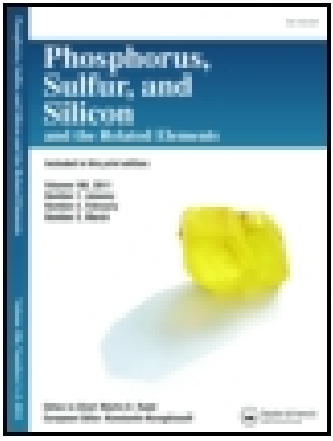


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

Synthesis of Novel Arylthio Derivatives of Mucochloric Acid

A. R. Kurbangalieva [a] , N. F. Devyatova [a] , A. V. Bogdanov [a] , E. A. Berdnikov [a] , T. G. Mannafov [a] , D. B. Krivolapov [b] , I. A. Litvinov [b] & G. A. Chmutova [c]

[a] Aleksandr Mikhailovich Butlerov Chemical Institute, Kazan State University , Kazan, Russia

[b] Aleksander Erminingeldovich Arbuzov Institute of Organic and Physical Chemistry, Kazan Scientific Center of the Russian Academy of Sciences , Kazan, Russia

[c] A. M. Butlerov Chemical Institute, Kazan State University , Kazan, Russia

Published online: 30 Jan 2007.

To cite this article: A. R. Kurbangalieva , N. F. Devyatova , A. V. Bogdanov , E. A. Berdnikov , T. G. Mannafov , D. B. Krivolapov , I. A. Litvinov & G. A. Chmutova (2007) Synthesis of Novel Arylthio Derivatives of Mucochloric Acid, Phosphorus, Sulfur, and Silicon and the Related Elements, 182:3, 607-630, DOI: 10.1080/10426500601015989

To link to this article: http://dx.doi.org/10.1080/10426500601015989

Phosphorus, Sulfur, and Silicon, 182:607–630, 2007

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500601015989

Synthesis of Novel Arylthio Derivatives of Mucochloric Acid

A. R. Kurbangalieva
N. F. Devyatova
A. V. Bogdanov
E. A. Berdnikov
T. G. Mannafov
Aleksandr Mikhailovich Butlerov Chemical Institute, Kazan State University, Kazan, Russia

D. B. Krivolapov
I. A. Litvinov
Aleksander Erminingeldovich Arbuzov Institute of Organic and Physical Chemistry, Kazan Scientific Center of the Russian Academy of Sciences, Kazan, Russia

G. A. Chmutova
A. M. Butlerov Chemical Institute, Kazan State University, Kazan, Russia

Stable reaction products of mucochloric acid with aromatic and heterocyclic thiols were synthesized and characterized. Under basic conditions the reactions proceeded with the substitution of the chlorine atom(s) by arylthiogroup(s), while in an acidic medium the hydroxy group at C_5 was substituted. Different types of new sulfur-containing products of di- and trisubstitution on the basis of mucochloric acid were obtained. In one case a new acyclic product—di-p-tolyl-2,3-bis-(p-tolylthio)butanedithioate—was isolated. The structure of all synthesized compounds was confirmed by IR, ^1H, and ^{13}C NMR spectroscopy; three compounds were characterized by single crystal X-ray diffraction.

Keywords Furanone; mucochloric acid; single crystal X-ray diffraction; sulfur; thioether

Received August 19, 2005; accepted August 22, 2006.

The grants given to A. R. Kurbangalieva and N. F. Devyatova by the Russian Ministry of Education and Science and U.S. Civilian Research and Development Foundation BRHE (REC-007, No. Y2-C-07-17) are gratefully acknowledged. This research was supported by grants from the Russian Foundation for Basic Research (grant No. 04-03-32156). The authors are thankful to Dr. E. G. Yarkova for recording the IR spectra and to Dr. O. A. Lodochnikova for assistance in X-ray analysis.

Address correspondence to A. R. Kurbangalieva, Department of Chemistry, Kazan State University, 18 Kremlyovskaya Street, Kazan, 420008 Republic of Tatarstan, Russian Federation. E-mail: almira@ksu.ru

INTRODUCTION

In recent years heterocyclic polyfunctional compounds have attracted considerable attention due to the wide spectrum of their biological activity. One of these systems is mucochloric acid **1**-3,4-dichloro-5-hydroxy-2(5*H*)-furanone, which is a commercially available polyfunctional heterocycle with high reactivity. Due to the presence of such reactive sites as a double bond, a lactone ring, two chlorine atoms, and a hydroxy-group mucochloric acid and its derivatives can react with nucleophilic as well as with electrophilic reagents. This allows the introduction of different functional groups into the lactone ring and to obtain new compounds with practically useful properties.[1–10]

It was shown earlier that chlorine atoms in positions 3 and 4 of the lactone ring are subjected to substitution in reactions of mucochloric acid with simple aliphatic and aromatic thiols[11,12] and selenophenols[13] under basic conditions; in the presence of inorganic acids the hydroxy group is substituted.[14–16] Nucleophilic substitution in an alkaline medium (a water–alcohol solution of potassium hydroxide) gives mainly 4-arylthiosubstituted derivatives, while 3,4-disubstituted derivatives of mucochloric acid are formed when an excess of the nucleophilic reagent is used.[12]

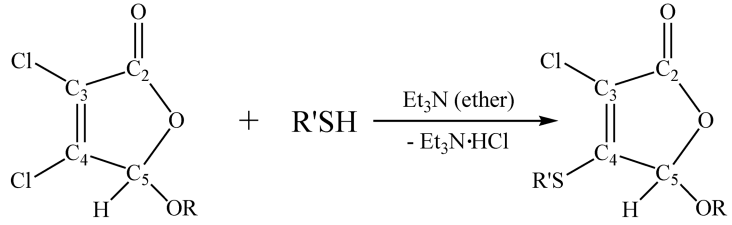
The main aim of the present work was the investigation of reactions of mucochloric acid with arylthiols under basic and acidic conditions in order to obtain pure regioisomers of sulfur-containing derivatives of the furanone series. Moreover, of particular interest are reactions of mucochloric acid with heterocyclic thiols and the synthesis of different di- and triarylthioderivatives. The reaction products were characterized by ^{13}C NMR spectroscopy and single crystal X-ray diffraction. IR and ^{1}H NMR spectroscopy were also used for the structure identification of the compounds. Identity and purity of the compounds were controlled by TLC as well as elemental analysis.

RESULTS AND DISCUSSION

Mucochloric acid **1** formed with arylthiols products **3–8** resulting from substitution of the chlorine atom in 4-position. The reaction was carried out in diethyl ether in the presence of triethylamine with an equimolar ratio of reagents and catalyst[11] (Scheme 1).

The new products **3–8** are stable solid compounds; their composition was determined by elemental analysis, and the position of the arylthio group was proven by the spectral data presented in Table I.

Characteristic features of the IR spectra of products **3–8** are a broad band of medium intensity in the range 3100–3400 cm^{-1} assigned to



1, 2 **3–9**

(**1**) R = H
(**2**) R = C_2H_5

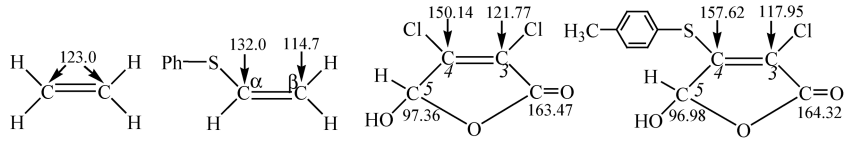
R = H, R' = 4-$CH_3C_6H_4$(**3**), 4-$C_2H_5C_6H_4$ (**4**), 1-Naphthyl (**5**), 4-ClC_6H_4 (**6**), 4-BrC_6H_4 (**7**), 3-BrC_6H_4 (**8**)
R = C_2H_5, R' = 4-ClC_6H_4 (**9**)

SCHEME 1

the stretching vibrations of the hydroxy group, a strong band at 1760–1780 cm^{-1} assigned to the stretching vibrations of the C=O bond of the γ-lactone, and a narrow intensive band in the range 1580–1600 cm^{-1} typical for the C=C bonds of the aromatic system. In the IR spectra of most of the products, the absorption band ν(C=O) was present either as a doublet (a strong signal at 1760–1780 cm^{-1} and a weak signal in the range 1730–1750 cm^{-1}) or as broad unsplit band. The comparison of the IR spectrum of mucochloric acid **1** with the IR spectra of compounds **3–8** gave evidence that the reaction proceeded with retention of the lactone ring.

In the ^{1}H NMR spectra of products **3–8**, there were three main types of signals: a singlet for the methine proton at C_5 (5.6–6.2 ppm); a multiplet in the range 7.0–8.0 ppm, characteristic for the aromatic protons, and a signal for the proton of the hydroxy group. The signal for the OH proton appeared as a broad singlet in the range 2.5–4.5 ppm in solutions of compounds **3–8** in $CDCl_3$ and at 8.1 ppm in the spectrum of compound **3**, which were recorded in DMSO-d_6 (Table I).

