

Heterocyclic Compounds from 3,3-Dimercapto-1-aryl-2-propen-1-ones.
Note 2. Condensation with *o*-Aminothiophenol and *o*-Aminophenol.

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The condensation of 3,3-dimercapto-1-phenyl-2-propen-1-one with *o*-aminothiophenol and *o*-aminophenol in hot xylene gave 2-phenacylbenzothiazole (**3**) and 2-phenacylbenzoxazole (**5**). When the reaction with *o*-aminophenol was carried out in hot benzene, 2-benzoylthioacetamidophenol (**4**) was obtained, which, heated in hot xylene gave **5**. Ethyl benzoylacetate by reaction with *o*-aminothiophenol gave **3**, whereas by reaction with *o*-aminophenol gave no heterocyclic compound. However, we were able to isolate 2-benzoylacetamidophenol (**6**), ethyl β -phenyl- β -(*o*-hydroxy)phenyliminopropionate (**7**), and 2-[β -(*o*-hydroxy)anilino]cinnamoylamidophenol (**8**). Ir and nmr spectra of synthesized compounds point out the existence of tautomers.

In a previous paper (1) we reported the synthesis of 4-phenyl-1,3-dihydro-2*H*-1,5-benzodiazepine-2-thione, obtained by condensing 3,3-dimercapto-1-phenyl-2-propen-1-one with *o*-phenyldiamine. Analogously, the synthesis of 4-phenyl-1,3-dihydro-2*H*-1,5-benzodiazepine-2-one by condensing *o*-phenyldiamine with ethyl benzoylacetate has been reported (2).

This paper describes the results obtained by condensing 3,3-dimercapto-1-phenyl-2-propen-1-one and ethyl benzoylacetate with *o*-aminothiophenol (**1**) and with *o*-aminophenol (**2**).

The condensation of 3,3-dimercapto-1-phenyl-2-propen-1-one with **1**, in hot xylene gave the compound **3**, which shows three tautomeric forms: the 2-phenacylbenzothiazole (**3a**), the 2-phenylglyoxyldenbenzothiazoline (**3b**), and the 2-(β -phenyl- β -hydroxy)vinylbenzothiazole (**3c**). Analogously the condensation of 3,3-dimercapto-1-phenyl-2-propen-1-one with **2** in hot xylene gave the compound **5**, which shows three tautomeric forms: the 2-phenacylbenzoxazole (**5a**), the 2-phenylglyoxyldenbenzoxazoline (**5b**), and the 2-(β -phenyl- β -hydroxy)vinylbenzoxazole (**5c**).

No seven-membered-ring compound was isolated from these reactions. When these reactions were carried out at a lower temperature (hot benzene), by condensation of 3,3-dimercapto-1-phenyl-2-propen-1-one with **1**, we obtained **3**, whereas by condensation with **2** we obtained 2-benzoylthioacetamidophenol (**4**). This product heated in hot xylene gave **5**.

Ethyl benzoylacetate under similar experimental conditions, by reaction in xylene with **1** gave **3**, as reported by A. Buzas *et al.* (3), whereas by reaction with **2** gave no heterocyclic compound. However we were able to isolate

