Ring-Opening Reactions of Thiophene Derivatives by the Use of the Birch Reduction

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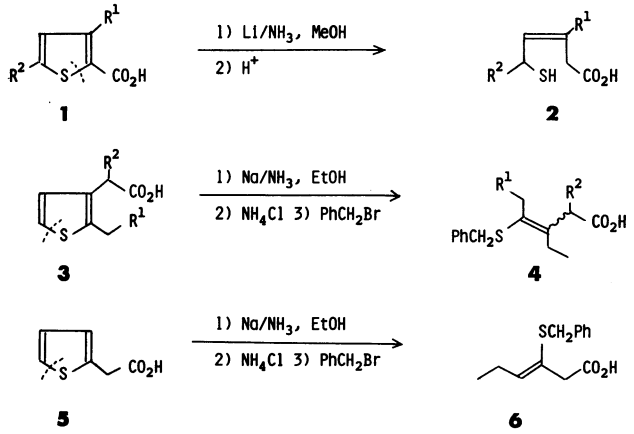
(Received December 14, 1985)

It was found that the Birch reduction of 2-(2-thienyl)alkanoic acid and subsequent alkylation with benzyl bromide resulted in the formation of 2-alkyl-3-benzylthio-3-hexenoic acid selectively. Further, the Birch reduction of a 2,3-dialkylthiophene and subsequent alkylation with benzyl bromide gave a tetrasubstituted olefin which was formed by a selective C-S bond fission between the 1 and 5 positions of the thiophene nuclei. In contrast to these results, the Birch reduction of 3-thiophenecarboxylic acid derivatives and subsequent benzylation gave 2-alkyl-4-benzylthio-3-butenoic acid which was formed by a C-S bond fission between the 1 and 2 positions of the thiophene nuclei.

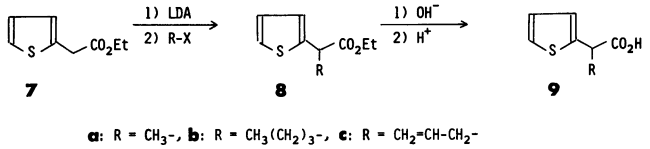
It is well-known that a Birch reduction of thiophene gives a mixture of dihydrothiophenes and ring-opening products, 2- and 3-butene-1-thiols.[1] In recent few years, several reports showed the formation of regioselective-ring-opening compounds by a Birch reduction of the thiophene derivatives. For example, Joullié et al. reported that the Birch reduction of 2-thiophenecarboxylic acid (**1**) gave (*Z*)-5-mercapto-3-pentenoic acid (**2**) which was formed by a reductive cleavage of the bond between the sulfur atom and C-2 of the thiophene nuclei.[2] However, we have reported that the product which was formed by the C-S bond fission between the 1 and 5 positions of the thiophene nuclei, 4-benzylthio-3-ethyl-3-alkenoic acid (**4**) or (*Z*)-3-benzylthio-3-hexenoic acid (**6**), was obtained by the Birch reduction of 2-(3-thienyl)alkanoic acid (**3**) or 2-thienylacetic acid (**5**) and subsequent alkylation with benzyl bromide.[3]



These results show that the regioselectivity of the C-S bond fission and the position of the double bond in the products are largely affected by the substituents of the thiophene derivatives. From this point of view, we investigated Birch reductions of several types of thiophenes in order to clarify the effects of the substituents on the regioselectivity of the ring-opening reactions.

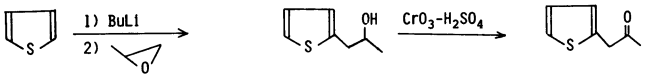
Results and Discussion

Preparations of Thiophenes. The preparations of 2-(2-thienyl)alkanoic acids (**9a—c**) were carried out as follows: The reaction of lithium enolate of ethyl 2-thienylacetate (**7**), prepared from **7** with lithium diisopropylamide (LDA) in THF, with alkyl halides gave ethyl 2-(2-thienyl)alkanoate (**8**) in good yields. Further, **9** was obtained by the hydrolysis of **8**.