The location of the arylthio group was determined by comparison of the ^{13}C NMR spectra of furanones **1** and **3** in DMSO-d_6 with those of the model compounds A and B (Scheme 2).[17,18]



A **B** **1** **3**

SCHEME 2

TABLE I Spectroscopic Data of Synthesized Compounds 2–24

No.	IR (ν cm^{-1}), ^{1}H NMR (δ ppm), and ^{13}C NMR (δ ppm)
2	2988 (C_5-H), 2940 (CH_2), 2912 (CH_3), 1792 (C═O), 1642 (C═C); ^{1}H NMR ($CDCl_3$, 200 MHz): 1.51 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_3), 4.01 (dq, $^3J_{HH}$ = 7.1 Hz, $^2J_{HH}$ = −9.4 Hz, 1H, CH_2), 4.11 (dq, $^3J_{HH}$ = 7.1 Hz, $^2J_{HH}$ = −9.4 Hz, 1H, CH_2), 6.03 (s, 1H, C_5-H); ^{13}C{^{1}H} NMR ($CDCl_3$, 50 MHz): 14.2 (CH_3); 65.6 (CH_2); 100.3 (C_5); 123.6 (C_3); 147.1 (C_4); 162.7 (C_2)
3	3272 (OH), 1782, 1748 (C═O), 1592, 1492 (C═C_{arom}); ^{1}H NMR ($CDCl_3$): 2.39 (s, 3H, CH_3), 3.98 (br s, 1H, OH), 5.77 (s, 1H, C_5-H), 7.22, 7.49 (AA′BB′, N = 7.5 Hz, 4H, H_{arom}); (DMSO-d_6): 2.35 (s, 3H, CH_3), 5.99 (s, 1H, C_5-H), 7.53, 7.28 (AA′BB′, N = 8.1 Hz, 4H, H_{arom}), 8.17 (s, 1H, OH); ^{13}C{^{1}H} NMR (DMSO-d_6, 75 MHz): 20.8 (CH_3), 97.0 (C_5), 118.0 (C_3), 121.7, 130.2, 134.7, 140.2 (C_{arom}), 157.6 (C_4), 164.3 (C_2)
4	3368 (OH), 1740 (C═O), 1584 (C═C_{arom}); ^{1}H NMR ($CDCl_3$): 1.25 (t, $^3J_{HH}$ = 7.6 Hz, 3H, CH_3), 2.69 (q, $^3J_{HH}$ = 7.6 Hz, 2H, CH_2), 3.50 (br s, 1H, OH), 5.80 (s, 1H, C_5-H), 7.25, 7.52 (AA′BB′, N = 7.9 Hz, 4H, H_{arom})
5	3248 (OH), 1754, 1732 (C═O), 1584 (C═C_{arom}); ^{1}H NMR ($CDCl_3$): 3.22 (br s, 1H, OH), 5.57 (s, 1H, C_5-H), 7.4–8.4 (m, 7H, naphthyl)
6	3400 (OH), 1772, 1738, 1700 (C═O), 1588 (C═C_{arom}); ^{1}H NMR ($CDCl_3$): 4.31 (br s, 1H, OH), 5.80 (s, 1H, C_5-H), 7.57, 7.41 (AA′BB′, N = 8.7 Hz, 4H, H_{arom})
7	3352 (OH), 1742 (C═O), 1592 (C═C_{arom}); ^{1}H NMR ($CDCl_3$): 4.03 (br s, 1H, OH), 5.79 (s, 1H, C_5-H), 7.48, 7.56 (AA′BB′, N = 8.6 Hz, 4H, H_{arom})
8	3244 (OH), 1762, 1736 (C═O), 1590 (C═C_{arom}); ^{1}H NMR ($CDCl_3$): 4.69 (br s, 1H, OH), 5.79 (s, 1H, C_5-H), 7.2-7.8 (m, 4H, H_{arom})
9	1766 (C═O), 1588 (C═C_{arom}); ^{1}H NMR ($CDCl_3$): 1.08 (t, $^3J_{HH}$ = 7.1 Hz, 3H, CH_3), 3.28 (dq, $^3J_{HH}$ = 7.1 Hz, $^2J_{HH}$ = −9.2 Hz, 1H, CH_2), 3.70 (dq, $^3J_{HH}$ = 7.1 Hz, $^2J_{HH}$ = −9.2 Hz, 1H, CH_2), 5.51 (s, 1H, C_5-H), 7.4–7.6 (m, 4H, H_{arom})
10	3120 (OH), 1762 (C═O), 1632 (C═N), 1594, 1498 (C═C_{arom}); ^{1}H NMR ($CDCl_3$): 2.37 (s, 3H, CH_3), 3.49 (br s, 1H, OH), 5.77 (s, 1H, C_5-H), 6.61 (s, 1H, H—C═), 7.2–8.0 (m, 5H, H_{arom})
11	3136 (OH), 1768 (C═O), 1648 (C═N), 1596, 1500 (C═C_{arom}); ^{1}H NMR ($CDCl_3$): 2.18 (s, 3H, CH_3), 3.46 (br s, 1H, OH), 5.89 (s, 1H, C_5-H), 7.4–7.9 (m, 10H, H_{arom})
12	1770 (C═O), 1622 (C═C), 1595, 1492 (C═C_{arom}); ^{1}H NMR ($CDCl_3$): 2.34 (s, 3H, CH_3), 6.03 (s, 1H, C_5-H), 7.16, 7.38 (AA′BB′, N = 8.1 Hz, 4H, H_{arom}); ^{13}C NMR ($CDCl_3$, 50 MHz): 21.3 (qt, $^1J_{CH}$ = 127.0 Hz, $^3J_{CH}$ = 4.4 Hz, CH_3), 86.1 (d, $^1J_{CH}$ = 171.3 Hz, C_5), 122.3 (d, $^3J_{CH}$ = 3.2 Hz, C_3), 121.8 (t, $^3J_{CH}$ = 5.0 Hz, C_i^S), 130.2 (ddq, $^1J_{CH}$ = 159.8 Hz, $^3J_{CH}$ = 5.4 Hz, C_m^S), 135.9 (dd, $^1J_{CH}$ = 164.0 Hz, $^3J_{CH}$ = 5.9 Hz, C_o^S), 141.1 (m, C_p^S), 149.2 (d, $^2J_{CH}$ = 5.5 Hz, C_4), 163.8 (s, C_2)
13	1768 (C═O), 1624 (C═C), 1591, 1502 (C═C_{arom}); ^{1}H NMR ($CDCl_3$): 6.1 (s, 1H, C_5-H), 7.4–8.6 (m, 7H, Naphthyl)
14	1790 (C═O), 1624 (C═C), 1597 (C═C_{arom}); ^{1}H NMR ($CDCl_3$): 6.03 (s, 1H, C_5-H), 7.32, 7.42 (AA′BB′, N = 7.8 Hz, 4H, H_{arom})
15	1772 (C═O), 1624 (C═C), 1592 (C═C_{arom}); ^{1}H NMR ($CDCl_3$): 6.10 (s, 1H, C_5-H), 7.2–7.8 (m, 4H, H_{arom})
16	1772 (C═O), 1626 (C═C), 1592, 1494 (C═C_{arom}); ^{1}H NMR ($CDCl_3$): 3.89 (s, 1H, OCH_3), 6.07 (s, 1H, C_5-H), 6.94, 7.50 (AA′BB′, N = 8.9 Hz, 4H, H_{arom})
17	3300 (O-H), 1762 (C═O), 1680 (C═C), 1588, 1492 (C═C_{arom}); ^{1}H NMR (DMSO-d_6): 6.23 (s, 1H, C_5-H), 7.1–7.6 (m, 5H, H_{arom}), 8.50 (s, 1H, O-H)

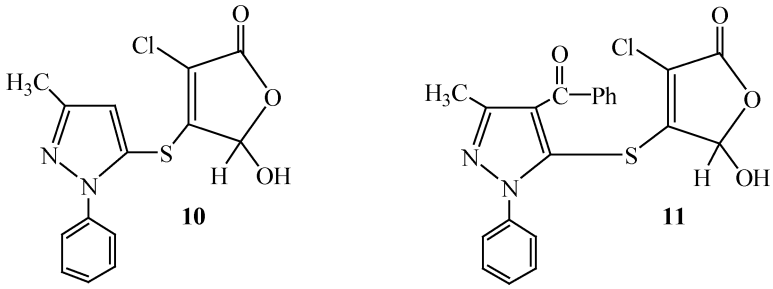
(Continued on next page)

TABLE I Spectroscopic Data of Synthesized Compounds 2–24 ***(Continued)***

No.	IR (ν cm^{-1}), ^1H NMR (δ ppm), and ^{13}— NMR (δ ppm)
18	3384 (O—H), 1746 (C═O), 1628 (C═C), 1596, 1496 (C═C_{arom}); ^1H NMR (DMSO-d_6): 2.29 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 5.95 (d, $^3J_{HH} = 8.9$ Hz, 1H, C_5-H), 7.16, 7.23 (AA′BB′, $N = 8.3$ Hz, 4H, H_{arom}), 7.24, 7.51 (AA′BB′, $N = 8.0$ Hz, 4H, H_{arom}), 7.93 (d, $^3J_{HH} = 8.9$ Hz, 1H, OH); ^{13}C NMR (DMSO-d_6, 50 ÃHz): 20.6 (q, $^1J_{CH} = 126.9$ Hz, CH_3), 20.8 (q, $^1J_{CH} = 126.9$ Hz, CH_3), 96.6 (d, $^1J_{CH} = 179.3$ Hz, C_5), 116.3 (s, C_3), 122.9, 128.4, 129.2, 130.0, 130.2, 134.7, 136.8, 140.0 (C_{arom}), 166.8 (s, C_4), 168.3 (s, C_2)
19	3276 (O-H), 1770 (C═O), 1600, 1492 (C═C_{arom}); ^1H NMR (DMSO-d_6, 200 MHz): 2.30 (s, 3H, CH_3), 6.17 (s, 1H, C_5-H), 7.20, 7.33 (AA′BB′, $N = 8.2$ Hz, 4H, H_{arom}), 8.47 (br s, 1H, OH); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 50 ÃHz): 20.7 (CH_3), 97.5 (C_5), 124.3 (C_3), 125.9, 130.1, 131.3, 138.1 (C_{arom}), 155.5 (C_4), 165.8 (C_2)
20	1768 (C═O), 1652 (C═C), 1596, 1492 (C═C_{arom}); ^1H NMR ($CDCl_3$): 2.33 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 5.70 (s, 1H, C_5-H), 7.0–7.6 (m, 8H, H_{arom}); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 50 MHz): 21.4, 21.4 (CH_3), 96.1 (C_5), 122.4 (C_3), 123.7, 130.0 (C_p^S), 130.5, 130.6 (C_m^S), 135.5, 135.7 (C_o^S), 140.7, 141.2 (C_i^S), 156.8 (C_4), 165.4 (C_2)
21	1784 (C═O), 1592, 1495 (C═C_{arom}); ^1H NMR ($CDCl_3$): 2.32 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 5.94 (s, 1H, C_5-H), 6.8–7.5 (m, 8H, H_{arom})
22	1790 (C═O), 1670 (C═$C_{furanone}$), 1588, 1488 (C═C_{arom}); ^1H NMR ($CDCl_3$): 2.42 (s, 1H, CH_3), 5.99 (s, 1H, C_5-H), 6.2–7.5 (m, 9H, H_{arom})
23	1766 (C═O), 1592, 1494 (C═C_{arom}); ^1H NMR ($CDCl_3$, 200 MHz): 2.31 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 5.65 (s, 1H, C_5-H), 6.7–7.6 (m, 12H, H_{arom}); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 50 MHz): 21.2, 21.4 (CH_3), 55.4 (OCH_3), 86.1 (C_5), 120.4 (C_3), 114.8, 117.5, 123.9, 127.9, 129.8, 130.5, 130.8, 135.3, 137.6, 138.0, 140.8, 161.4 (C_{arom}), 164.6 (C_4), 167.8 (C_2)
24	1700 (C═O), 1596, 1494 (C═C_{arom}); ^1H NMR ($CDCl_3$, 200 MHz): 2.33 (s, 6H, CH_3), 2.38 (s, 6H, CH_3), 4.16 (s, 2H, C-H), 7.0–7.5 (m, 16H, H_{arom}); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 50 MHz): 21.3, 21.4 (CH_3), 58.6 (C-H), 123.8, 128.0 (C_p^S), 130.0, 130.1 (C_m^S), 134.5, 134.9 (C_o^S), 139.5, 139.9 (C_i^S), 193.1 (C═O)