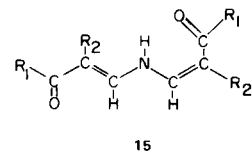
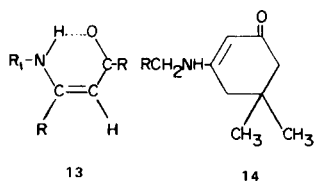
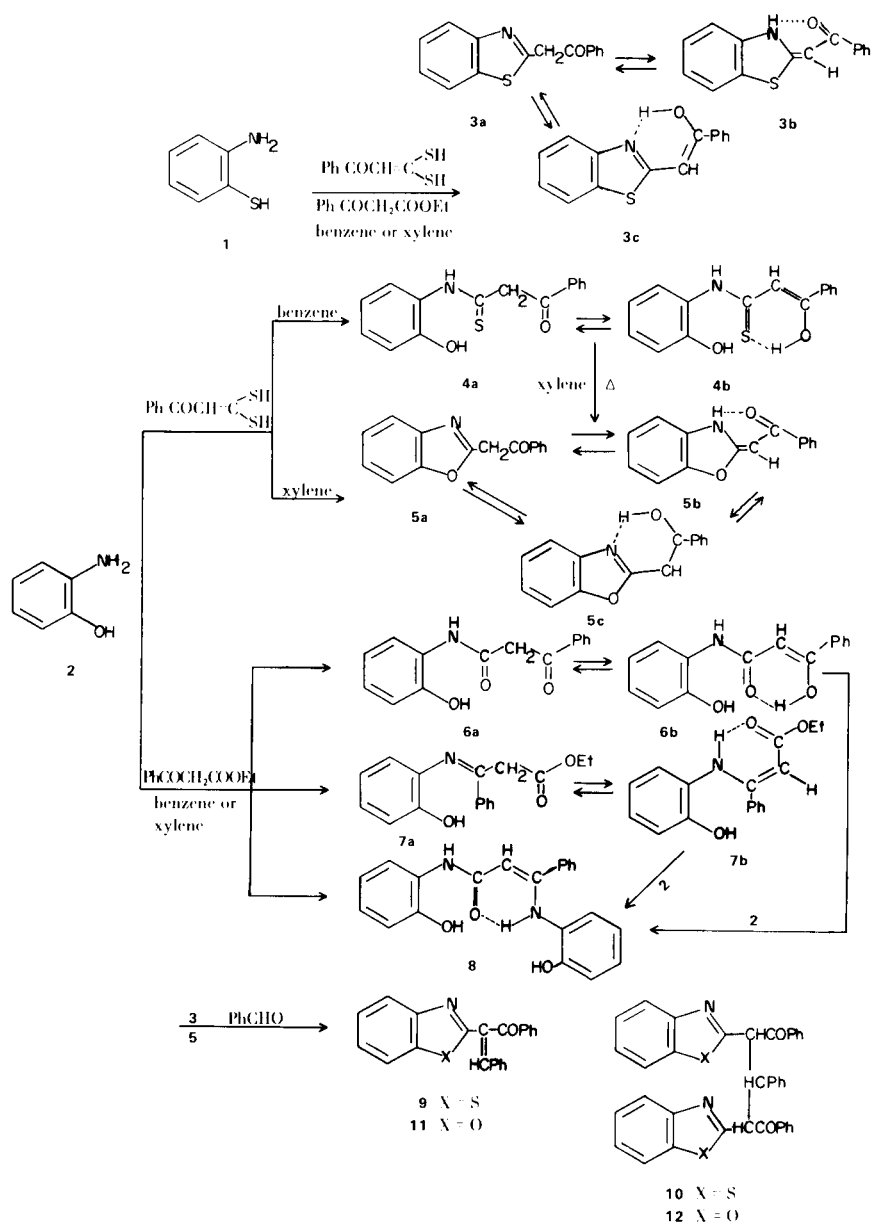
2-benzoylacetamidophenol (**6**); ethyl β -phenyl- β -(*o*-hydroxy)phenyliminopropionate (**7**), and 2-[β -(*o*-hydroxy)anilino]cinnamoylamidophenol (**8**).

Compound **8** was also obtained by reaction of **6** or **7** with **2**.

The structures of **3** and **5** were confirmed by elemental analysis, nmr, and ir spectra and by comparison with authentic samples prepared according to the literature (4-6).

F. N. Stepanov, *et al.* (4) reported that **3** by condensation with benzaldehyde gave the benzylidene derivative **9** with m.p. 119°. From this reaction we obtained, besides **9**, a side-product, m.p. 171°, which was isolated by column chromatography on silica gel and identified as 1,3-bis-(2-benzothiazoly)-1,3-dibenzoyl-2-phenylpropane (**10**). Analogously by reaction of benzaldehyde with **5** we were able to isolate 2-(α -benzoyl- β -phenyl)vinylbenzoxazole (**11**), and 1,3-bis-(2-benzoxazoly)-1,3-dibenzoyl-2-phenylpropane (**12**). These results point out the existence of tautomers **3a** and **5a**. The nmr (δ) and ir (cm^{-1}) spectra of **3** and **5** also indicate the existence of tautomers **b**, and **c** in addition to tautomer **a**. The presence of tautomer **a** is confirmed by a CH_2 singlet at 4.8 δ for **3** (35%), and at 4.6 δ for **5** (20%). The spectra show also =CH signals at 6.4 δ for **3** (65%) and at 6.1 δ for **5** (80%) which are related to tautomers **b** and **c**. The broad bands at 12.1 δ for **3** (23%) and at 11.4 δ for **5** (43%) may be related to the NH protons of tautomer **b**. The large paramagnetic shift of NH signal supports the hypothesis that an intramolecular hydrogen bond occurs between NH proton and CO group of tautomer **b**.