a: R = CH_3-, **b**: R = $CH_3(CH_2)_3$-, **c**: R = CH_2=CH-CH_2-

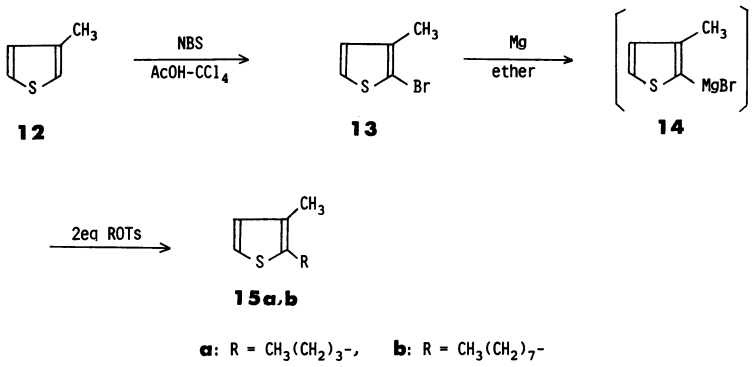
2-Thienylacetone (**11**) was prepared by the Jones oxidation of 1-(2-thienyl)-2-propanol (**10**) which was obtained by successive treatments of thiophene at −30 °C with butyllithium and propylene oxide.



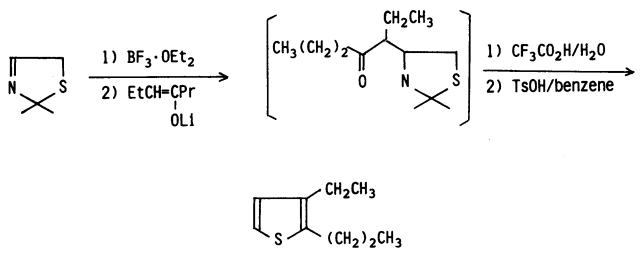
2,3-Dialkylthiophenes (**15a—c**) were prepared by the following two methods. Commercially available 3-methylthiophene (**12**) was used as the starting material for the preparation of 2-alkyl-3-methylthiophenes (**15a, b**). 2-Bromo-3-methylthiophene (**13**) was prepared from **12** and *N*-bromosuccinimide (NBS) by the procedure of Kellogg et al.[4] The resulting **13** was converted to the Grignard reagent **14** in ether and **14** was allowed to react with two equivalents of an alkyl *p*-toluenesulfonate[5] to give **15a, b** in good yields (Scheme 1).

3-Ethyl-2-propylthiophene (**15c**) was prepared by modifing the method reported by Meltz et al.[6] as shown in Scheme 2.

The Birch Reductions of Thiophenes. The Birch reduction of 2-(2-thienyl)propanoic acid (**9a**) with 5 equivalents of sodium in liquid ammonia in the presence of ethanol and a subsequent treatment with ammonium chloride and benzyl bromide resulted in

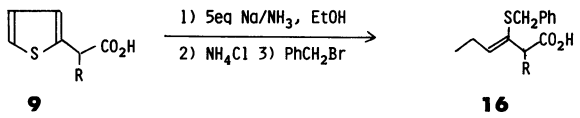


Scheme 1.

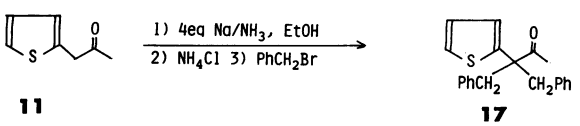


Scheme 2.

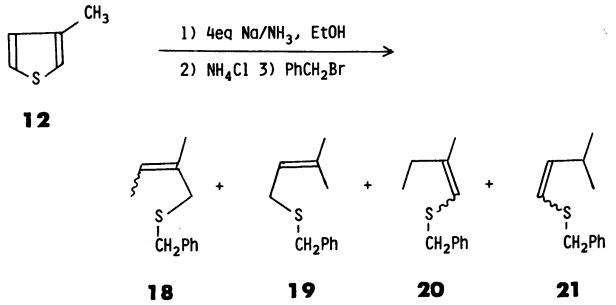
the formation of (*Z*)-3-benzylthio-2-methyl-3-hexenoic acid (**16a**) in 63% yield. The Birch reductions of 2-(2-thienyl)hexanoic acid (**9b**) and 2-(2-thienyl)-4-pentenoic acid (**9c**) under similar reaction conditions also gave (*Z*)-3-benzylthio-2-butyl-3-hexenoic acid (**16b**) and (*Z*)-2-allyl-3-benzylthio-3-hexenoic acid (**16c**) in 77 and 76% yields, respectively. These products were formed by the cleavage of the bond between the sulfur atom and C-5 of the thiophene nuclei.