The characteristic changes of the chemical shifts of the ethylene carbon atoms on introducing the arylthio group—a significant downfield shift for the signal $C^{\alpha}(C_4)$ and an upfield shift for the signal $C^{\beta}(C_3)$—prove the substitution of the chlorine atom at C_4. Thioethers **4–8** and the compound **9**, which is the interaction product of 4-chlorothiophenol with the ethyl ester of mucochloric acid **2**, have similar structure. A characteristic feature of the ^1H NMR spectrum of compound **9** is the presence of signals for the ethoxy group in the form of a triplet for the methyl protons (δ 1.08 ppm) and two multiplets for the two diastereotopic methylene protons. The diastereotopy ($\Delta\delta$ 0.42 ppm) was noticeably larger than in the ethyl ester of mucochloric acid **2** itself ($\Delta\delta$ 0.10 ppm).

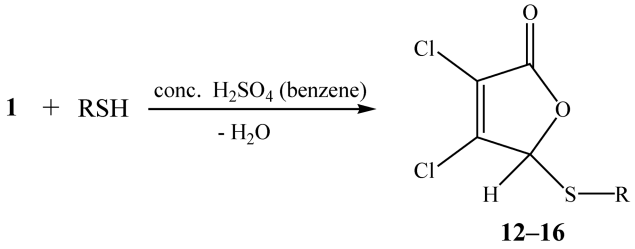
The reactions of mucochloric acid with heterocyclic thiols with the purpose to introduce sulfur as well as known pharmacophoric fragments at the 2(5*H*)-furanone framework are of particular interest. To the best of our knowledge, there is only one example of the reaction of mucobromic acid and its methyl ester with disodium 2-oxo-1,3-dithiole-4,5-dithiolate, leading to the formation of sulfur-containing heterocyclic compounds.[19] Reactions of mucochloric acid with 3-methyl-1-phenylpyrazol-5-thiol and 4-benzoyl-3-methyl-1-phenylpyrazol-5-thiol were carried out in analogy to the reaction outlined in Scheme 1. Products **10–11** showed similar IR and ^{1}H NMR spectral data for the lactone fragment as those previously described (Table I) and are novel 4-substituted derivatives of mucochloric acid (Scheme 3).



SCHEME 3

However, reactions with heterocyclic thiols were accompanied by strong resinification of the reaction mixture, which is the reason for low yields of pure final products **10** and **11**.

The synthesis of 5-thiosubstituted derivatives of mucochloric acid was performed by prolonged heating of **1** with arylthiols in benzene in the presence of sulfuric acid according to [14] (Scheme 4):



R = 4-$CH_3C_6H_4$ (**12**), 1-Naphthyl (**13**), 4-ClC_6H_4 (**14**), 3-BrC_6H_4 (**15**), 4-$CH_3OC_6H_4$(**16**)

SCHEME 4

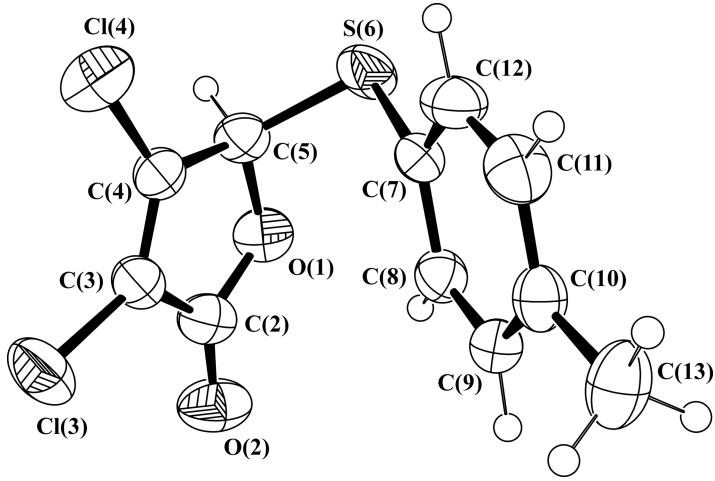


FIGURE 1 Molecular structure of 3,4-dichloro-5-[(4-methylphenyl)thio]-2(5*H*)-furanone **12** in the crystal.

Products **12–16** were isolated with yields of 70–84%. IR spectra of compounds **12–16** displayed bands for the aromatic system in the range 1500–1515 cm^{-1}; an intensive band for the carbonyl group of the lactone ring at 1768–1772 cm^{-1}; and no absorption band for a hydroxy group, characteristic of **1**. Together with the ^1H NMR data (a singlet for the proton at saturated carbon C_5 and a multiplet for aryl protons) and the ^{13}C NMR data (Table I), they confirmed the substitution of the hydroxy group at C_5 in an acidic medium.

Products **12–16** are crystalline substances. The structure of 3,4-dichloro-5-[(4-methylphenyl)thio]-2(5*H*)-furanone **12** was determined by single crystal X-ray diffraction (Figure 1).

In molecule **12**, the furanone ring was planar within 0.009(2) Å with the carbonyl group and the chlorine atoms lying in the same plane. The C=O bond length was 1.200(4) Å (Table II). The conjugation in the $O{=}C_2{-}C_3{=}C_4$ fragment was negligible as indicated by the bond lengths of $C_3{=}C_4$, 1.321(4), and the $C_2{-}C_3$, 1.459(5) Å. In spite of the remarkable steric repulsion between the chlorine atoms, which became evident in the increased exocyclic bond angles $Cl_3C_3C_4$ 128.9(2)° and $Cl_4C_4C_3$ 127.9(2)°, the double bond was not twisted (torsion angle $Cl_4C_4C_3Cl_3$ -1.5[4]°). The torsion angle between the planes of the furanone and the benzene rings was 63.5(1)°. The bond angle $C_5S_6C_7$ of 104.1(1)° suggests some repulsion between these rings. Bond length and bond angles in the molecule were as expected. Apparently, the crystal packing of **12** was determined by stacking interactions between the benzene rings.

TABLE II Selected Bond Distances (Å), and Bond and Torsion Angles (°) for Compounds 12, 18, and 24

