4-Benzoyl-5-phenyl-1,3-oxathiol-2-one. Synthesis and Reaction with *N*-Nucleophiles

Chang He-Xi and Gert Kollenz*

Institute of Organic Chemistry, Isotope Department,
University of Graz, A-8010 Graz, Austria

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The synthesis of 4-benzoyl-5-phenyl-1,3-oxathiol-2-ones **1** and the behaviour of **1a** against several amines were investigated to afford aminomercaptoethenes **2** or thiocarbamates **3**, as well as complete cleavage to sulfur, dibenzoylmethane and the corresponding urea, depending on the nature of the *N*-nucleophile used.

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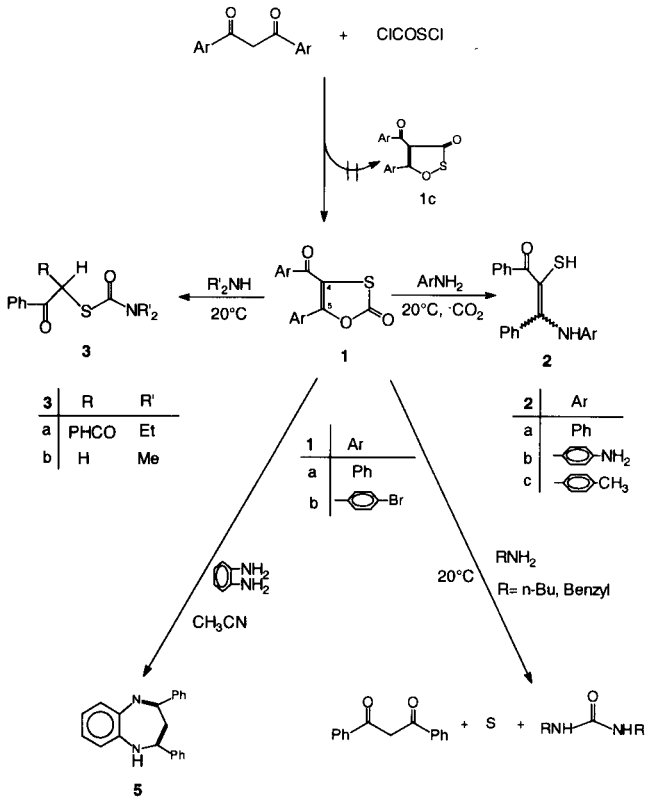
Chlorocarbonylsulfenyl chloride, easily prepared from trichloromethansulfenyl chloride by an improved method [1], was found to be a suitable cyclization reagent [2], in particular to prepare heterocyclic systems possessing biological activity in the herbicide and insecticide area [3].

Oxathiolones, in general usually obtained from cyclocondensation reaction of ketones and chlorocarbonylsulfenyl chloride [4,6], have found practical application as agricultural bactericides [5]. In this paper, 1,3-diketones (dibenzoylmethane, *p,p'*-dibromodibenzoylmethane) are used as ketones and cyclized with chlorocarbonylsulfenyl chloride to afford new oxathiolones, namely 4-aroyl-5-aryl-1,3-oxathiol-2-ones **1**. The yield of **1a** (from dibenzoylmethane) is 93%, using di-*p*-bromobenzoylmethane **1b** was obtained in 26% yield only. Obviously the bromo-substituent decreases the nucleophilic activity of the 1,3-diketone.

Scheme 1



Besides elemental analysis, the structure of **1a** was confirmed from ir and ^{13}C nmr spectroscopic data: In the ir spectrum, the absorption band at 1745 cm^{-1} is assigned to the lactone carbonyl, which agrees well with data found from similar oxathiolones [6]. In the ^{13}C nmr spectrum, the signals due to C=O and O=C-O appeared at 189 (t) and 170 ppm (s) respectively, the signals at 118.8 (s) and 153.5 ppm (t) were assigned to C-4 and C-5. Deduced from an INADEQUATE-one dimensional experiment, which exhibited no coupling of the ring C=O carbon, the isomeric 1,2-oxathiol-3-one structure **1c** was ruled out.