However, the Birch reduction of 2-thienylacetone (**11**) (which contains a carbonyl group at the same position as **9**) did not give ring-opening products. When **11** was treated with 4 equivalents of sodium and benzyl bromide, a dialkylated compound **17** was obtained without the formation of ring-opening products. This result shows that the formation of a carbanion at the α-carbon of the carbonyl group of **11** is faster than the reduction of the thiophene nuclei.

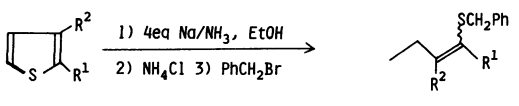


In a previous report,[3] we found that the Birch reduction of 2-propylthiophene under similar reaction conditions gave (*Z*)-4-benzylthio-3-heptene. In the present report, the Birch reduction and alkylation of 3-methylthiophene (**12**) was examined. The reduction of **12** with 4 equivalents of sodium under reaction conditions similar to those reported before gave a mixture of many products. A careful separation of the products by silica-gel column chromatography and an NMR study clarified that 1-benzylthio-2-methyl-2-butene (**18**), 1-benzylthio-3-methyl-2-butene (**19**), 1-benzylthio-2-methyl-1-butene (**20**), and 1-benzylthio-3-methyl-1-butene (**21**) were formed in the ratio of 10:4:4:1.



The ratio of the trisubstituted and disubstituted olefins in the above products was 18:1. This result indicates that the product distribution is dependent on the thermodynamic stability of the olefins. Therfore, Birch reductions of 2,3-dialkylthiophene (**15**) were examined with an expectation that tetrasubstituted olefins would be formed.

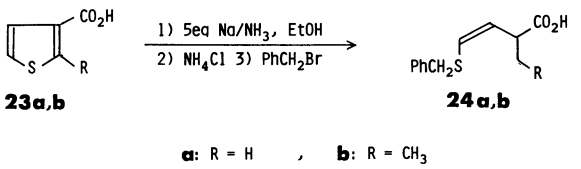
When 2-butyl-3-methylthiophene (**15a**) was allowed to react with 4 equivalents of sodium by the procedure reported previously, 4-benzylthio-3-methyl-3-octene (**22a**) was obtained in 60% yield as expected. Similarly, a Birch reduction of 3-methyl-2-octylthiophene (**15b**) and 3-ethyl-2-propylthiophene (**15c**) also gave tetrasubstituted olefins **22b** and **22c** in 37 and 52% yields, respectively. These results show that the reductive



a: R^1= $CH_3(CH_2)_3$- R^2= CH_3-
b: R^1= $CH_3(CH_2)_7$- R^2= CH_3-
c: R^1= $CH_3(CH_2)_2$- R^2= CH_3CH_2-

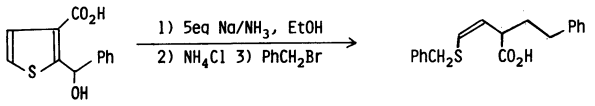
cleavage of the bond between the sulfur atom and C-5 of the thiophene nuclei gave thermodynamically stable tetrasubstituted olefins.

