HETEROCYCLES, Vol. 29, No. 2, 1989

AN EFFICIENT CYCLODESULFURIZATION OF N-(2-HYDROXYPHENYL)THIOAMIDES WITH SUPEROXIDE. A NOVEL ROUTE TO BENZOXAZOLES

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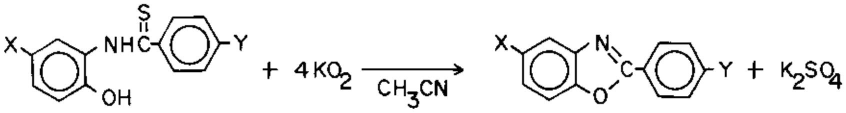
Abstract - *Treatment of N-(2-hydroxyphenyl)thioamides (1) with superoxide ($O_2^{-\cdot}$) at* room temperature in dry acetonitrile resulted in the formation of 2-substituted benzoxazoles (7) in excellent yields.

Superoxide ($O_2^{-\cdot}$), one-electron reduction product of molecular oxygen, has recently become the subject of considerable chemical[1] and biological[2] interest and investigation. It is known to have the potential of acting as a redox agent, as a nucleophile or as a base.[3] In the previous papers,[4,5] we reported that thioamides and thioureas reacted with superoxide anion to afford the corresponding amides and ureas respectively, and proposed that the desulfurization involves formation of sulfur dioxide or sulfur trioxide intermediate. During a study on the sulfur oxide intermediate, we have found that N-(2-hydroxyphenyl)benzthioamides reacted readily with superoxide anion at 20 °C to give the corresponding benzoxazoles by one step reaction in excellent yields. The results are shown in Table I.

In a typical procedure, a solution of N-(2-hydroxyphenyl)benzthioamide (114.5 mg, 0.5 mmol) in CH_3CN (2 ml) was added to a heterogeneous solution of potassium superoxide (148 mg, 2 mmol) in CH_3CN (2 ml) under nitrogen atomsphere. After being stirred for 6 h at 20 °C with vigorous stirring, the reaction mixture was poured into cold water and then extracted with dichloromethane (25 ml x 3). The CH_2Cl_2 solution was dried over anhydrous magnesium sulfate, filtered, and then concentrated under reduced pressure to give crude 2-phenylbenzoxazole (7a: 97%), which was purified by a silica gel column chromatography (Kiesel gel 60, 70-230 mesh, 1cm x 20cm, Et_2O:n-hexane = 1:2) to get pure 7a (93% in Run 1; mp 99-101 °C (lit.[6] 97-98 °C), ^1H nmr δ 7.5 (H7), δ 8.3 (H2); m/z 195; ir (KBr) 3050, 1600, 1530, 1450, 1230, 1050 cm^{-1}). The products obtained were identified by comparing their mp, ^1H nmr, ir and mass spectra with those from the authentic samples.[7] The workup is simple: after monitoring the complete reaction by tlc on silica gel, filtration, and then concentration give a highly pure product, 2. When the reaction is carried

Table I. Cyclodesulfurization of N-(2-Hydroxyphenyl)thioamides.



1 7

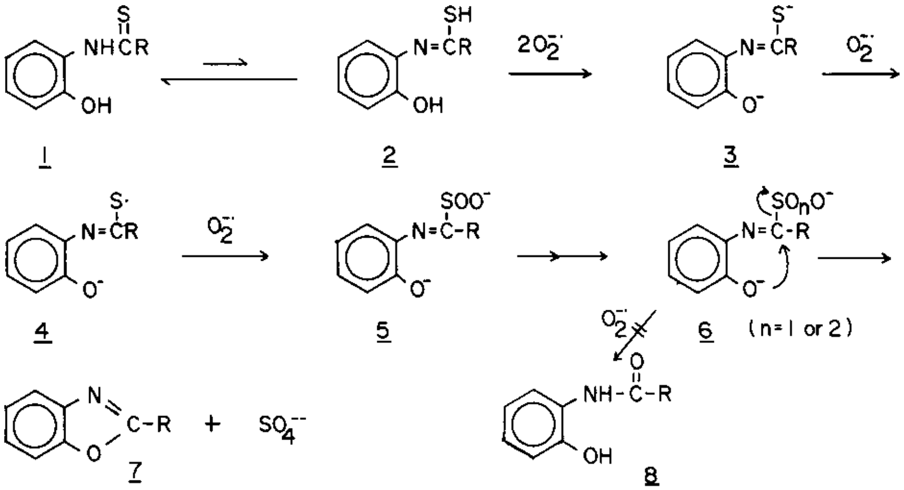
Run	X	Y	Reactn. Time (h)	Reactn. Temp (°C)	Products	Yield(%)[a]
1	H	H	6	20	7a	93
2	H	H	7	-20	7a	67[b]
3	H	H	15	-20	7a	90
4	Me	H	6	20	7b	86
5	Me	OMe	11	10	7c	89
6	Me	OMe	6	20	7c	90
7	Me	Cl	11	10	7d	92
8	Me	Cl	15	-35	7d	62[c]
9	Me	Ph	11	10	7e	91
10	Cl	H	11	10	7f	87
11	Cl	Br	11	10	7g	87