The oxathiolone **1a** then was subjected to reactions with several amines (Scheme 1), which showed a surprising reaction pattern depending on the nature of the amine.

Primary aromatic amines obviously attack C-5 of the oxathiolone ring. After ring opening decarboxylation occurs leading to the aminomercapto-ethenes **2**. This reaction pathway is close to the well known nucleophilic substitution at a vinyl carbon. Due to several mechanistic alternatives for such reactions no evidence can be given concerning *E*/*Z* isomerism [7]. The 1,2-aminomercapto-ethene moiety (*Z*-configuration) is usually present in *o*-mercaptoaniline, 1,4-thiazines, and related cyclic systems [8], but very seldom found in open chain compounds [9].

The basic structure of **2a** is strongly supported by its ^{13}C nmr spectrum: The signal at 199.16 ppm (t) is assigned to Ph-C=O, the signals of -N-C= and =C-SH appear at 169.5 ppm (m) and 101.67 ppm (d), respectively. In the ir spectra of **2b**, the NH_2 is found at 3340, 3440 cm^{-1}, the ^1H nmr spectrum of **2b** exhibits a signal at 5.15 ppm (broad, 2H, NH_2) besides the aromatic protons. The ^{13}C nmr spectrum of **2b** is similar to that of **2a**. Signals at 197, 169 and 99 ppm were assigned to Ph-C=O, NH-C= and HS-C= carbons. Further reactions of **1a** with *p*-nitroaniline and diphenylamine failed.

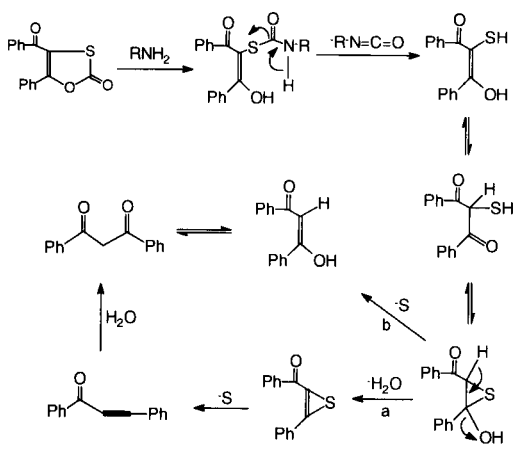
Unlike the primary aromatic amines dialkyl amines attack C-2 of the oxathiolone ring and with cleavage of the lactone moiety compounds **3** were obtained in 81-84% yield. In the case of dimethylamine, which was used in 40% water solution, additional hydrolytic cleavage of the benzoyl group (→ benzoic acid) took place. Obviously the considerable stronger basicity of secondary amines (p*K*

value differences approximately 5-6) [10] should be responsible for that different behaviour.

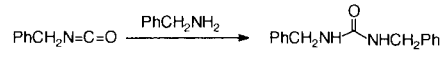
In principle two types of urethanes, namely thiocarbamates or carbamates, could be formed after the amine's attack to the carbonyl group of the oxathiolone ring, depending on wether the C-S- or the C-O- bond is broken. To distinguish between those molecules slight differences in their ir spectra could be helpful, but nevertheless some overlap could be observed. Usually the carbonyl absorption band of thiocarbamates is found between 1690-1640 cm^{-1}, while the carbamates absorb in the 1720-1680 cm^{-1} region [11]. In the ir spectra of **3a**, the carbonyls absorb at 1700, 1660 cm^{-1}, respectively, but no -SH absorption was found, which normally should be observed at 2600-2550 cm^{-1} (weak) [12,13b]. In the ^1H nmr of **3a** besides the ethyl group (1.2, 3.4 ppm) and the characteristical C-H signal (s, 7.01 ppm) the aromatic signals at 7.40-7.64 ppm (m, 6H) and 8.0-8.1 ppm (d, 4H) support the existence of two highly symmetrical benzoyl groups. This was further confirmed by the ^{13}C nmr spectrum of **3a**. Only one signal is found for the benzoyl-carbons at 192.3 ppm (t), the thiocarbamate carbonyl is observed at 164.1 ppm (dt), respectively. The signal for the sp^3 C-H appears at 57.3 ppm (d) thus ruling out the carbamate structure and confirming the presence of the diketo-tautomeric form of **3a** in solution. The ^1H nmr of **3b** also strongly supports the *S*-urethan-structure by the signal at 4.45 ppm (s, 2H, CH_2), since from the isomeric *O*-urethane formation of a Ph-C(O)CH_2-S- moiety could hardly be understandable. Here it is worthwhile to note, that with unsubstituted 4,5-dihydro-oxathiol-2-one itself, attacked by several primary and secondary amines, the C-S- bond is broken exclusively to afford carbamates and/or - after decarboxylation - the corresponding aminoethanethiols [13].