Analogously Dudek, *et al.*, (7) observed signals at 10.6-11.8 δ for β -acylvinylamines (**13**), which exist in hydrogen-bonded form, whereas NH proton signals appear in 4.7-5.9 δ



range for 3-amino-5,5-dimethyl-2-cyclohexene-1-ones (**14**), which cannot give an intramolecular hydrogen bond. Dabrosky, *et al.*, (8) reported signals at 11.3-11.6 δ for the NH protons of hydrogen-bonded β -acylvinylamines (**15**).

The nmr spectra possessed no signals related to the enolic OH of the tautomer **c**, but the ir spectra in solution did indicate this evidence. In fact in carbon tetrachloride solution a series of bands appear in the range 3250-2640 cm^{-1} . The bands at higher frequencies may be attributed

to the NH or the OH groups, the bands at lower frequencies only to the OH group chelated through a strong intramolecular hydrogen bond. By deuteration with deuterium oxide, the OH and NH bands disappear in time.

The tautomers **a** of **3** and **5** exist only in solution. In fact in the ir spectra in the solid state the expected conjugated carbonyl absorptions in the range 1700-1680 cm^{-1} are lacking. The ir spectra in solution, however, show bands at 1686 cm^{-1} for **3** and 1692 cm^{-1} for **5**, which indicate that the keto form is also present. Similar observations are reported by Branch, *et al.*, (9) for a series of 2-phenacylpyridines.

The ir spectra of **3**, and **5**, in both the solid state and in solution show bands in the range 1631-1600 cm^{-1} , which may be related to the stretching vibration of the carbonyl group hydrogen-bonded with the NH proton of tautomer **b**. Similar data are reported by Dabrosky, *et al.*, (8) and by Cromwell, *et al.*, (10) for hydrogen bonded β -acylvinylamines.

The derivative **4** shows two tautomers. In fact we observed in nmr spectra an enolic OH signal at 14.1 δ (75%) and =CH signal at 6.9 δ (75%) for tautomer **4b**, and a CH_2 singlet at 4.75 δ (25%) for tautomer **4a**. We also observed different NHCS signals at 10.4 δ and at 10.9 δ , and different phenolic OH signals at 9.3 δ , and at 9.10 δ .

Also the derivatives **6** and **7** show tautomeric forms. The presence of **6a** is indicated by CH_2 singlet at 4.30 δ (65%), whereas a CH= singlet at 6.45 δ (35%), and a broad band at 14.1 δ indicated the presence of enolic tautomer **6b**.

Compound **7** in the solid state exists only as **7b**. In fact the ir spectrum shows at 1639-1563 cm^{-1} , a large band centered at 1613 cm^{-1} , but no band in the 1740-1700 cm^{-1} range. The ir spectrum in chloroform solution shows in addition to the above band, a weak band at 1706 cm^{-1} , which may be related to CO stretching of tautomer **7a**. In the nmr spectrum the signal of NH at 9.8 δ (80%), and that of =CH at 6.45 δ (80%) support the hypothesis that an intramolecular hydrogen bond occurs between the NH proton and the CO group of tautomer **7b**.

We observed no tautomer for **8**. The ir spectrum in the solid state shows a band at 1668 cm^{-1} related to the stretching of hydrogen-bonded CO, whereas we observed no band in the 1680-1650 cm^{-1} range. The nmr spectrum shows a CH= singlet at 5.4 δ , but no CH_2 signal.

From the above reported results, we can conclude: a) the 3,3-dimercapto-1-phenyl-2-propen-1-one is a more useful reagent than ethyl benzoylacetate to obtain heterocyclic compounds; b) *o*-phenyldiamine by reaction with 3,3-dimercapto-1-phenyl-2-propen-1-one or ethyl benzoylacetate gives seven-membered ring compounds, whereas *o*-aminothiophenol and *o*-aminophenol give five-membered compounds.