Next, it was found that the regioselectivity of the ring-opening reactions of 3-thiophenecarboxylic acid (**23a**) and its derivatives was different from that of the above-mentioned reactions. When **23a** was allowed to react with 5 equivalents of sodium and benzyl bromide, (*Z*)-4-benzylthio-2-methyl-3-butenoic acid (**24a**) was obtained in 51% yield. Similarly, the Birch reduction and alkylation of 2-methyl-3-thiophenecarboxylic acid (**23b**) gave (*Z*)-4-benzylthio-2-ethyl-3-butenoic acid (**24b**) in 69% yield. In these reactions, a reductive cleavage of the thiophene ring occurred between the sulfur atom and C-2 of the thiophene nuclei and the resulting products were disubstituted olefins rather than trisubstituted olefins. Further, the Birch reduction and alkylation of 2-(α-hydroxybenzyl)-3-thiophenecarboxylic acid (**25**) resulted in the formation of an over-reduced product, (*Z*)-4-benzylthio-2-(2-phenylethyl)-3-butenoic acid (**26**) in 48% yield.



23a,b **24a,b**

a: R = H , **b**: R = CH_3

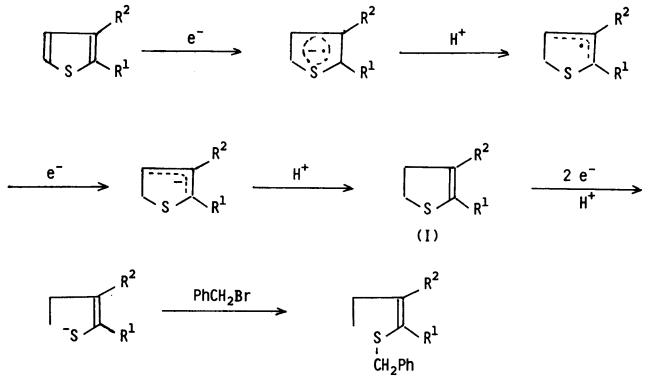


25 **26**

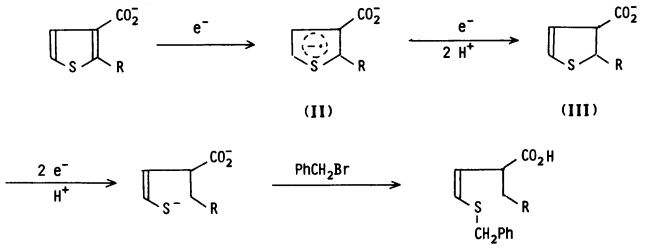
In conclusion, the ring-opening reactions of thiophene derivatives are classified into three types. (A) The ring-opening reaction occurs between the sulfur atom and C-5 of the thiophene nuclei and the double bond remains at the 2 position. Birch reductions of **3**, **5**, **9**, and **15** belong to type-A. (B) The ring-opening reaction occurs between the sulfur atom and C-2 of thiophene and the double bond remains at the 3 position. A Birch reduction of **1** belongs to type-B. (C) The position of a C-S bond fission is the same as type-B, but the double bond remains at the 4 position. Birch reductions of **23** and **25** belong to type-C.

These selectivities of the ring-opening reaction can be reasonably explained by the two mechanisms shown in Shemes 3 and 4.

In these mechanisms, the reduction and the protonation of the thiophene derivatives of type-A forms thermodynamically stable dihydrothiophene (**I**) as the intermediate (Scheme 3). The formation of 2,3-dihydrothiophene (**III**) as the intermediate in Scheme 4 by the reduction and the protonation of radical anion **II**, which is produced by the reduction of the thiophene derivatives of the type-C, can be affected by the



Scheme 3.



Scheme 4.

position of the carboxyl group. However, the reason of the formation of **III** is not clear.

Experimental

The Preparation of 2-(2-Thienyl)propanoic Acid (9a). A solution of ethyl 2-thienylacetate (**7**) (1.72g, 10 mmol) in 10 ml of THF was added into a solution of lithium diisopropylamide which was prepared from diisopropylamine (1.11 g, 11 mmol) and butyllithium (11 mmol) in 15 ml of THF at −30 °C under argon. After the addition of **7**, a white precipitate was observed in the reaction mixture. The reaction mixture was stirred for 0.5 h and was added to methyl iodide (2.13 g, 15 mmol) in 10 ml of THF at −30 °C. Additional stirring was continued for 1 h and the reaction mixture was quenched with 10% hydrochloric acid. The mixture was extracted with ether and the ether layer was dried over magnesium sulfate. After removing the solvent, the residue was chromatographed on silica gel using benzene as the solvent to give ethyl 2-(2-thienyl)propanoate (**8a**) [1.72 g (94%)]. IR (NaCl) 1730 cm^{-1} (C=O); NMR ($CDCl_3$) δ=1.27 (3H, t), 1.63 (3H, d), 4.03 (1H, q), 4.20 (2H, q), 6.90—7.47 (3H, m); MS *m/z* 184 (M^+).