12				18				24		
				Bond distances					Molecule A	Molecule B
Cl^3-C^3	1.691(3)	O^1-C^2	1.350(3)	S^6-C^3	1.728(8)	C^2-C^3	1.470(1)	S^2-C^2	1.780(5)	1.765(6)
C^9-C^{10}	1.381(4)	O^1-C^5	1.446(3)	C^{16}-C^{17}	1.370(1)	C^3-C^4	1.350(1)	S^2-C^6	1.773(6)	1.772(7)
Cl^4-C^4	1.690(3)	O^2-C^2	1.200(4)	S^6-C^7	1.760(1)	C^4-C^5	1.490(1)	S^3-C^3	1.822(5)	1.815(5)
C^{10}-C^{11}	1.380(4)	C^2-C^3	1.459(5)	C^{17}-C^{18}	1.380(2)	C^{19}-C^{20}	1.400(1)	S^4-C^4	1.829(5)	1.817(5)
S^6-C^5	1.795(3)	C^3-C^4	1.321(4)	S^{14}-C^4	1.713(9)	O^1-C^5	1.450(1)	O^1-C^5	1.212(7)	1.212(6)
C^{10}-C^{13}	1.512(4)	C^4-C^5	1.483(4)	C^{18}-C^{21}	1.510(1)	O^2-C^2	1.210(1)	O^2-C^2	1.198(7)	1.207(7)
S^6-C^7	1.772(3)	C^7-C^8	1.389(4)	S^{14}-C^{15}	1.750(1)	O^5-C^5	1.370(1)	C^2-C^3	1.520(7)	1.513(8)
C^{11}-C^{12}	1.379(4)	C^7-C^{12}	1.383(4)	C^{18}-C^{19}	1.380(2)	O^1-C^2	1.350(1)	C^3-C^4	1.510(7)	1.518(7)
C^8-C^9	1.377(4)							C^4-C^5	1.500(8)	1.511(7)
				Bond angles						
C^5-S^6-C^7	104.1(1)	Cl^4-C^4-C^5	122.3(2)	C^3-S^6-C^7	103.3(5)	S^{14}-C^4-C^3	126.2(6)	C^2-S^2-C^6	105.3(3)	105.3(3)
C^{11}-C^{10}-C^{13}	121.0(2)	C^3-C^4-C^5	109.8(2)	S^{14}-C^{15}-C^{16}	119.6(8)	C^3-C^4-C^5	109.3(7)	C^3-S^3-C^{13}	102.2(2)	101.8(2)
C^2-O^1-C^5	110.3(2)	S^6-C^5-O^1	112.41(2)	C^4-S^{14}-C^{15}	100.8(4)	S^{14}-C^4-C^5	124.5(6)	S^3-C^{13}-C^{14}	122.0(5)	120.7(4)
C^{10}-C^{11}-C^{12}	121.2(3)	S^6-C^5-C^4	116.47(2)	C^{15}-C^{16}-C^{17}	121.6(9)	O^1-C^5-O^5	109.2(7)	S^2-C^2-O^2	118.3(4)	116.8(4)
O^1-C^2-O^2	122.4(3)	O^1-C^5-C^4	103.3(2)	C^2-O^1-C^5	108.6(7)	O^5-C^5-C^4	116.1(8)	O^2-C^2-C^3	122.6(4)	120.8(4)
C^7-C^{12}-C^{11}	120.7(3)	S^6-C^7-C^8	123.1(2)	C^{16}-C^{17}-C^{18}	120(1)	O^1-C^5-C^4	104.7(7)	S^2-C^2-C^3	119.1(4)	122.3(4)
O^1-C^2-C^3	107.8(2)	S^6-C^7-C^{12}	118.1(2)	C^{17}-C^{18}-C^{19}	118(1)	S^6-C^7-C^8	120.1(8)	S^3-C^3-C^2	107.7(3)	108.9(3)
O^2-C^2-C^3	129.8(3)	C^8-C^7-C^{12}	118.6(2)	O^1-C^2-O^2	120.7(9)	S^6-C^7-C^{12}	120.7(9)	S^3-C^3-C^4	114.8(3)	114.8(3)
Cl^3-C^3-C^2	122.3(2)	C^7-C^8-C^9	119.9(2)	C^{17}-C^{18}-C^{21}	121(1)	S^{14}-C^{15}-C^{20}	123.0(8)	C^2-C^3-C^4	110.5(4)	109.5(4)
Cl^3-C^3-C^4	128.9(2)	C^8-C^9-C^{10}	121.9(2)	O^2-C^2-C^3	129.1(9)	C^2-C^3-C^4	107.3(7)	S^4-C^4-C^5	108.3(3)	107.6(3)
C^2-C^3-C^4	108.8(2)	C^9-C^{10}-C^{11}	117.7(2)	O^1-C^2-C^3	110.2(8)	S^6-C^3-C^2	117.0(7)	S^5-C^5-C^4	121.7(4)	120.6(4)
Cl^4-C^4-C^3	127.9(2)	C^9-C^{10}-C^{13}	121.3(2)	S^6-C^3-C^4	135.7(7)			O^1-C^5-C^4	122.0(5)	121.9(4)

Torsion angles

C^7-S^6-C^5-C^4	−45.2(2)	C^2-C^3-C^4-Cl^4	179.8(2)	$C^7S^6C^3C^4$	35(1)	$C^2O^1C^5O^5$	−125.1(8)	C^6-S^2-C^2-O^2	171.4(4)	−173.5(4)
C^5-S^6-C^7-C^{12}	128.2(2)	Cl^4-C^4-C^5-S^6	−56.7(3)	$C^3S^6C^7C^{12}$	−131.8(9)	$C^2O^1C^5C^4$	−0.2(9)	C^6-S^2-C^2-C^3	−9.9(5)	9.9(5)
C^5-S^6-C^7-C^8	−57.6(3)	C^3-C^4-C^5-O^1	0.3(3)	$C^3S^6C^7C^8$	54(1)	$C^5O^1C^2C^3$	1(1)	C^{13}-S^3-C^3-C^2	−70.8(4)	67.8(4)
C^7-S^6-C^5-O^1	73.7(2)	C^3-C^4-C^5-S^6	124.1(2)	$C^7S^6C^3C^2$	−147.3(7)	$O^1C^2C^3C^4$	−1(1)	C^{13}-S^3-C^3-C^4	52.6(4)	−55.2(4)
C^2-O^1-C^5-C^4	0.5(3)	Cl^4-C^4-C^5-O^1	179.6(2)	$C^4S^{14}C^{15}C^{16}$	-61.1(9)	$O^2C^2C^3C^4$	175(1)	C^4-S^4-C^{20}-C^{25}	86.6(5)	−89.1(5)
C^5-O^1-C^2-O^2	178.0(3)	C^{12}-C^7-C^8-C^9	−0.3(4)	$C^{15}S^{14}C^4C^3$	152.7(9)	$O^2C^2C^3S^6$	−2(1)	S^2-C^2-C^3-C^4	153.7(3)	−157.5(3)
C^2-O^1-C^5-S^6	−125.9(2)	S^6-C^7-C^8-C^9	−174.4(2)	$C^5O^1C^2O^2$	−176.4(8)	$O^1C^2C^3S^6$	−179.8(6)	O^2-C^2-C^3-S^3	98.4(5)	−100.1(5)
C^5-O^1-C^2-C^3	−1.1(3)	S^6-C^7-C^{12}-C^{11}	172.3(2)	$S^{14}C^4C^5O^5$	−58(1)	$S^6C^3C^4C^5$	179.1(8)	O^2-C^2-C^3-C^4	−27.7(6)	26.1(6)
O^2-C^2-C^3-Cl^3	3.5(4)	O^1-C^2-C^3-Cl^3	−177.5(2)	$C^3C^4C^5O^1$	−1(1)	$S^6C^3C^4S^{14}$	−2(1)	S^2-C^2-C^3-S^3	−80.3(4)	76.3(4)
O^2-C^2-C^3-C^4	−177.7(3)	Cl^3-C^3-C^4-C^5	177.8(2)	$S^6C^7C^8C^9$	175.5(8)	$C^2C^3C^4C^5$	1(1)	S^3-C^3-C^4-C^5	−175.4(3)	177.5(3)
O^1-C^2-C^3-C^4	1.3(3)	Cl^3-C^3-C^4-Cl^4	−1.5(4)	$S^6C^7C^{12}C^{11}$	−175.4(8)	$C^2C^3C^4S^{14}$	179.7(7)	C^2-C^3-C^4-C^5	−53.4(5)	54.8(5)
C^2-C^3-C^4-C^5	−1.0(3)			$C^3C^4C^5O^5$	119.5(9)	$S^{14}C^4C^5O^1$	−179.1(6)	S^4-C^4-C^5-S^5	−75.4(4)	79.5(4)

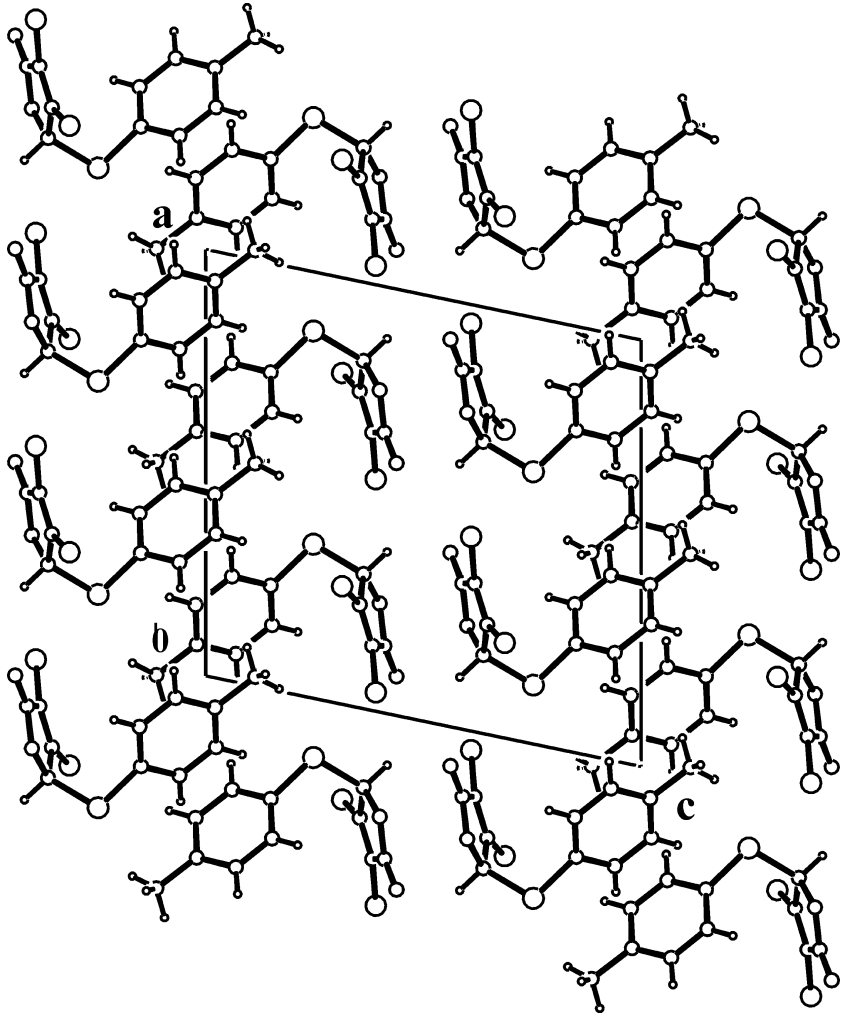


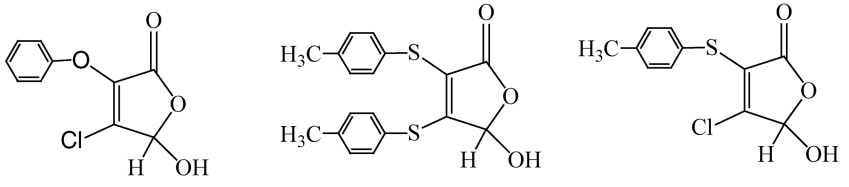
FIGURE 2 Packing in the crystal of compound **12**; projection is along the *b*-axis.