EXPERIMENTAL

Melting points were determined in open glass capillaries on a Büchi apparatus and are uncorrected. Nmr spectra were recorded on a Jeol C-60 HL spectrometer and chemical shifts are expressed in δ units, ppm downfield from TMS as the internal standard. Ir spectra were recorded on a Perkin-Elmer 357 spectrophotometer.

2-Phenacylbenzothiazole (**3**) (4-6).

a) A stirred mixture of 1.96 g. (0.01 mole) of 3,3-dimercapto-1-phenyl-2-propen-1-one, (11) 1.25 g. (0.01 mole) of *o*-aminothiophenol (**1**) and 20 ml. of xylene, under a stream of nitrogen was refluxed for 4 hours. The solution was concentrated under reduced pressure to one third and cooled. The separated crystals were collected and recrystallized from hexane, yield 1.6 g. (63%), m.p. 114°.

b) A mixture of 1.92 g. (0.01 mole) of ethyl benzoylacetate, 1.25 g. (0.01 mole) of *o*-aminothiophenol (**1**) and 5 ml. of xylene under a stream of nitrogen was stirred at 20-25° for 2 hours and then refluxed for 4 hours. The solution was concentrated under reduced pressure to one third and cooled. The crystals which separated were collected and recrystallized from hexane, yield 1.63 g. (64%), m.p. 114°; ir (nujol): cm^{-1} 1620-1600 (CO...H-bonded of tautomer **b**); ir (carbon tetrachloride): 2810, 2640 (intramol. H-bonded OH of tautomer **c**) 1686 (CO of tautomer **a**), and 1616 (CO...H-bonded of tautomer **b**); nmr (deuteriochloroform): δ 4.8 (0.7 H, singlet, CH_2 of tautomer **a**), 6.4 (0.65 H, singlet, =CH of tautomers **b** and **c**), 12.1 (broad band, NH of tautomer **b**).

Anal. Calcd. for $\text{C}_{15}\text{H}_{11}\text{NOS}$: C, 71.14; H, 4.37; N, 5.53; S, 12.63. Found: C, 70.87; H, 4.42; N, 5.55; S, 12.45.

2-Phenacylbenzoxazole (**5**) (4,5).

A stirred mixture of 1.96 g. (0.01 mole) of 3,3-dimercapto-1-phenyl-2-propen-1-one, 1.09 g. (0.01 mole) of *o*-aminophenol (**2**) and 20 ml. of xylene under a stream of nitrogen was refluxed for 4 hours. After evaporation of the solvent under reduced pressure, the residue was chromatographed on a silica gel column eluting with petroleum ether-benzene (9:1). The crude product was crystallized from petroleum ether, yield 1.5 g. (42%), m.p. 97-98°; ir (nujol): cm^{-1} 1630-1600 (CO...H-bonded of tautomer **b**); ir (carbon tetrachloride): 2835, 2690 (intramol. H-bonded OH of tautomer **c**) 1692 (CO of tautomer **a**), and 1631-1603 (CO...H-bonded of tautomer **b**); nmr (deuteriochloroform): δ 4.6 (0.4 H, singlet, CH_2 of tautomer **a**), 6.1 (0.8 H, singlet, =CH of tautomers **b** and **c**), 11.4 (0.7 H, broad band, NH of tautomer **b**).

Anal. Calcd. for $\text{C}_{15}\text{H}_{11}\text{NO}_2$: C, 75.93; H, 4.67; N, 5.90. Found: C, 75.70; H, 4.78; N, 6.02.

2-Benzoylthioacetamidophenol (**4**).

A mixture of 1.96 g. (0.01 mole) of 3,3-dimercapto-1-phenyl-2-propen-1-one, 1.09 g. (0.01 mole) of *o*-aminophenol (**2**), and 20 ml. of benzene under a stream of nitrogen was refluxed with stirring for 4 hours. After cooling, the separated crystals were collected and dried. The product was washed with 0.5 *N* hydrochloric acid to remove impurities of **2**, and then crystallized from 2-propanol, yield 1.5 g. (55%), m.p. 135°.

