.65 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz): δ = 187.4 (CS), 175.5/174.5 (CO/C-2′), 136.6/128.9/127.9/126.8 (Ph), 126.1 (C-3′), 73.9 and 73.7 (C-5), 57.8 (C-1′), 54.2 (C-7′), 51.4 (C-4′), 39.7 and 39.6 (C-4), 33.9 and 33.7 (C-3), 29.6 (C-6′), 25.8 (C-5′), 19.7 (CH_3), 18.9 (CH_3), 13.0 (CH_3) ppm. MS: *m*/*z* (%) = 387 (17) [M^+], 303 (28), 301 (59), 270 (100), 226 (22), 212 (20), 194 (41), 77 (47), 55 (24), 45 (33), 41 (38). $C_{21}H_{25}NO_2S_2$ (387.56): calcd. C 65.08, H 6.50, N 3.61, S 16.55; found C 65.10, H 6.49, N 3.65, S 16.50.

4-Ethoxy(thiocarbonyl)thio-4,5-dihydro-2(3*H*)-furanone (25): A solution of the xanthate **11** (216 mg, 1.35 mmol) in $CHCl_3$ (2 mL) at room temperature was treated with the butenolide **1** (88 μL, 1.25 mmol) and glacial acetic acid (153 μL, 2.50 mmol). The mixture was stirred at room temperature for 4 days, acidified with 10% HCl solution to pH 2 and extracted with chloroform (3 × 5 mL). The organic phases were combined and concentrated to yield an oil (167 mg), which was purified by flash chromatography (hexane/ethyl acetate, 2:1) to afford 91 mg (0.44 mmol, 35% yield) of **25** as an oil. IR (film): $\tilde{\nu}$ = 2987, 1785, 1229, 1166, 1053 cm^{-1}. ^1H NMR (400 MHz): δ = 4.75 (dd, $J_{5,5}$ = 9.8, $J_{5,4}$ = 7.0 Hz, 1 H, 5-H), 4.61 (q, J = 7.3 Hz, 2 H, CH_2), 4.41 (m, 1 H, 4-H), 4.30 (dd, $J_{5,5}$ = 9.8, $J_{5,4}$ = 5.2 Hz, 1 H, 5-H), 3.03 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 9.2 Hz, 1 H, 3-H), 2.56 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 6.1 Hz, 1 H, 3-H), 1.40 (t, J = 7.3 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz): δ = 211.4 (CS), 174.2 (CO), 72.5/70.6 (C-5/CH_2), 42.6 (C-4), 33.2 (C-3), 13.6 (CH_3) ppm. MS: *m*/*z* (%) = 206 (8) [M^+], 161 (1), 122 (45), 85 (100), 84 (21), 75 (72), 55 (36), 45 (25). $C_7H_{10}O_3S_2$ (206.28): calcd. C 40.76, H 4.89, S 31.09; found C 40.79, H 4.86, S 31.28.