The planes of the benzene rings of neighboring molecules were parallel with an interplanar distance of 3.385 Å (Figure 2).

Thus, it was shown that in acidic and basic media, the attack of a nucleophile goes to different centers; differences in regioselectivity are connected with different mechanisms of reaction. We believe that in the presence of triethylamine, the substitution of the halogen atom at C_4 proceeds according to the well-known scheme of nucleophilic vinyl

substitution, which was shown earlier for related systems.[20] Under acidic conditions, the increasing electrophilicity of C_5 in the protonated form of mucochloric acid directs the nucleophilic attack of arylthiol (RSH) to this position of the lactone ring, which is followed by the elimination of a water molecule and of a proton to form the 5-thiosubstituted derivative of mucochloric acid.

The product of the chlorine substitution at C_3—4-chloro-5-hydroxy-3-phenoxy-2(5*H*)-furanone **17** (Scheme 5)—was obtained from the reaction of compound **1** with phenol in an aqueous solution containing an excess of potassium hydroxide.[21] It was shown that the opening of the lactone ring in the molecule of mucochloric acid and further attack of the nucleophile at the carbon atom in α-position to the carboxy group occurred in a basic medium; the cyclic product **17** was isolated after acidification of the reaction mixture.[21] It should be noted that in the case of 4-methylthiophenol, the product of 3,4-disubstitution **18** is the only compound formed under the same conditions: an aqueous solution of alkali (4.1 mol), 4-methylthiophenol (3.4 mol), and **1** (1 mol).



17 **18** **19**

SCHEME 5

The formation of the disubstitution product 3,4-di[(4-methylphenyl)thio]-5-hydroxy-2(5*H*)-furanone **18** was revealed by spectral data (Table I). Its crystal structure was determined by single crystal X-ray diffraction (Figure 3).

As in **12**, in **18** the furanone ring was planar. The carbonyl group and the sulfur atoms were positioned in the plane of the heterocycle. The corresponding bond length in the molecules of **12** and **18** coincided within the experimental error (Table II). A twisting of the double bond was not observed (torsion angle S_6-C_3=C_4-S_{14} -2[1]°), in spite of the even greater increase of bond angles $S_6C_3C_4$ 135.7(7) and $S_{14}C_4C_3$ 126.2(6)°. The dihedral angles between the planes of the benzene rings and the furanone ring in **18** were 67.9(5)° and 69.0(5)°. Interestingly, a difference in sulfur bond angles ($C_3S_6C_7$ 103.3[5]°, $C_4S_{14}C_{15}$ 100.8(4)°) was observed, most probably connected with a different steric strain of these arylthio fragments. The presence of the hydroxy group at C_5 determined

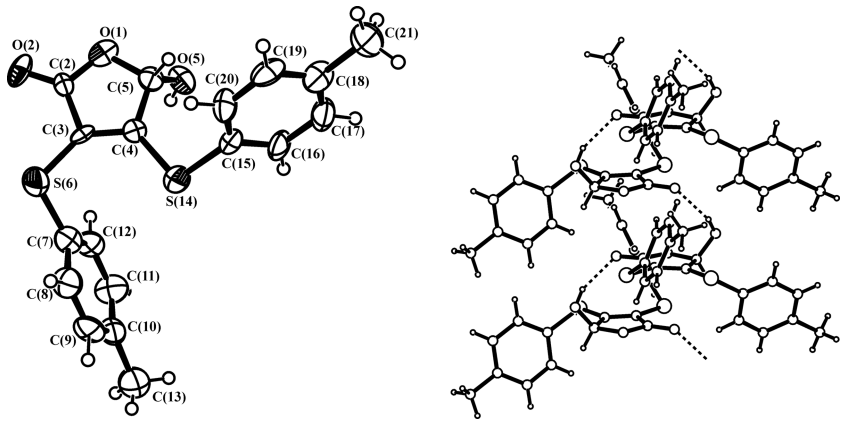


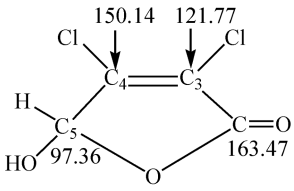
FIGURE 3 Molecular structure of 3,4-di[(4-methylphenyl)thio]-5-hydroxy-2(5*H*)-furanone **18** and hydrogen bonds in crystal.

packing in the crystal. The molecules of **18** formed infinite chains along the *b*-axis via O_5-$H_{51}\cdots O_2'$ (1−x,−1/2+y,1/2−z) hydrogen bonds (O─H 0.82, $H\cdots O_2'$ 2.04, $O_5\cdots O_2'$ 2.79[1] Å, O_5-$H_{51}\cdots O_2'$ is 154°). It must be noted that as in the case of **12**, stacking interactions in the crystal between the benzene rings at S_3 of neighboring molecules were observed (Figure 4). The benzene rings of neighboring molecules, connected by a center of symmetry, were parallel; the distance between the planes of the rings was 3.69 Å.

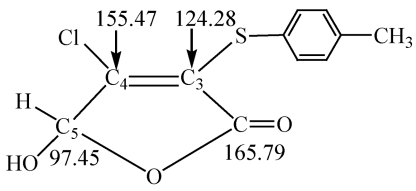
Variation of the reaction conditions allowed us to obtain the monosubstitution product at C_3 of the lactone ring **19**. Thus, two products, **18** and **19**, in a 1:1 ratio were isolated using the reagents in a 1:1:1 ratio and the same order of their mixing.

The ^{1}H NMR spectrum of **19** showed a singlet for the methine proton at C_5 (6.17 ppm), a singlet for methyl protons (2.30 ppm), signals of aromatic protons (7.1–7.6 ppm), and a broad signal for the OH proton (8.47 ppm) (Table I). The analysis of the ^{13}C NMR spectrum of compound **19** reveald, that the introduction of the thiotolyl moiety in place of the chlorine atom at C_3 results in the shift of all signals of carbon atoms of the lactone ring to a lower field compared to those of mucochloric acid (Scheme 6).

Interestingly, when the order mixing the reagents was different, viz. the alkaline solution of **1** was added dropwise to the alkaline solution of 4-methylthiophenol (ratio **1**:4-methylthiophenol:KOH of 1:1:2), products **18** and **19** were isolated in a ratio of 1:4. The monosubstituted furanone **19** was the only product of the reaction when the ratio of the reagents was 1:1:2 and when the alkaline solution of



1



19

SCHEME 6

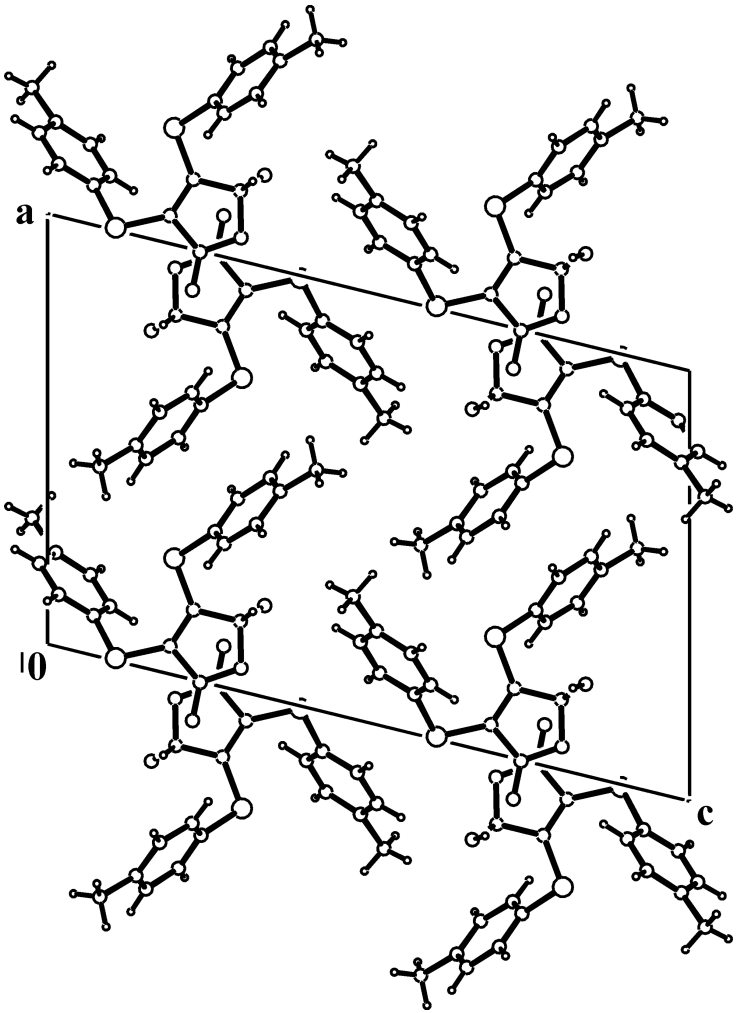
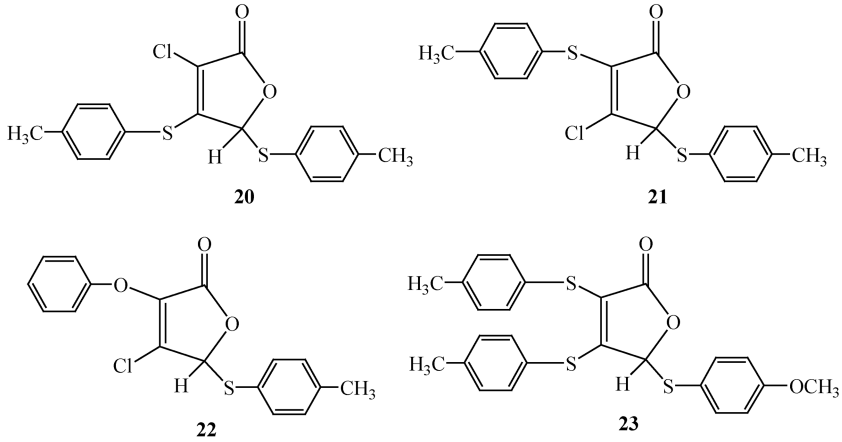


FIGURE 4 Packing in the crystal of compound **18**; projection is along the *b*-axis.