This compound by heating in xylene yielded 2-phenacylbenzoxazole (**5**); ir (nujol): cm^{-1} 1672, 1616, 1608, 1563; nmr (DMSO- d_6): δ 4.75 (0.5 H, singlet, CH_2 of tautomer **a**), 6.9 (0.75 H, singlet, =CH of tautomer **b**), 9.3 (0.25 H, singlet, phenolic-OH of tautomer **a**), 9.4 (0.75 H, singlet, phenolic-OH of tautomer **b**), 10.4 (0.75 H, broad band, NHCS of tautomer **b**), 10.9 (0.25 H, broad band, NHCS of tautomer **a**), 14.1 (0.75 H, broad band, enolic-OH of tautomer **b**).

Anal. Calcd. for $C_{15}H_{13}NO_2S$: C, 66.41; H, 4.83; N, 5.16; S, 11.79. Found: C, 66.48; H, 4.99; N, 5.37; S, 11.64.

Reaction of Ethyl Benzoylacetate with *o*-Aminophenol.

A stirred mixture of 11.54 g. (0.06 mole) of ethyl benzoyl acetate, 6.54 g. (0.06 mole) of *o*-aminophenol (**2**), and 30 ml. of xylene under a stream of nitrogen was refluxed for 4 hours. After cooling, the separated crystals were collected.* This product was a mixture of **2**, **6**, and **8**. The mixture was washed with cold 0.5 *N* hydrochloric acid to remove **2**, and the residue was suspended in 150 ml. of methanol and shaken for 5 minutes. The insoluble product was collected** and crystallized from ethanol, yield 6.05 g. (39.5%), m.p. 195-196°.

This compound was identified as 2-benzoylacetamidophenol (**6**); *ir* (nujol): cm^{-1} 3330-3320, 2700-2600, 1690, 1661, 1613, 1587; *nmr* (DMSO- d_6): δ 4.3 (1.3 H, singlet, CH_2 of tautomer **a**), 6.45 (0.35 H, singlet, =CH of tautomer **b**), 9.3 (0.35 H, broad band, NHCO of tautomer **b**), 9.55 (0.65 H, broad band, NHCO of tautomer **a**), 9.75 (1H, broad band, phenolic OH), 14.1 (broad band, molic OH).

Anal. Calcd. for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.87; H, 5.25; N, 5.71.

*The filtrate was evaporated and the residue was extracted with hot petroleum ether. After cooling, the separated crystals were collected, yield 1.5 g. (9%), m.p. 109°. This compound was identified as ethyl β -phenyl- β -(*o*-hydroxy)phenyliminopropionate (**7**); *ir* (nujol): cm^{-1} 3247, 1639-1563; *ir* (chloroform) 3400-3030 centered at 3145, 2900, 1706, 1645-1563 (series of bands); *nmr* (deuteriochloroform): δ 1.35 (3H, triplet, CH_3), 4.3 (2H, quartet, CH_2), 5.15 (1.2 H, CH_2CO of tautomer **a** and phenolic OH of tautomer **b**), 6.45 (0.8 H, singlet, =CH of tautomer **b**), 6.25-7.5 (9.2 H multiplet, phenolic OH of tautomer **a**, and aromatic protons), 9.8 (0.8 H, singlet, NH of tautomer **b**).

Anal. Calcd. for $C_{17}H_{17}NO_3$: C, 72.06; H, 6.05; N, 4.94; O, 16.94; C_2H_5O -15.90. Found: C, 71.94; H, 5.93; N, 4.85; O, 17.01; C_2H_5O -15.91.

The solution was evaporated and the residue was crystallized from 2-propanol, yield 2 g. (20%), m.p. 219-220°. This compound was identified as 2- $[\beta$ -(*o*-hydroxy)anilino]cinnamoylamidophenol (8**); *ir* (nujol): 3330, 3175, 1613 cm^{-1} ; *nmr* (DMSO- d_6): δ 5.40 (1H, singlet, =CH), 9.05 (singlet, phenolic OH), 9.6 and 9.75 (2H, two unresolved bands, NH and NHCO), 10.4 (1H, singlet, phenolic OH).

Anal. Calcd. for $C_{21}H_{18}N_2O_3$: C, 72.82; H, 5.24; N, 8.09. Found: C, 72.98; H, 5.42; N, 7.87.

When a ratio of 1:2 between ethyl benzoylacetate and **2** was used, we were able to isolate 12% of **6**, 6% of **7** and 29% of **8**.