a) Isolated Yields.

b) The starting material was recovered in 30%.

c) The starting material was recovered in 35%.

out at low temperature, longer reaction time is required but a control of reaction time resulted in good yield (Run 3). The cyclodesulfurization of N-(2-hydroxyphenyl)benzthioamides appears to involve the formation of a key intermediate of peroxysulfur dioxide and/or trioxide (6) as in the case of desulfurization of thioamides.[5] The cyclization seems to be initiated *via* the formation of phenolate anion 3 in the basic condition of $O_2^{-\cdot}$[1] and then thiyl radical (4) by one electron transfer from the thiolate anion to $O_2^{-\cdot}$ followed by proton transfer to the resultant HOO·.[1]



Hydrogen abstraction of diphenols by $O_2^{-\cdot}$ to form semiquinones has been reported for a number of catecols.[8] A behavior of $O_2^{-\cdot}$ as an oxidizing agent to accept one electron has been reported. The thiyl radical (4) may couple with $O_2^{-\cdot}$ to form a peroxysulfenate followed by undergoing further oxidation to peroxysulfur intermediate (6). An intramolecular nucleophilic attack by the phenolic hydroxyl anion on the imine carbon should be more favorable than the direct attack of $O_2^{-\cdot}$: The amide product, 8 could not be actually detected. In this cyclization, the combination of a neighboring group effect of a hydroxylate anion and the leaving group of SO_nO^- seems to play an important role. Since benzoxazole derivatives are important intermediates for the syntheses of polyether antibiotics,[9] of fluorescent whitening agents,[10] and of dye releasers in instant color photography.[11] They are conventionally prepared from o-aminophenols by cyclization with carboxylic acids, imino ethers, and nitriles in moderate yields.[12] Beckmann rearrangement of o-acylphenol oximes[13] has been reported to produce benzoxazoles successfully to some extent. Formation of benzoxazoles by intramolecular trapping of an aryne intermediate from 2- or 3-haloanilides has been reported.[6,14] Recently, photolysis of ortho-thallated anilides was reported to give benzoxazoles in moderate yields.[15] In summary, benzoxazoles may be readily prepared from N-(2-hydroxyphenyl)thioamides and superoxide under mild conditions in the wide range of reaction temperature ($-35 \sim 20$ °C). Extensions and scope of this methodology are under investigation.

ACKNOWLEDGMENTS

This investigation was supported by the Korea Science and Engineering Foundation.

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7. 7b: mp 103-104 °C; mass spec. m/z 209; ^{1}H nmr ($CDCl_3$) 2.6 (H3), 7.2-7.4 (H1), 7.4-7.8 (H5), 8.2-8.4 (H2); ir (KBr) 2950, 1550, 1480, 1450, 1270 cm^{-1}. 7c: mp 104-106 °C, ^{1}H nmr ($CDCl_3$) δ 2.4 (H3), 3.8 (H3), 6.8-7.4 (H5), 8.0-8.2 (H2), ir (KBr) 3010, 1510, 1450, 1240, 1060 cm^{-1}. 7d: mp 143-144 °C; mass spec. m/z 243, ^{1}H nmr ($CDCl_3$) δ 2.6 (H3), 7.8-8.0 (H5), 8.2-8.4 (H2); ir (KBr) 3060, 1590, 1520, 1330, 1260 cm^{-1}. 7e; mp 144-145 °C, mass spec. m/z 285; ir (KBr) 3080, 1560, 1500, 1450, 1340, 1280 cm^{-1}. 7f; mp 100-101 °C (lit[16] 101-102 °C), mass spec. m/z 229; ir (KBr) 3080, 1560, 1500, 1450, 1340, 1280 cm^{-1}. 7g; mp 174-176 °C, mass spec. m/z 307; ir (KBr) 1600, 1550, 1480, 1400, 1080 cm^{-1}.

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Received, 22nd September, 1988