4-methylthiophenol was added dropwise to the alkaline solution of mucochloric acid.

Thus we have found that the variation of the ratio of the reagents and the order of their mixing affected the type and ratio of products of the reaction of mucochloric acid with 4-methylthiophenol in potassium hydroxide solution. Some suggestions can be offered for the explanation of this fact. When the solution of potassium mucochlorate is added to the alkaline solution of 4-methylthiophenol, in the moment of mixing there is an excess of thiol, which can attack the molecule of mucochloric acid at the two electrophilic centers C_3 and C_4; therefore, the disubstitution product **18** is formed along with the monosubstitution product **19**. On the contrary, when the alkaline solution of 4-methylthiophenol is added dropwise to the solution of potassium mucochlorate, there is a lack of *S*-nucleophile, which may cause the formation of only the α-monosubstitution product **19**.

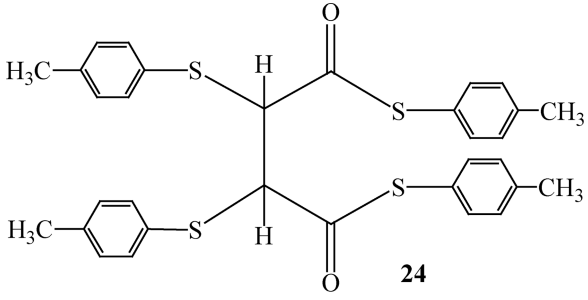
Products of 4,5-disubstitution (compound **20**) and 3,5-disubstitution (compounds **21** and **22**) were obtained for the first time under acidic conditions from the reaction of 4-methylthiophenol with the furanones **3**, **19**, and **17**, respectively (Scheme 7). Furanone **23** substituted in the three position was synthesized in a similar manner. Under boiling of 3,4-di[(4-methylphenyl)thio]-5-hydroxy-2(5*H*)-furanone **18** with 4-methoxythiophenol in benzene in the presence of concentrated sulfuric



SCHEME 7

acid, only one product was isolated, which, according to the spectral data (Table I), has the structure of 3,4-di[(4-methylphenyl)thio]-5-[(4-methoxyphenyl)thio]-2(5*H*)-furanone **23**.

In an attempt to obtain the product of 4,5-disubstitution **20** from 3,4-dichloro-5-[(4-methylphenyl)thio]-2-(5*H*)-furanone **12** and 4-methylthiophenol under basic conditions with triethylamine as a base, the acyclic product **24** was unexpectedly isolated (Scheme 8).



24

SCHEME 8

The IR spectrum of **24** showed the absorption band of the stretching vibration of the carbonyl group at 1700 cm^{-1} (strongly shifted to lower frequencies compared to the C=O bands of γ-lactones) and two bands in the range 1494 and 1596 cm^{-1}, assigned to the stretching vibrations of the aromatic system. The ^1H NMR spectrum of **24** displayed a singlet for methine protons at 4.16 ppm, two singlets for methyl protons at 2.38 and 2.33 ppm, and a multiplet for aromatic protons in the range 7.0–7.5 ppm (Table I). Structure determination by single crystal X-ray diffraction identified **24** as di-p-tolyl-2,3-bis-(p-tolylthio)butanedithioate (Figure 5).

There were two independent molecules A and B observed in the crystal of **24**. These independent molecules represent an enantiomeric pair. Chiral centers in the molecule A had an RR configuration, and in the molecule B, they had an SS configuration. The bond lengths and bond angles in the independent molecules were identical within experimental error (Table II). Both molecules slightly differed in conformation, with the maximal difference in the module of torsion angles not exceeding 10°.

Functional groups able to form hydrogen bonding were absent in **24**, but there was a large number of aromatic substituents. Therefore, the packing in the crystal of **24** was determined predominantly by stacking interactions. Parallel arrangement of benzene rings $C_{27} \div C_{32}$

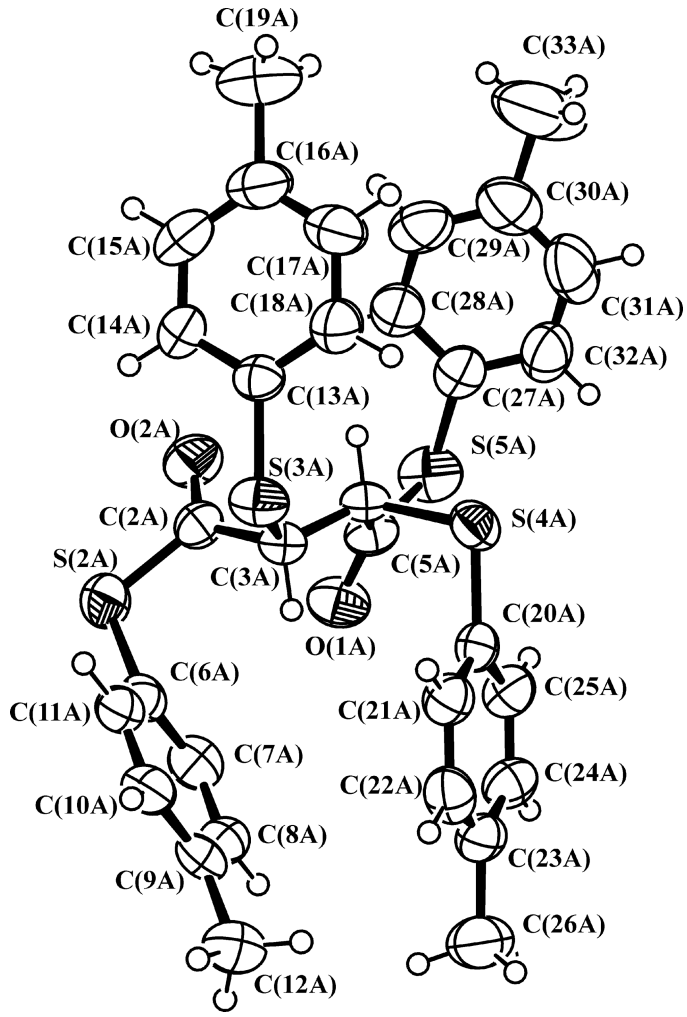


FIGURE 5 Molecular structure of the independent molecule A of compound **24** in the crystal.

of molecule A and $C_6 \div C_{11}$ of molecule B was observed with an interplanar distance of 3.62 Å (Figure 6).

Although for the moment it is difficult to explain the mechanism of the formation of the acyclic product **24**, we assume that this compound may be formed according to the mechanism outlined in Scheme 9.

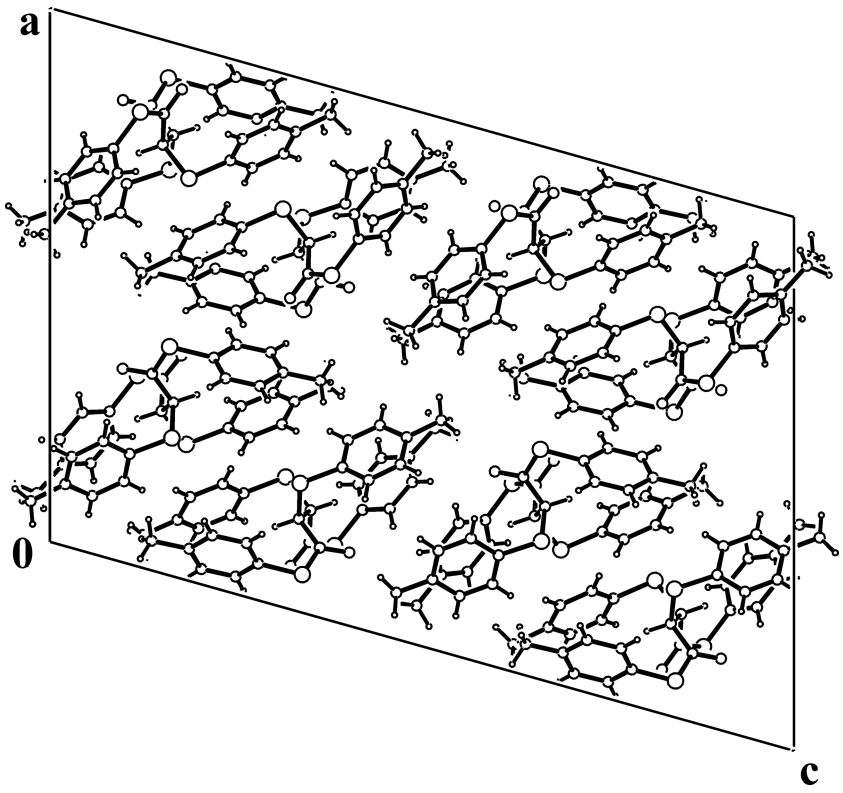
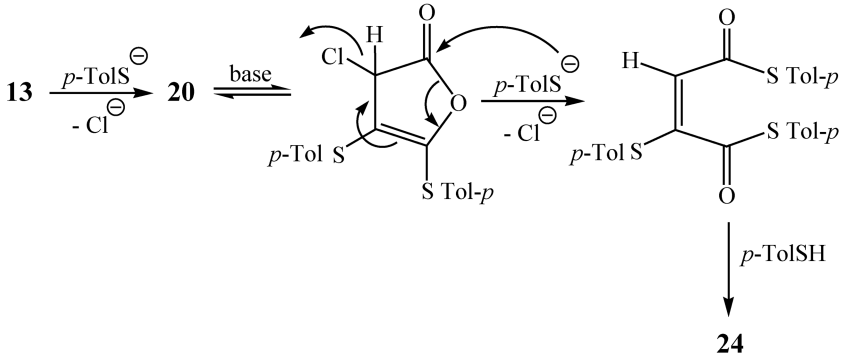


FIGURE 6 Packing in the crystal of compound **24**; projection is along the *b*-axis.



