Oxidation of *N*-Acyl-, *N*-Sulfonyl-, and *N*-Arylsulfilimines to Sulfoximines by *m*-Chloroperoxybenzoate Anion[1]

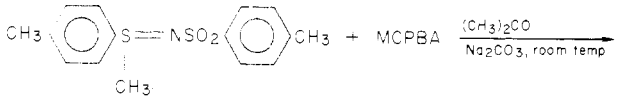
Shui-Lung Huang and Daniel Swern*

Fels Research Institute and the Department of Chemistry, Temple University, Philadelphia, Pennsylvania 19122

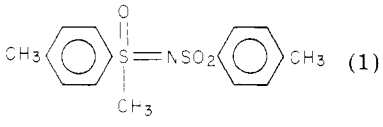
Received January 30, 1979

N-Acyl-, *N*-sulfonyl-, and *N*-arylsulfilimines are rapidly oxidized to the corresponding sulfoximines in high to virtually quantitative yields by *m*-chloroperoxybenzoate anion generated in situ in basic aqueous alcoholic media. In the one *N*-aryl case studied, *S*,*S*-dimethyl-*N*-(*p*-nitrophenyl)sulfilimine is converted unexpectedly to *p*-nitrosonitrobenzene in excellent yield by *m*-chloroperoxybenzoic acid but if the *m*-chloroperoxybenzoate anion is *completely* formed before sulfilimine is added, sulfoximine is obtained in over 90% yield. Reaction pathways are proposed.

In 1968 Cram and co-workers[2a] oxidized optically active *S*-tolyl-*S*-methyl-*N*-(*p*-toluenesulfonyl)sulfilimine (**1**) to the corresponding sulfoximine (**2**) with a large excess of *m*-chloroperoxybenzoic acid (MCPBA) in acetone containing a slurry of sodium carbonate (eq 1). Yields were



1



(1)

2 (55–65%)

only fair, a large (fivefold) excess of oxidant was used, and long reaction times (24 h) were employed. When we repeated the oxidation with *S*,*S*-dimethyl-*N*-(*p*-toluenesulfonyl)sulfilimine (**3**), it was slowly but completely consumed (TLC) and we obtained less than a 40% yield of the expected sulfoximine (**4**) along with a complex mixture of unidentified byproducts. Oae and co-workers[2b] oxidized *S*,*S*-diphenylsulfilimine with *p*-methylperoxybenzoic acid and obtained a mixture of sulfoximine (40%), sulfone (20%), and sulfoxide (trace). Thus, the oxidation of sulfilimines to sulfoximines by peroxy acids does not appear promising.

For some time we have been interested in peroxy acid anions rather than peroxy acid as oxidizing agents but, owing to peroxy anion instability[3] and solubility considerations, suitable reaction conditions are not easily developed. Recently, Griffin and co-workers[4] succeeded in using excess MCPBA (estimated $pK_a \approx 7.5$[3,5]) in a two-phase system consisting of aqueous sodium bicarbonate–methylene chloride at room temperature or 37–38 °C to convert a series of polynuclear aromatic hydrocarbons to arene oxides in good yields. The oxidations appeared to be enhanced by the presence of water but its role remained to be defined.[4] We came to the tentative conclusion that although the major role of aqueous sodium bicarbonate was to neutralize *m*-chlorobenzoic acid ($pK_a \approx 3.8$) as it formed,[3] it might also be generating *m*-chloroperoxybenzoate anions albeit in low concentrations.

Using **3** as a model sulfilimine, we repeated Griffin's oxidation procedure at room temperature and obtained an approximately 60% yield of sulfoximine (**4**) within 30 min (Table I, experiment 1). All of the sulfilimine was consumed within that time but we also obtained an unidentified byproduct; material balance was good. At this stage we had no basis for concluding that the oxidation was effected by the peroxy acid anion or whether the use of a biphasic system was dominating. This encouraging result, however, prompted us to study the oxidation of **3** to **4** with MCPBA under various (stronger) basic conditions to optimize the yields and possibly develop a new general method for efficient oxidation of other sulfilimines to sulfoximines. The reaction was monitored by TLC and ^{1}H NMR, using authentic **3**[6] and **4**[1b] as reference compounds; results are summarized in Table I.