2- $[\beta$ -(*o*-Hydroxy)anilino]cinnamoylamidophenol (**8**).

a) A mixture of 1.28 g. (0.005 mole) of 2-benzoylacetamidophenol (**6**), 0.54 g. (0.005 mole) of *o*-aminophenol (**2**), and 3.5 ml. of xylene was refluxed with stirring for 4 hours under a stream of nitrogen. After cooling, the crystals which separated were collected, dried, and washed with 0.5 *N* hydrochloric acid to remove unchanged **2**. The residue was shaken with 50 ml. of methanol. The insoluble matter was identified as unchanged **6**, (0.70 g., 55%). Evaporation of the filtrate gave 0.63 g. (36.7%) of **8**, m.p. 215°.

b) A stirred mixture of 1.42 g. (0.005 mole) of ethyl β -phenyl- β -(*o*-hydroxy)phenyliminopropionate (**7**), 0.54 g. (0.005 mole) of *o*-aminophenol (**2**), and 3.5 ml. of xylene was refluxed for 4 hours under a stream of nitrogen. After cooling, the crystals which separated were collected. The crude product was washed with hot petroleum ether to remove unchanged **7** (0.65 g., 46%), and with 0.5 *N* hydrochloric acid to remove unchanged **2**. The residue was identified as **8** (0.56 g., 32.5%, m.p. 215°).

Reaction of 2-Phenacylbenzothiazole with Benzaldehyde.

A mixture of 2.53 g. (0.01 mole) of 2-phenacylbenzothiazole (**3**), 1.06 g. (0.01 mole) of benzaldehyde, 20 ml. of pyridine, and 0.05 ml. of piperidine was stirred for 24 hours at 20-25° and then poured into water. The mixture was extracted with diethyl ether. After drying and evaporation of the solvent, the residue was chromatographed on a silica gel column eluting at first with benzene and then with ethyl acetate. By evaporation of benzene we obtained 2 g. (58%), m.p. 119° of 2-(α -benzoyl- β -phenyl)vinylbenzothiazole (**9**) (**4**).

Evaporation of ethyl acetate gave 0.6 g. (20%), m.p. 171°.

This compound was identified as 1,3-bis(2-benzothiazolyl)-1,3-dibenzoyl-2-phenylpropane (**10**); *nmr* (deuteriochloroform): AB_2 system; δ 5.17 (ν_A), 6.20 (ν_B), J_{AB} 9.5 cps.

Anal. Calcd. for $C_{37}H_{26}N_2O_2S_2$: C, 74.74; H, 4.41; N, 4.71; S, 10.10. Found: C, 74.49; H, 4.40; N, 4.77; S, 10.40.

Reaction of 2-Phenacylbenzoxazole with Benzaldehyde.

A mixture of 9.4 g. (0.04 mole) of 2-phenacylbenzoxazole (**5**), 4.77 g. (0.045 mole) of benzaldehyde, 60 ml. of pyridine, and 0.05 ml. of piperidine was refluxed for 4 hours. After cooling the mixture was poured into water and allowed to stand for several hours. The separated precipitate was collected and dried, yield 13 g. This product was chromatographed on a silica gel column eluting at first with diethyl ether-petroleum ether 2:8 and then with a mixture containing higher ratio of diethyl ether.

The first fraction gave unchanged **5**, then a mixture of **5** and **11** was obtained, and then 7.4 g. (57%) of 2-(α -benzoyl- β -phenyl)vinylbenzoxazole (**11**). This compound crystallized from ethanol m.p. 123-124°.

Anal. Calcd. for $C_{22}H_{15}NO_2$: C, 81.21; H, 4.65; N, 4.31. Found: C, 81.41; H, 4.73; N, 4.20.

The last fractions gave 0.24 g. (2.1%) of 1,3-bis(2-benzoxazolyl)-1,3-dibenzoyl-2-phenylpropane (**12**). This compound was crystallized from ethyl acetate m.p. 198°; *nmr* (deuteriochloroform): AB_2 system: δ 5.39 (ν_A), 6.01 (ν_B), J_{AB} 9.5 cps.

Anal. Calcd. for $C_{37}H_{26}N_2O_4$: C, 78.99; H, 4.66; N, 4.98. Found: C, 79.09; H, 4.90; N, 4.89.

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