SCHEME 9

CONCLUSION

Reactions of mucochloric acid with aromatic and heterocyclic thiols were carried out under basic and acidic conditions. Different regioisomers as well as novel sulfur-containing products of trisubstitution and various types of disubstitution products were obtained when reactions were performed under different conditions.

EXPERIMENTAL

IR spectra were recorded on a Specord–M80 spectrometer in a solid state (in Nujol); the thickness of cell was $d = 0.1$–0.12 mm. NMR spectra were obtained on a Varian Unity–300 spectrometer at 299.94 MHz (^{1}H) and 75.13 MHz (^{13}C) and a Varian Gemini–200 spectrometer at 200 MHz (^{1}H) and 50.46 MHz (^{13}C) at 25°C with $CDCl_3$, and DMSO-d_6 was taken as internal standards. TLC was performed using Silufol UV-254 plates, processed in an iodide camera, and was fixed in water. Acetone–benzene 1:8 mixture was used as the eluent.

Mucochloric acid **1** was commercially available and was further recrystallised from water. M.p. 127°C (m.p. 127°C[22]). TLC, R_f 0.42. 3,4-Dichloro-5-ethoxy-2(5*H*)-furanone[20] **2** and 4-chloro-5-hydroxy-3-phenoxy-2(5*H*)-furanone[21] **17** were synthesized according to the known methods.

X-Ray Structure Determinations

The X-ray diffraction data for the crystals of **12**, **18**, and **24** were collected on a CAD4 Enraf-Nonius automatic diffractometer using graphite-monochromated MoK_α ($\lambda = 0.71073$ Å) radiation. Details of crystal data, data collection, and refinement are given in Table III. The stability of the crystals and the experimental conditions were checked every 2 h using three control reflections, while the orientation was monitored every 200 reflections by centering two standards. No significant decay was observed. Corrections for Lorentz and polarization effects were applied. Absorption correction was not applied. The structure was solved by direct method using the SIR[23] program and refined by full matrix least-squares using SHELXL97[24] program. All non–hydrogen atoms were refined anisotropically. The positions of the hydrogen atoms were idealized. All calculations were performed on a PC using the WinGX[25] program. Cell parameters, data collection, and data reduction were performed on an Alpha Station 200 computer

TABLE III Single-Crystal X-Ray Data for Structures of Compounds 12, 18, and 24

	12	**18**	**24**
Chemical formula	$C_{11}H_8O_2SCl_2$	$C_{18}H_{16}O_3S_2$	$C_{32}H_{30}O_2S_4$
Chemical formula weight	275.16	344.45	574.84
Space group	$P2_1/a$	$P2_1/c$	$P2_1/n$
	Cell parameters		
a(Å)	12.662(2)	13.380(4)	20.836(6)
b(Å)	7.167(2)	6.271(4)	9.860(2)
c(Å)	13.207(2)	20.559(8)	30.15(1)
β(deg)	101.77(1)	103.75(3)	105.69(5)
V (Å^3)	1173.3(3)	1676(1)	5962(6)
Z	4	4	8
D_x (mg m^{-3})	1.56	1.37	1.28
F(000)	560	720	2288
Crystal color	Colorless	Yellow	Colorless
Crystal form	Prismatic	Needle	Prismatic
Crystal size (mm)	0.8 × 0.6 × 0.5	0.9 × 0.06 × 0.02	0.4 × 0.4 × 0.2
Diffractometer used	Enraf-Nonius CAD-4		
Radiation (Å)	0.71073		
Temperature, (deg K)	293		
Scan mode	ω		
θ_{max} (deg)	26.29	22.77	26.32
Absorption correction	Not applied		
μ(cm^{-1})	7.05	3.15	3.32
Scan speed (deg · min^{-1})	Variable, 1–16.4		
Recorded reflections	2504	1766	5598
Independent reflections with $F^2 \geq 2\sigma(F^2)$	1659	568	3525
R_{int}	0.026	0.224	0.044
R_1	0.041	0.049	0.044
R_1 all data	0.065	0.282	0.096
ωR_2	0.110	0.050	0.102
ωR_2 all data	0.122	0.082	0.122
S	1.032	0.918	0.997

using the MoLEN[26] program. All figures were made using the programs ORTEP[27] and PLATON.[28]

Crystallographic data for the structures of **12**, **18**, and **24** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication No. CCDC-607651, CCDC-607652, and CCDC-607650, respectively. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk, www:http://www.ccdc.cam.ac.uk).

General Procedure for the Preparation of Furanones (3–11)

To a solution of mucochloric acid (1.00 g, 6 mmol) in absolute ether with intense stirring was added dropwise a solution of thiol (6 mmol) in ether and an ether solution of triethylamine (6 mmol). Weak warming of the reaction mixture and the formation of a white precipitate of $(C_2H_5)_3N{\cdot}\underline{HCl}$ was observed. The precipitate was filtered off and washed with ether (20 mL). The combined filtrates were evaporated to dryness and the obtained residue was crystallized from benzene.

3-Chloro-5-hydroxy-4-[(4-methylphenyl)thio]-2(5H)-furanone (3)

Yield 1.32 g (86%), m.p. 126°C, TLC R_f: 0.36. Anal. calcd. for $C_{11}H_9ClO_3S$: C, 51.47; H, 3.53; Cl, 13.81; S, 12.49%. Found: C, 51.28; 51.10; H, 3.27, 3.24; Cl, 13.36, 13.22; S, 12.23, 12.29%.

3-Chloro-4-[(4-ethylphenyl)thio]-5-hydroxy-2(5H)-furanone (4)

Yield 1.14 g (70%), m.p. 112°C, TLC R_f: 0.39. Anal. calcd. for $C_{12}H_{11}ClO_3S$: C, 53.24; H, 4.10; Cl, 13.10; S, 11.84%. Found: C, 53.32, 53.35; H, 4.27, 4.31; Cl, 13.79, 14.06; S, 12.10, 12.16%.

3-Chloro-5-hydroxy-4-[(1-naphthyl)thio]-2(5H)-furanone (5)

Yield 0.47 g (27%), m.p. 179°C, TLC R_f: 0.30. Anal. calcd. for $C_{14}H_9ClO_3S$: C, 57.44; H, 3.10; Cl, 12.11; S, 10.95%. Found: C, 57.32, 57.64; H, 3.18, 3.14; Cl, 12.68; S, 11.22, 11.22%.

3-Chloro-4-[(4-chlorophenyl)thio]-5-hydroxy-2(5H)-furanone (6)

Yield 1.63 g (98%), m.p. 138°C, TLC R_f: 0.71. Anal. calcd. for $C_{10}H_6Cl_2O_3S$: C, 43.34; H, 2.18; Cl, 25.59; S, 11.57%. Found: C, 45.69; H, 3.94; Cl, 25.37; S, 11.29%.

4-[(4-Bromophenyl)thio]-3-chloro-5-hydroxy-2(5H)-furanone (7)

Yield 1.79 g (93%), m.p. 158°C, TLC R_f: 0.41. Anal. calcd. for $C_{10}H_6BrClO_3S$: C, 37.35; H, 1.88; Br, 24.85; Cl, 11.02; S, 9.97%. Found: C, 36.52, 36.27; H, 1.28, 1.42; Br, 23.62, 23.52; Cl, 10.49, 10.45; S, 9.70, 9.67%.

4-[(3-Bromophenyl)thio]-3-chloro-5-hydroxy-2(5H)-furanone (8)

Yield 1.10 g (57%), m.p. 108°C (from hexane), TLC R_f: 0.39. Anal. calcd. for $C_{10}H_6BrClO_3S$: Br, 24.85; Cl, 11.02; S, 9.97%. Found: Br, 23.42; Cl, 10.39; S, 9.62%.

3-Chloro-4-[(4-chlorophenyl)thio]-5-etoxy-2(5H)-furanone (9)

This was synthesized from ether **2** (6 mmol) and 4-chlorothiophenol following a general procedure. Yield 1.70 g (93%), m.p. 72°C (from petroleum ether), TLC R_f: 0.68. Anal. calcd. for $C_{12}H_{10}Cl_2O_3S$: C, 47.23; H, 3.30; Cl, 23.23; S, 10.51%. Found: C, 49.95; H, 4.33; Cl, 22.77; S, 10.90%.

3-Chloro-5-hydroxy-4-[(3-methyl-1-phenylpyrazolyl-5)thio]-2(5 H)-furanone (10).

Yield 0.87 g (45%), m.p. 185°C, TLC R_f: 0.46.

4-[(4-Benzoyl-3-methyl-1-phenylpyrazolyl-5)thio]-3-chloro-5-hydroxy-2(5H)-furanone (11)

Yield 1.23 g (48%), m.p. 128°C, TLC R_f: 0.29. Anal. calcd. for $C_{21}H_{15}ClN_2O_4S$: C, 59.09; H, 3.54; Cl, 8.31; S, 7.51%. Found: C, 58.60; H, 3.91; Cl, 9.78; S, 6.64%.

General Procedure for the Preparation of Furanones (12–16) and (20–23)

A solution of mucochloric acid (5.77 g, 34.2 mmol), thiophenol (34.2 mmol), and concentrated sulfuric acid (0.7 mL) in benzene (75 mL) was refluxed in a round-bottom flask supplied with a reflux condenser and adapter for the azeotropic evaporation of water for 3 h. After cooling to r.t. the benzene solution was washed with water until neutral reaction and dried over $MgSO_4$. The solvent was evaporated, and the residue was mixed with petroleum ether and cooled to −10–0°C. The solid thus obtained was filtered and crystallized from hexane.

3,4-Dichloro-5-[(4-methylphenyl)thio]-2(5H)-furanone (12)

Yield 7.81 g (83%), m.p. 46°C, TLC R_f: 0.80. Anal. calcd. for $C_{11}H_8Cl_2O_2S$: C, 48.02; H, 2.93; Cl, 25.77; S, 11.65%. Found: C, 47.34; H, 2.44; Cl, 26.30; S, 14.27%.