When aliphatic primary amines reacted with **1a**, the overall reaction proceeds *via* a different way. From a complete fragmentation of **1a** elemental sulfur, dibenzoylmethane and the corresponding urea (with benzylamine) were obtained, separated by chromatography (see Experimental). A possible reaction mechanism for that surprising fragmentation sequence is shown in Scheme 2.

Scheme 2



The primary attack of the amine - similar to the reaction with secondary amines - should open the oxathiolone ring to afford the corresponding *S*-urethane. This could eliminate isocyanate [14] leading to a thioenole system which should tautomerize to the mercaptodiketone intermediate [15]. Mercaptoketones are described to extrude sulfur after treatment with primary amines thus regenerating the ketones themselves, but no further mechanistic considerations on that desulfurization process are discussed [16]. We consider an oxo-cyclotautomerism to a thiirane intermediate to be the next step, followed (route a) by elimination of water thus generating a highly reactic thiirene [17]. Thiirenes are known to be able to decompose to acetylene derivatives, affording elemental sufur as by-product [17]. The ketone (dibenzoylmethane) then can easily come out from addition of water to the benzoylphenylacetylene intermediate. It is also reported - route b - that thiiranes themselves can extrude sulfur forming the corresponding ethene derivatives, in particular, if they have aryl- and/or electron withdrawing substituents [18]. Consequently, the thiirane intermediate here could directly afford dibenzoylmethane. The formation of the *N,N'*-dibenzylurea should be the result of addition of further amine to the primary formed isocyanate:



In the case of *n*-butylamine, no urea was detected, but this could be due to the fact that the eliminated butyl isocyanate (bp 115°) is removed during work-up of the reaction mixture (evaporating).

2,4-Diphenyl-1,5-benzodiazepine **5** [19] is the product from reaction of **1a** with *o*-phenylendiamine. As proved by an independent synthesis, this apparently is the result of condensation between *o*-phenylendiamine and dibenzoylmethane, the latter again derived from the decomposition of the oxathiolone **1a** (see discussion above).

EXPERIMENTAL

Melting points were determined on a Tottoli Apparatus and are uncorrected. Elemental Analyses were performed with a Carlo Erba Elemental Analyzer. Ir spectra were recorded on a Perkin-Elmer 421. The ^1H and ^{13}C nmr spectra were obtained on a Varian 200 Gemini spectrometer with TMS as internal standard.

4-Benzoyl-5-phenyl-1,3-oxathiol-2-one (**1a**).

Dibenzoylmethane (2.17 g, 9.7 mmoles) mixed with 3.52 g (27 mmoles) of chlorocarbonylsulfenyl chloride, was heated at 80° for 2 hours. Then the temperature was increased to 100° for an additional 2 hours. After cooling, the faint yellow solid was washed with petroleum ether and ether; it is already of high purity, yield

2.56 g (93%). The product can also be recrystallized from *n*-butanol, mp 92°; ir (potassium bromide): 1745, 1630 cm^{-1}; ^{13}C nmr (deuteriochloroform): 189.7 (t, Ph-C=O), 170.3 (s, O=C-O), 153.5 (t, O-C=), 118.8 (s, S-C=), 128-138.5 (aromatic carbons).