Thus prepared, **8a** (1.66 g, 9 mmol) was stirred with 50 ml of 5% sodium hydroxide solution at room temperature for 2h. The reaction mixture was acidified with 10% hydrochloric acid and extracted with ether. The ether layer was washed with a saturated sodium chloride solution and dried over magnesium sulfate. After removing the solvent, the residue was chromatographed on silica gel using benzene-ether (2:1) as the solvent to give 2-(2-thienyl)propanoic acid (**9a**) [1.35 g (96%)]. Further purification of **9a** was performed by distillation, bp 138—140 °C (11 mmHg, 1 mmHg=133.32 Pa). IR (NaCl) 3600—2300 cm^{-1} (CO_2H), 1700 cm^{-1} (C=O); NMR ($CDCl_3$) δ=1.63 (3H, d), 4.07 (1H, q), 6.87—7.43 (3H, m), 11.30 (1H, brs); MS *m/z* 156 (M^+).

Similarly, ethyl 2-(2-thienyl)hexanoate (**8b**), 2-(2-thienyl)-hexanoic acid (**9b**), ethyl 2-(2-thienyl)-4-pentenoate (**8c**), and 2-(2-thienyl)-4-pentenoic acid (**9c**) were prepared by the reactions of **7** with corresponding alkyl halides. The yields and spectral data are as follows.

8b: Yield 71%; IR (NaCl) 1720 cm^{-1} (C=O); NMR ($CDCl_3$) δ=0.75—1.62 (10H, m), 2.01 (2H, m), 3.92 (1H, t), 4.52 (2H, q), 6.92—7.53 (3H, m); MS *m/z* 226 (M^+).

9b: Yield 86%; IR (NaCl) 3600—2400 cm^{-1} (CO_2H), 1700 cm^{-1} (C=O); NMR ($CDCl_3$) δ=0.72—2.22 (9H, m), 3.78 (1H, t), 6.72—7.18 (3H, m), 11.32 (1H, s); MS *m/z* 198 (M^+).

8c: Yield 87%; IR (NaCl) 1720 cm^{-1} (C=O), 1640 cm^{-1} (CH=CH_2); NMR ($CDCl_3$) δ=1.22 (3H, t), 2.17—3.04 (2H, m), 3.86 (1H, t), 4.05 (2H, q), 4.78—5.17 (2H, m), 5.35—6.03 (1H, m), 6.63—7.20 (3H, m); MS *m/z* 210 (M^+).

9c: Yield 99%; IR (NaCl) 3600—2300 cm^{-1} (CO_2H), 1710 cm^{-1} (C=O), 1650 cm^{-1} (CH=CH_2); NMR ($CDCl_3$) δ=2.23—3.08 (2H, m), 3.85 (1H, t), 4.76—5.19 (2H, m), 5.31—6.01 (1H, m), 6.67—7.19 (3H, m), 11.34 (1H, s); MS *m/z* 182 (M^+). Found: C, 54.17; H, 5.36%. Calcd for $C_9H_{10}O_2S$: C, 54.29; H, 5.54%.