(4*RS*)-4-[(1*R*,2*S*,5*R*)-Menthyloxy(thiocarbonyl)thio]-4,5-dihydro-2(3*H*)-furanone (26): A solution of xanthate **12** (1.0 g of 47% purity, 2.5 mmol) in $CHCl_3$ (3 mL) at room temperature was treated with butenolide **1** (88 μL, 1.25 mmol) and glacial acetic acid (142 μL, 2.50 mmol). The mixture was stirred at room temperature for 20 h, acidified with 1 M HCl solution to pH 2 and extracted with chloroform (3 × 5 mL). The organic phases were combined and concentrated to yield an oil (575 mg), which was purified by flash chromatography (CH_2Cl_2/diethyl ether, 9:1) affording the following fractions: i) 335 mg of a complex mixture; ii) 10 mg (0.05 mmol, 4% yield) of disulfide **28**[20] as a solid; and iii) 35 mg (0.13 mmol, 10% yield) of thioether **27**[19] as a solid. A second chromatography (hexane/CH_2Cl_2, 1:3) of the less-polar fraction afforded menthol (136 mg, 0.88 mmol), furanone **1** (23 mg, 0.27 mmol) and a 1:1 mixture of both diastereoisomers of **26** (73 mg, 0.23 mmol, 18% yield) as an oil. IR (film): $\tilde{\nu}$ = 2959, 2913, 2823, 1785, 1257, 1222, 1166, 1053 cm^{-1}. ^1H NMR (400 MHz): δ = 5.45 (m, 1 H, CHO), 4.77 (dd, $J_{5,5}$ = 9.5, $J_{5,4}$ = 7.6 Hz) and 4.76 (dd, $J_{5,5}$ = 9.7, $J_{5,4}$ = 7.9 Hz) (1 H, 5-H), 4.40 (m, 1 H, 4-H), 4.30 (dd, $J_{5,5}$ = 9.7, $J_{5,4}$ = 5.5 Hz, 1 H, 5-H), 3.02 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 8.5 Hz, 1 H, 3-H), 2.56 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 6.1 Hz) and 2.55 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 6.1 Hz) (1 H, 3-H), 2.15 (m, 1 H), 1.85−1.40 (m, 5 H), 1.15−0.95 (m, 2 H), 0.90 (m, 1 H), 0.90 (d, J = 7.3 Hz, 3 H, CH_3), 0.89 (d, J = 7.3 Hz, 3 H, CH_3), 0.78 (d, J = 7.3 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz): δ = 210.8 and 210.7 (CS), 174.2 (CO), 85.3 (C-1′), 72.54 and 72.50 (C-5), 47.1 (C-2′), 42.41 and 42.38 (C-4), 39.4 (C-6′), 33.9 (C-4′), 33.3 (C-3), 31.3 (C-5′), 26.5 (C-7′), 23.6 (C-3′), 21.8 (CH_3), 20.4 (CH_3), 16.8 (CH_3) ppm. MS: *m*/*z* (%) = 316 (1) [M^+], 138 (21), 123 (26), 96 (27), 95 (56), 82 (36), 81 (86), 71 (100), 69 (30), 67 (33), 57 (26), 55 (43), 43 (34), 41 (43). $C_{15}H_{24}O_3S_2$ (316.48): calcd. C 56.93, H 7.64, S 20.26; found C 56.73, H 7.62, S 20.40.

(4*RS*)-4-{[(*R*)-*N*-α-Methylbenzylamino](thiocarbonyl)thio}-4,5-dihydro-2(3*H*)-furanone (29): A solution of butenolide **1** (191 μL, 2.7 mmol) in $CHCl_3$ (6 mL) at room temperature was treated with dithiocarbamate **13** (1.06 g, 3.3 mmol) and glacial acetic acid (158 μL, 2.7 mmol). The mixture was stirred at room temperature for 3 days, acidified with 10% HCl solution to pH 2 and extracted with CH_2Cl_2 (3 × 6 mL). The organic phases were combined and concentrated to yield a solid (939 mg), which was purified by flash chromatography (hexane/ethyl acetate, 3:1) affording the following fractions: i) 565 mg of a complex mixture; ii) 98 mg (0.4 mmol, 15% yield) of disulfide **28**[20] as a solid; and iii) 102 mg (0.5 mmol, 19% yield) of thioether **27**[19] as a solid. A second chromatography (hexane/ethyl acetate, 4:1) of the less-polar fraction afforded 370 mg (1.30 mmol, 50% yield) of a 1:1 mixture of both diastereoisomers of **29** as a white solid and the thiourea derived from carbamate **13** (180 mg, 0.55 mmol). **29:** M.p. 122−123 °C (ethyl acetate/pentane). IR (film): $\tilde{\nu}$ = 3268, 2998, 2980, 2860, 1778, 1496, 1377, 1173, 1018, 969, 702 cm^{-1}. ^1H NMR (400 MHz): δ = 7.33−7.25 (m, 5 H, 5 Ph), 5.65 (m, 1 H, C*H*NH), 4.70 (m, 1 H, 5-H), 4.63 (m, 1 H, 4-H), 4.32 (dd, $J_{5,5}$ = 9.8, $J_{5,4}$ = 4.3 Hz) and 4.27 (dd, $J_{5,5}$ = 9.8, $J_{5,4}$ = 3.7 Hz) (1 H, 5-H), 3.01 (dd, $J_{3,3}$ = 18.6, $J_{3,4}$ = 9.1 Hz) and 2.98 (dd, $J_{3,3}$ = 18.6, $J_{3,4}$ = 8.5 Hz) (1 H, 3-H), 2.54 (dd, $J_{3,3}$ = 18.6, $J_{3,4}$ = 5.2 Hz) and 2.51 (dd, $J_{3,3}$ = 18.6, $J_{3,4}$ = 4.9 Hz) (1 H, 3-H), 1.55 (d, J = 6.7 Hz, 3 H, CH_3) ppm. ^{13}C NMR (62.5 MHz): δ = 193.1 (CS), 175.2 (CO), 141.0/128.8/127.9/126.4 (Ph), 73.6 and 73.4 (C-5), 56.1 (CH-NH), 43.6 (C-4), 33.6 (C-3), 21.0 (CH_3) ppm. MS: *m*/*z* (%) = 281 (1) [M^+], 197 (7), 163 (8), 105 (100). $C_{13}H_{15}NO_2S_2$ (281.39): calcd. C 55.49, H 5.37, N 4.98, S 22.79; found C 55.42, H 5.28, N 4.94, S 22.67.