Anal. Calcd. for $C_{16}H_{10}O_3S$: C, 68.09; H, 3.55; S, 11.35. Found: C, 68.20; H, 3.60; S, 11.55.

4-*p*-Bromobenzoyl-5-*p*-bromophenyl-1,3-oxathiol-2-one (**1b**).

Di-*p*-bromobenzoylmethane (0.5 g, 1.3 mmoles) and 1 g of chlorocarbonylsulfenyl chloride (7.6 mmoles) were heated at 85-100° for 8 hours. After cooling, ether and petroleum ether (2:1) were added to the mixture and a light yellow crude material precipitated, which was recrystallized from *n*-butanol, yield 0.15 g (26%), mp 130°; ir (potassium bromide): 1740, 1640 cm^{-1}.

Anal. Calcd. for $C_{16}H_8O_3SBr_2$: C, 43.64; H, 1.82. Found: C, 43.65; H, 1.98.

1-Benzoyl-1-mercapto-2-phenyl-2-phenylaminoethylene (**2a**).

Compound **1a** (0.4 g, 1.4 mmoles) was mixed with 0.6 ml (6.6 mmoles) of freshly distilled aniline and stirred at room temperature for 2 days. Ether was then added to the mixture to afford 0.3 g of crude product which was recrystallized from ethanol, yield 0.15 g (33%), mp 190°; ir (potassium bromide): 1600, 1540, 1500 cm^{-1}; ^{13}C nmr (deuteriochloroform): 199.16 (t, Ph-C=O), 169.54 (m, N-C=), 101.67 (d, HS-C=), 123-143 (aromatic carbons).

Anal. Calcd. for $C_{21}H_{17}NOS$: C, 76.13; H, 5.14; N, 4.23; S, 9.67. Found: C, 75.85; H, 4.94; N, 4.14; S, 9.38.

1-Benzoyl-1-mercapto-2-phenyl-2-(*p*-phenylendiamino)ethylene (**2b**).

Compound **1a** (0.3 g, 1.05 mmoles) and 0.2 g (1.85 mmoles) of *p*-phenylendiamine, mixed with 5 ml of acetonitrile, were stirred at room temperature for 20 hours to give 0.25 g of yellow solid, recrystallized twice from acetone, yield 0.15 g (41%), mp 162°; ir (potassium bromide): 3440, 3340, 1625, 1540, 1515 cm^{-1}; ^1H nmr (DMSO-d_6): 5.15 (s, 2H, NH_2), 6-7.5 (m, Ar-H, NH, SH); ^{13}C nmr (DMSO-d_6): 197 (Ph-C=O), 169 (N-C=), 99 (HS-C=O), 113-147 (aromatic carbons).

Anal. Calcd. for $C_{21}H_{18}N_2OS$: C, 72.83; H, 5.20; N, 8.09; S, 9.25. Found: C, 72.64; H, 4.85; N, 7.81; S, 8.92.

1-Benzoyl-1-mercapto-2-phenyl-2-(4-tolylamino)ethylene (**2c**).

To 0.3 g (2.8 mmoles) of *p*-toluidine, dissolved in 4 ml of ether, 0.2 g (0.7 mmole) of **1a** was added and the mixture was stirred at room temperature for 2 days. After suction, 0.22 g yellow solid was obtained and recrystallized twice from ethanol, yield 0.14 g (57%), mp 200°; ir (potassium bromide): 1600, 1540 cm^{-1}.

Anal. Calcd. for $C_{22}H_{19}NOS$: C, 76.52; H, 5.51; N, 4.06; S, 9.28. Found: C, 76.70; H, 5.43; N, 4.01; S, 9.37.

N,N-Diethyl-*S*-dibenzoylmethylthiocarbamate (**3a**).