The Preparation of 2-Thienylacetone (11). To a solution of thiophene (1.72 g, 20 mmol) in 20 ml of THF, a solution of butyllithium in hexane (22 mmol) was added at −30 °C with stirring under an argon atmosphere. After stirring for one hour at −30 °C, the reaction mixture was cooled to −70 °C. Into the reaction mixture, a solution of propylene oxide (1.22 g, 22 mmol) in 20 ml of THF was added at −70 °C. The reaction temperature was maintained at −70 °C for 0.5 h and then slowly raised to room temperature. Further, the reaction mixture was refluxed for 3 h. The mixture was acidified with 10% hydrochloric acid and extracted with ether. After the ether layer was washed with saturated sodium chloride solution, it was dried over magnesium sulfate. The solvent was removed under a reduced pressure and the residue was chromatographed on silica gel using benzene-ether (1 : 1) as the solvent to give 1-(2-thienyl)-2-propanol (**10**) [1.77 g (63%)]. IR (NaCl) 3500 cm^{-1} (OH); NMR ($CDCl_3$) δ=1.19 (3H, d), 2.31—2.62 (1H, brs), 3.89 (2H, d), 3.95 (1H, sex), 6.73—7.27 (3H, m); MS *m/z* 142 (M^+).

Into a solution of **10** (2.84 g, 20 mmol) in 50 ml of acetone, a mixture of chromium trioxide (2.60 g, 26 mmol), concd sulfuric acid (23 ml), and water (5 ml) was added at −20 °C over a period of 1 h. Further, additional stirring was continued for 1 h at −20 °C and the mixture was poured into 2-propanol (20 ml) and sodium hydrogencarbonate solution. After the precipitate was filtered, the filtrate was extracted with ether. The ether layer was washed with a saturated sodium chloride solution and was dried over magnesium sulfate. After removing the solvent, the residue was chromatographed on silica gel using benzene-petroleum ether (4 : 1) as the solvent to give 2-thienylacetone (**11**) [1.16 g (41%)]. IR (NaCl) 1700 cm^{-1} (C=O); NMR ($CDCl_3$) δ=2.22 (3H, s), 3.93 (2H, s), 6.92—7.48 (3H, m); MS *m/z* 140 (M^+).

Preparation of 2-Butyl-3-methylthiophene (15a). The preparation of 2-bromo-3-methylthiophene (**13**) was performed by the procedure of Kellog et al.[4] from 3-methylthiophene (**12**) and *N*-bromosuccinimide.

A solution of **13** (5.31 g, 30 mmol) in 25 ml of ether was added to magnesium (0.74 g, 31 mmol) with stirring at room temperature under nitrogen. The reaction mixture was stirred for 2.5 h at room temperature and was refluxed for 15 min. Into the reaction mixture, a solution of butyl *p*-toluenesulfonate (13.08 g, 60 mmol) in 25 ml of ether was added at reflux temperature. After refluxing was continued for 7.5 h, the solution was acidified with 10% hydrochloric acid. The resulting mixture was extracted with ether and the ether layer was washed with saturated sodium chloride solution. The layer was dried over magnesium sulfate. After removing the ether, the residue was chromatographed on silica gel and 2-butyl-3-methylthiophene (**15a**) was obtained by the elution with petroleum ether [2.27 g (49%)]. Thus prepared **15a** was further purified by distillation, bp 78—82 °C (18 mmHg). IR (NaCl) 700 cm^{-1} (thiophene); NMR ($CDCl_3$) δ=0.70—1.90 (7H, m), 2.09 (3H, s), 2.65 (2H, t), 6.83 (1H, d), 6.87 (1H, d); MS *m/z* 154 (M^+).

In a similar procedure, 3-methyl-2-octylthiophene (**15b**) was prepared. The spectral data and boiling point of **15b** are as follows: yield 60%, bp 140—142 °C (14 mmHg). IR (NaCl) 700 cm^{-1} (thiophene); NMR ($CDCl_3$) δ=0.63—1.81 (15H, m), 2.09 (3H, s), 2.65 (2H, t), 6.59 (1H, d), 6.81 (1H, d); MS *m/z* 210 (M^+).