4-Mercapto-4,5-dihydro-2(3*H*)-furanone (30):[10b] A solution of **14** (1.09 g, 6.8 mmol) in benzene (1 mL) was treated with *p*-toluidine (729 mg, 6.8 mmol). After stirring the solution under reflux for 1 h, a few drops of hexane were added and the mixture was cooled to 0 °C. The resulting precipitate was filtered and washed with benzene (2 mL). The filtrate was washed with 1 M HCl solution and concentrated under reduced pressure to yield an oil (1.6 g), which was purified by flash chromatography (hexane/ethyl acetate, 2:1) to afford 627 mg (5.3 mmol, 78% yield) of **30**. An analytical sample was obtained by distillation, b.p. 80 °C/0.2 Torr. IR (KBr): $\tilde{\nu}$ = 2910, 2558, 1778, 1166, 1011 cm^{-1}. ^1H NMR (400 MHz): δ = 4.48 (dd, $J_{5,5}$ = 9.5, $J_{5,4}$ = 6.6 Hz, 1 H, 5-H), 3.99 (dd, $J_{5,5}$ = 9.5, $J_{5,4}$ = 5.8 Hz, 1 H, 5-H), 3.62 (m, 1 H, 4-H), 2.84 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 8.0 Hz, 1 H, 3-H), 2.34 (dd, $J_{3,3}$ = 18.3, $J_{3,4}$ = 7.3 Hz, 1 H, 3-H), 1.89 (d, J = 7.3 Hz, 1 H, SH) ppm. ^{13}C NMR (100 MHz): δ = 174.7 (CO), 75.5 (C-5), 38.2 (C-4), 32.7 (C-3) ppm. MS: *m*/*z* (%) = 118 (48) [M^+], 100 (44), 60 (100), 59 (33), 58 (31), 45 (31), 43 (42). $C_4H_6O_2S$ (118.15): calcd. C 40.66, H 5.12, S 27.14; found C 41.07, H 5.27, S 27.24.

***cis*-4-Mercapto-3-methyl-4,5-dihydro-2(3*H*)-furanone (31):** A solution of **16** (1.18 g, 6.8 mmol) in benzene (1 mL) was treated with *p*-toluidine (729 mg, 6.8 mmol). After stirring the solution under reflux for 1 h, a few drops of hexane were added and the mixture was cooled to 0 °C. The resulting precipitate was filtered and washed with benzene (2 mL). The filtrate was washed with 1 M HCl solution and concentrated under reduced pressure to yield an oil (1.7 g), which was purified by flash chromatography (hexane/ethyl acetate, 2:1) to afford 627 mg (5.1 mmol, 75% yield) of **31**. An analytical sample was obtained by distillation, b.p. 25 °C/0.01 Torr. IR (KBr): $\tilde{\nu}$ = 2980, 2931, 2565, 1771, 1166, 1039 cm^{-1}. ^1H NMR (400 MHz): δ = 4.44 (dd, $J_{5,5}$ = 10.2, $J_{5,4}$ = 5.8 Hz, 1 H, 5-H), 4.09 (dd, $J_{5,5}$ = 10.2, $J_{5,4}$ = 3.3 Hz, 1 H, 5-H), 3.76 (m, 1 H, 4-H), 2.80 (q, J = 7.3 Hz, 1 H, 3-H), 1.53 (d, J = 7.3 Hz, 1 H, SH), 1.20 (d, $J_{Me,3}$ = 7.3 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz): δ = 177.3 (CO), 73.8 (C-5), 39.6/39.2 (C-3/C-4), 10.7 (CH_3) ppm. MS: *m*/*z* (%) = 132 (19) [M^+], 74 (90), 72 (80), 59 (36), 55 (100), 45 (53), 41 (91). $C_5H_8O_2S$ (132.18): calcd. C 45.43, H 6.10, S 24.26; found C 45.51, H 6.20, S 24.24.

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