3,4-Dichloro-5-[(1-naphthyl)thio]-2(5H)-furanone (13)

Yield 7.55 g (71%), m.p. 122°C (from CCl_4), TLC R_f: 0.77.

5-[(4-Chlorophenyl)thio]-3,4-dichloro-2(5H)-furanone (14)

Yield 8.49 g (84%), m.p. 80°C, TLC R_f: 0.79. Anal. calcd. for $C_{10}H_5Cl_3O_2S$: C, 40.64; H, 1.71; Cl, 35.98; S, 10.85%. Found: C, 40.38; H, 1.73; Cl, 36.85; S, 11.70%.

5-[(3-Bromophenyl)thio]-3,4-dichloro-2(5H)-furanone (15)

Yield 8.60 g (74%), m.p. 58°C (from a hexane/CCl_4 mixture), TLC R_f: 0.80. Anal. calcd. for $C_{10}H_5BrCl_2O_2S$: C, 35.33; H, 1.48; Br, 23.50; Cl, 20.85; S, 9.43%. Found: C, 31.19; H, 1.33; Br, 20.89; Cl, 18.54; S, 11.79%.

3,4-Dichloro-5-[(4-methoxyphenyl)thio]-2(5H)-furanone (16)

Yield 8.26 g (83%), m.p. 67°C, TLC R_f: 0.69. Anal. calcd. for $C_{11}H_8Cl_2O_3S$: C, 45.38; H, 2.77; Cl, 24.35; S, 11.02%. Found: C, 46.19, 46.48; H, 3.83, 3.65; Cl, 23.61; S, 14.41%.

Synthesis of 3,4-Di[(4-methylphenyl)thio]-5-hydroxy-2(5 H)-furanone (18)

To a solution of 4-methylthiophenol (2 g, 16.1 mmol) and potassium hydroxide (1.09 g, 19.4 mmol) in water (2.5 mL) was added mucochloric acid (1.2 g, 4.7 mmol) slowly with intense stirring. A weak warming of the reaction mixture and the formation of a precipitate was observed. The precipitate was filtered off, and dissolved in water, and the solution was acidified by diluted hydrochloric acid. The bright yellow solid thus obtained was filtered and recrystallized from a benzene/petroleum ether mixture (the ratio was 2:1). Yield 1.05 g (65%), m.p. 158°C, TLC R_f: 0.84. Anal. calcd. for $C_{18}H_{16}O_3S_2$: C, 62.76; H, 4.68; S, 18.62%. Found: C, 62.19; H, 4.82; S, 21.32%.

Synthesis of 4-Chloro-5-hydroxy-3-[(4-methylphenyl)thio]-2(5 H)-furanone (19)

To a solution of mucochloric acid (2.47 g, 14.6 mmol) and potassium hydroxide (0.82 g, 14.6 mmol) in water (10 mL) was added slowly with intense stirring a solution of 4-methylthiophenol (1.81 g, 14.6 mmol) and potassium hydroxide (0.82 g, 14.6 mmol) in water (20 mL). Weak warming of the reaction mixture and the formation of a precipitate were observed. The precipitate was filtered off and dissolved in water, and the solution was acidified by diluted hydrochloric acid. The obtained oil was recrystallized from carbon tetrachloride. Yield 2.51 g (67%), m.p. 95°C, TLC R_f: 0.29. Anal. calcd. for $C_{18}H_{16}ClO_3S$: C, 51.46; H, 3.53; Cl, 13.81; S, 12.49%. Found: C, 51.37; H, 3.60; Cl, 13.60; S, 15.06%.

3-Chloro-4,5-di[(4-methylphenyl)thio]-2(5 H)-furanone (20)

This was synthesized following the general procedure from furanone **3** (0.8 g, 3.1 mmol) and 4-methylthiophenol. Yield 0.65 g (58%), m.p. 113°C, TLC R_f: 0.90.

4-Chloro-3,5-di[(4-methylphenyl)thio]-2(5 H)-furanone (21)

This was synthesized following the general procedure from furanone **19** (0.8 g, 3.1 mmol) and 4-methylthiophenol. Yield 0.69 g (61%), m.p. 90°C. Anal. calcd. for $C_{18}H_{15}ClO_2S_2$: C, 59.57; H, 4.17%. Found: C, 61.03; H, 3.61%.

4-Chloro-5-[(4-methylphenyl)thio]-3-phenoxy-2(5 H)-furanone (22)

This was synthesized following the general procedure from furanone **17** (2.0 g, 8.3 mmol) and 4-methylthiophenol. Yield 2.0 g (73%), m.p. 88°C. Anal. calcd. for $C_{17}H_{13}ClO_3S$: C, 61.35; H, 3.94%. Found: C, 62.54; H, 3.92%.

3,4-Di[(4-methylphenyl)thio]-5-[(4-methoxylphenyl)thio]-2(5 H)-furanone (23)

This was synthesized following the general procedure from furanone **18** (0.8 g, 2.3 mmol) and 4-methoxythiophenol. Yield 0.62 g (57%), m.p. 109°C (from hexane / CCl_4), TLC R_f: 0.67.

Synthesis of Di-p-tolyl-2,3-bis-(p-tolylthio)butanedithioate (24)

To a solution of furanone **12** (1.18 g, 4.3 mmol) in absolute ether (10 mL) with intense stirring was added dropwise a solution of 4-methylthiophenol (0.53 g, 4.3 mmol) in ether and an ether solution of triethylamine (0.60 mL, 4.3 mmol). The precipitated $(C_2H_5)_3N{\bullet}HCl$ was filtered off and washed with ether (20 mL). The filtrate was evaporated, and the obtained white solid residue was crystallized from petroleum ether. Yield 0.57 g (69%), m.p. 107°C, TLC R_f: 0.76. Anal. calcd. for $C_{32}H_{30}O_2S_4$: C, 66.86; H, 5.26; S, 22.31%. Found: C, 67.01; H, 5.16; S, 22.13%.

REFERENCES

[1] A. A. Avetisyan and M. T. Dangyan, *Usp. Khim.*, **46,** 1250 (1977).
[2] Y. S. Rao, *Chem. Rev.,* **64,** 353 (1964).
[3] F. Bellina and R. Rossi, *Curr. Org. Chem*., **8,** 1089 (2004).
[4] J. Zhang, P. G. Blazecka, D. Belmont, and J. G. Davidson, *Org. Lett*., **4,** 4559 (2002).

[5] J. Zhang, P. G. Blazecka, H. Berven, and D. Belmont, *Tetrahedron Lett*., **44,** 5579 (2003).
[6] J. Zhang, P. G. Blazecka, and J. G. Davidson, *Org. Lett*., **5,** 553 (2003).
[7] P. G. Blazecka, D. Belmont, T. Curran, D. Pfum, and J. Zhang, *Org. Lett*., **5,** 5015 (2003).
[8] J. Zhang, K. Das Sarma, T. T. Curran, D. T. Belmont, and J. G. Davidson, *J. Org. Chem*., **70,** 5890 (2005).
[9] J. Maki, R. Sjoholm, and L. Kronberg, *J. Chem. Soc., Perkin Trans. 1.,* **20,** 2923 (1999).
[10] D. Asplund, L. Kronberg, R. Sjoholm, and T. Munter, *Chem. Res. Toxicol.,* **8,** 841 (1995).
[11] F. Zanker and F. Reicheneder, Ger. Offen. 2,032,709 (1972); *Chem. Abstr.,* **76,** 140252 (1972).
[12] T. I. Bobrova, S. D. Volodkovich, and S. S. Kukalenko, *Zh. Obshch. Khim*., **44,** 390 (1972).
[13] A. R. Kurbangalieva, A. V. Bogdanov, A. I. Movchan, and G. A. Chmutova, *Zh. Org. Khim*.,**40,** 1263 (2004).
[14] T. I. Bobrova, S. D. Volodkovich, and S. S. Kukalenko, *Zh. Obshch. Khim*., **45,** 1123 (1975).
[15] H. Arahori and N. Sato, Jpn. Kokai Tokkyo Koho 63,170,370 (1988); *Chem. Abstr.*, **110,** 8030 (1988).
[16] H. Arahori and N. Sato, Jpn. Kokai Tokkyo Koho 63,170,371 (1988); *Chem. Abstr.*, **110,** 8031 (1988).
[17] V. M. Bzhezovsky, Ph.D. Thesis, Irkutsk, USSR, 1977.
[18] V. D. Simonov, E. N. Shitova, Ya. B. Yasman, A. F. Galieva, and V. Z. Estrina, *Zh. Org. Khim*., **14,** 519 (1978).
[19] K. Hartke and F. Rauschen, *J. Pract. Chem.*, **1,** 15 (1997).
[20] S. Ducher and A. Michet, *Bull. Soc. Chim. Fr*., **11,** 1923 (1976).
[21] N. P. Buu-Hoï, M. Dufour, and P. Jacquignon, *Bull. Soc. Chim. Fr.*, **8,** 2999 (1971).
[22] L. M. Kogan, T. I. Bobrova, and N. M. Burmakin, *Zh. Prikl. Khim*., **43,** 926 (1970).
[23] A. Altomare, G. Cascarano, C. Giacovazzo, and D. Viterbo, *Acta Crystallogr. A.*, **47,** 744 (1991).
[24] G. M. Sheldrick, SHELXL97, V. 5.10, 1997, Bruker AXS Inc., Madison, WI, USA.
[25] L. J. Farrugia, *J. Appl. Cryst.*, **32,** 837 (1999).
[26] L. H. Straver and A. J. Schierbeek, MolEN. Structure Determination System, Program Description (Nonius B.V., Delft, Netherlands, 1994), Vol. 1, Part 2, 180p.
[27] L. J. Farrugia, *J. Appl. Cryst.*, **30,** 565 (1997).
[28] A. L. Spek, *Acta Cryst. A*, **46,** 34 (1990).