The Preparation of 3-Ethyl-2-propylthiophene (15c). The preparation of 3-ethyl-2-propylthiophene (**15c**) was performed by the modified procedure of Meltz et al.[6] The adduct, prepared from 4-heptanone (3.42 g, 30 mmol) and 2,2-dimethyl-3-thiazoline (3.45 g, 30 mmol) by the reported method, was hydrolyzed with trifluoroacetic acid (3.5 ml) in ethanol (15 ml) and water (5 ml) under stirring for 1 h. After removing the solvent, the residue was refluxed in benzene (100 ml) for 10 h with catalytic amounts of *p*-toluenesulfonic acid using a water-separating apparatus. The reaction mixture was washed with 10% sodium hydrogencarbonate solution and a saturated sodium chloride solution. The benzene layer was dried over magnesium sulfate. After removing the solvent, the residue was chromatographed on silica gel and **15c** was obtained by the elution with petroleum ether [0.95 g (21%)]. IR (NaCl) 700 cm^{-1} (thiophene); NMR ($CDCl_3$) δ=0.98 (3H, t), 1.18 (3H, t), 1.45—2.12 (2H, m), 2.32—2.90 (4H, m), 6.77 (1H, d), 6.98 (1H, d); MS *m/z* 154 (M^+).

General Procedure for the Birch Reduction and Benzylation of Thiophene Derivatives. To a mixture of thiophene derivatives (10 mmol), absolute ethanol (4 ml) and liquid ammonia (50 ml), small pieces of sodium (4.4 or 5.5 equivalents) were added over a period of 1 h under reflux. After the mixture then had been stirred for 1 h in refluxing ammonia, solid ammonium chloride (3 equivalents) was added and the mixture was stirred for 0.5 h. Next, benzyl bromide (2.0 ml) was added to the mixture, and the mixture was stirred for 0.5 h. Further, additional benzyl bromide (1.0 ml) was added into the mixture and the mixture was stirred for 1 h with refluxing. The ammonia was then evaporated and the residue was added 20 ml of 10% hydrochloric acid and 20 ml of ether. The mixture was stirred for 1 h and then the ether layer was separated. The ether layer was washed with saturated sodium chloride solution and dried over magnesium sulfate. After removing the solvent, the residue was chromatographed on silica gel. The yield, the solvent of chromatography, spectral data, and analytical data of the products are as follows.

(*Z*)-3-Benzylthio-2-methyl-3-hexenoic acid (**16a**); yield 63% [elution with benzene-ether (5 : 1)]; an oily product; IR (NaCl) 3250—2950 cm^{-1} (CO_2H), 1700 cm^{-1} (C=O); NMR ($CDCl_3$) δ=0.90 (3H, t), 1.34 (3H, d), 2.25 (2H, qu), 3.42 (1H, q), 3.87 (2H, s), 6.01 (1H, t, J=8.4 Hz), 7.35 (5H, s), 12.31 (1H, brs); MS *m/z* 206 (M^+). Found: C, 67.06; H, 7.72%. Calcd for

$C_{14}H_{18}O_2S$: C, 67.17; H, 7.26%.

(*Z*)-3-Benzylthio-2-butyl-3-hexenoic acid (**16b**); yield 77% [elution with benzene-ether (5:1)]; an oily product; IR (NaCl) 3700—2300 cm^{-1} (CO_2H), 1700 cm^{-1} (C=O); NMR ($CDCl_3$) δ=0.70—1.97 (12H, m), 2.20 (2H, qu), 3.21 (1H, t), 3.81 (2H, s), 5.92 (1H, t, J=7.0 Hz), 7.19 (5H, s), 10.54 (1H, brs); MS m/z 248 (M^+). Found: C, 69.77; H, 8.46%. Calcd for $C_{17}H_{24}O_2S$: C, 69.82; H, 8.29%.

(*Z*)-2-Allyl-3-benzylthio-3-hexenoic acid (**16c**); yield 76% [elution with benzene-ether (4:1)]; an oily product; IR (NaCl) 3550—2200 cm^{-1} (CO_2H), 1700 cm^{-1} (C=O), 1640 cm^{-1} (CH=CH_2); NMR ($CDCl_3$) δ=0.86 (3H, t), 1.92—2.66 (4H, m), 3.32 (1H, t), 3.82 (2H, s), 4.85—5.83 (3H, m), 5.96 (1H, t, J=7.0 Hz), 7.22 (5H, s), 11.40 (1H, brs); MS m/z 214 (M^+). Found: C, 69.64; H, 7.53%. Calcd for $C_{16}H_{20}O_2S$: C, 69.50; H, 7.31%.