Diethylamine (0.37 ml, 3.6 mmoles) was added dropwise to an etheral solution of 0.2 g (0.7 mmole) of **1a**. The mixture was kept at room temperature for 6 hours with stirring. After suction, the light yellow solid was recrystallized from petroleum ether, yield 0.2 g (81%), mp 105°; ir (potassium bromide): 1700, 1660 cm^{-1}; ^1H nmr (deuteriochloroform): 1.2 (t, 6H, 2 CH_3), 3.4 (4H, 2 CH_2), 7.01 (s, 1H, C-H), 7.2-8.2 (m, 10H, Ar-H); ^{13}C nmr (deuteriochloroform): 192.3 (t, C=O), 164.1 (dt, O=C-N), 135.2, 133.9, 129.1, 128.9 (aromatic carbons), 57.3 (d, C-H), 42.8 (t, CH_2), 12.5 ppm (q, CH_3).

Anal. Calcd. for $C_{20}H_{21}NO_3S$: C, 67.61; H, 5.92; N, 3.94; S, 9.01. Found: C, 67.51; H, 5.99; N, 3.87; S, 8.80.

N,N-Dimethyl-*S*-benzoylmethylthiocarbamate (**3b**).

Compound **1a** (0.3 g, 1.05 mmoles) and 0.5 ml (9.9 mmoles) of dimethylamine (40% aqueous solution) was stirred at room temperature for 15 hours. Then 10 ml of ether was added to the mixture and the ether layer separated and evaporated. The residue was recrystallized from petroleum ether, yield 0.2 g (84%), mp 80°; ir (potassium bromide): 1695, 1645 cm^{-1}; ^1H nmr (deuteriochloroform): 3.05 (s, 6H, 2 CH_3), 4.45 (s, 2H, CH_2), 7.3-8.2 (m, 5H, Ar-H).

Anal. Calcd. for $C_{11}H_{13}NO_2S$: C, 59.19; H, 5.83; N, 6.28. Found: C, 59.32; H, 5.68; N, 6.21.

Reaction of Benzylamine with **1a**.

Benzylamine (0.43 ml, 3.9 mmoles) was added dropwise to an ether solution of 0.2 g (0.7 mmole) of **1a** and stirred at room temperature for 5 hours. After suction, the crude product was recrystallized from ethanol, identified [20] from mp and tlc as *N,N'*-dibenzylurea, yield 0.1 g (59%), mp 165°, (167°) [20]; ir (potassium bromide): 3320, 1625 cm^{-1}.

Anal. Calcd. for $C_{15}H_{16}N_2O$: C, 75.00; H, 6.66; N, 11.66. Found: C, 74.90; H, 6.54; N, 11.57.

The ether filtrate of *N,N'*-dibenzylurea was evaporated to dryness and the residue separated by silica gel column chromatography, using chloroform and petroleum ether (1:1, 6:4, 7:3) as eluents. Two fractions were obtained: elemental sulfur (11 mg, 49%) and dibenzoylmethane (50 mg, 32%), mp 76°.

Reaction of *n*-Butylamine with **1a**.

Diluted butylamine (0.2 ml of butylamine in 2 ml of ether, 2 mmoles) was added dropwise to an ether solution of 0.2 g (0.7 mmole) of **1a**. The mixture was stirred at room temperature for 3 hours, then evaporated to dryness. A small amount of ether was added again to the residue forming a crystalline solid, recrystallized from *n*-butanol. Elemental analysis shows that it is pure sulfur (98%), mp 118°, yield 13 mg (58%).

The ether filtrate of sulfur was concentrated. The residue was crystallized from methanol, yield 35 mg (22%), mp 78°. This product was identified as dibenzoylmethane (mp, tlc).

2,4-Diphenyl-1,5-benzodiazepine (**5**).

A mixture of 0.3 g (1.05 mmoles) of **1a**, 0.22 g (2 mmoles) of *o*-phenylendiamine and 3 ml of acetonitrile was refluxed for 12 hours. After evaporation 5 ml of ether was added to the residue. The solid obtained was then recrystallized from ethanol, yield 0.12 g (40%), mp 130°; ^1H nmr (deuteriochloroform): 3-4.5 (s, 1H, NH), 7.2-8.1 (m, Ar-H, HC=).

Anal. Calcd. for $C_{21}H_{16}N_2$: C, 85.14; H, 5.41; N, 9.46. Found: C, 85.17; H, 5.43; N, 9.24.

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