4-Benzylthio-3-methyl-3-octene (**22a**); yield 60% (elution with petroleum ether); an oily product; IR (NaCl) 2950 cm^{-1} (CH_2), 2920 cm^{-1} (CH_2), 700 cm^{-1} (C_6H_5); NMR ($CDCl_3$) δ=0.63—1.62 (10H, m), 1.67 (3H, s), 1.97—2.42 (4H, m), 3.62 (2H, s), 7.02 (5H, s); MS m/z 248 (M^+). Found: C, 77.54; H, 9.63%. Calcd for $C_{16}H_{24}S$: C, 77.37; H, 9.74%.

4-Benzylthio-3-methyl-3-dodecene (**22b**); yield 37% (elution with petroleum ether); an oily product; IR (NaCl) 2920 cm^{-1} (CH_2), 2850 cm^{-1} (CH_2), 700 cm^{-1} (C_6H_5); NMR ($CDCl_3$) δ=0.61—1.64 (18H, m), 1.67 (3H, s), 1.97—2.46 (4H, m), 3.69 (2H, s), 7.27 (5H, s); MS m/z 304 (M^+). Found: C, 78.92; H, 10.72%. Calcd for $C_{20}H_{32}S$: C, 78.89; H, 10.59%.

4-Benzylthio-3-ethyl-3-heptene (**22c**); yield 52% (elution with petroleum ether); an oily product; IR (NaCl) 2950 cm^{-1} (CH_2), 2870 cm^{-1} (CH_2), 690 cm^{-1} (C_6H_5); NMR ($CDCl_3$) δ=0.64—1.12 (9H, m), 1.22—1.78 (2H, m), 1.80—2.50 (6H, m), 3.72 (2H, s), 7.21 (5H, s); MS m/z 248 (M^+). Found: C, 77.38; H, 10.20%. Calcd for $C_{16}H_{24}S$: C, 77.37; H, 9.74%.

(*Z*)-4-Benzylthio-2-methyl-3-butenoic acid (**24a**); yield 51% (elution with benzene); an oily product; IR (NaCl) 3400—2300 cm^{-1} (CO_2H), 1700 cm^{-1} (C=O); NMR ($CDCl_3$) δ=1.26 (3H, d), 3.29—3.86 (1H, m), 3.92 (2H, s), 5.72 (1H, t), 6.20 (1H, d, J=10 Hz), 7.33—7.65 (5H, m), 11.29 (1H, s); MS m/z 222 (M^+). Found: C, 64.75; H, 6.60%. Calcd for $C_{12}H_{14}O_2S$: C, 64.85; H, 6.35%.

(*Z*)-4-Benzylthio-2-ethyl-3-butenoic acid (**24b**); yield 69% [elution with petroleum ether-ethyl acetate (1:1)]; an oily product; IR (NaCl) 3300—2200 cm^{-1} (CO_2H), 1690 cm^{-1} (C=O); NMR ($CDCl_3$) δ=0.98 (3H, t), 1.05—1.51 (2H, m), 1.51—2.13 (1H, m), 3.97 (2H, s), 5.79 (1H, t), 6.40 (1H, d, J=8 Hz), 7.56 (5H, s), 11.54 (1H, brs); MS m/z 236 (M^+). Found: C, 66.36; H, 7.01%. Calcd for $C_{13}H_{16}O_2S$: C, 66.08; H, 6.83%.

(*Z*)-4-Benzylthio-2-(2-phenylethyl)-3-butenoic acid (**26**); yield 48% [elution with petroleum ether-ethyl acetate (1:1)]; mp 104—105 °C (recrystallization from petroleum ether-benzene); IR (KBr) 3400—2300 cm^{-1} (CO_2H), 1700 cm^{-1} (C=O); NMR ($CDCl_3$) δ=2.00 (2H, q), 2.60 (2H, t), 3.50 (1H, q), 3.88 (2H, s), 5.65 (1H, t), 6.24 (1H, d, J=10 Hz), 7.05—7.52 (10H, m), 11.59 (1H, s); MS m/z 312 (M^+). Found: C, 73.64; H, 6.54%. Calcd for $C_{19}H_{20}O_2S$: C, 73.06; H, 6.45%.

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