The importance of base strength is vividly demonstrated by experiments 4–6 in which methanol- or ethanol-saturated aqueous base reaction systems are used. These systems are biphasic as ethanol (or methanol) and saturated aqueous potassium carbonate are not completely miscible at room temperature. To ensure substantial conversion of MCPBA to its anion in situ, oxidations were run by adding a solution of MCPBA in ethanol to stirred solutions of **3** in ethanol containing the requisite excess of saturated aqueous base. With a molar ratio of MCPBA/base (K_2CO_3)/**3** of 1.05:1.3:1 almost complete oxidation to **4** occurs within 1 h; some unreacted **3** is still present and is a contaminant of **4** (experiment 6). Best results are obtained with a somewhat larger excess of MCPBA and base to **3**; preferred molar ratios for MCPBA/K_2CO_3/**3** are (1.5–2):(1.9–2.5):1 (experiments 7 and 8). Sulfoximine **4** of good quality is obtained in over 85% yield in less than 1 h (experiments 7–9). Some excess of MCPBA to **3** is always required presumably to compensate for anion decomposition. By spectral and TLC examination, crude **4** is virtually pure without further workup although its melting point may be slightly lower than analytical samples.

In one experiment (experiment 10), an organic base was used in a homogeneous methylene chloride solution consisting of a MCPBA/DIPEA/**3** ratio of 2:3:1. No **4** was obtained although most of the **3** was consumed; this line was not investigated further.

(1) (a) Huang, S. L.; Swern, D., presented in part at the 12th Middle Atlantic Regional Meeting of the American Chemical Society, Baltimore, Md., April 1978. (b) This paper is part 5 of the series Sulfoximines. Part 4: Veale, H. S.; Levin, J.; Swern, D. *Tetrahedron Lett.* **1978**, 503.

(2) (a) Rayner, D. R.; Von Schriltz, D. M.; Day, J.; Cram, D. J. *J. Am. Chem. Soc.* **1968**, *90*, 2721. Cram, D. J.; Day, J.; Rayner, D. R.; Von Schriltz, D. M.; Duchamp, D.; Garwood, D. C. *Ibid.* **1970**, *92*, 7369. (b) Yoshimura, Y.; Omata, T.; Furukawa, N.; Oae, S. *J. Org. Chem.* **1976**, *41*, 1728.

(3) Swern, D. "Organic Peroxides"; Swern, D., Ed.; Wiley: New York, 1970; Vol. 1, Chapter VII, p 503.

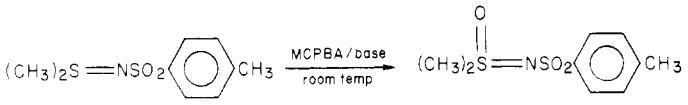
(4) Ishikawa, K.; Charles, H. C.; Griffin, G. W. *Tetrahedron Lett.* **1977**, 427. Ishikawa, K.; Griffin, G. W. *Angew Chem., Int. Ed. Engl.* **1977**, *16*, 171; *Angew. Chem.* **1977**, *89*, 181.

(5) Schwartz, N. N.; Blumbergs, J. H. *J. Org. Chem.* **1964**, *29*, 1976.

(6) Varkey, T. E.; Whitfield, G. F.; Swern, D. *J. Org. Chem.* **1974**, *39*, 3365.

0022-3263/79/1944-2510$01.00/0

Table I



3 4

expt no.	reactn medium	molar ratio MCPBA/3	molar ratio base/3	reactn time, h	mp of 4,[a] °C	yield of 4, %
1	CH_2Cl_2-H_2O[4]	5	⩾25 ($NaHCO_3$)	0.5	166-168[b]	60[b]
2	CH_3OH-H_2O	2	2 ($NaHCO_3$)	1	156-158	<27 (mixture of 3 and 4)
3		2	4 ($NaHCO_3$)	1	163-165	57
4		2	2.5 (K_2CO_3)	1	163-165	78
5	C_2H_5OH-H_2O	2	5 ($NaHCO_3$)	1		[c]
6		1.05	1.3 (K_2CO_3)	1	161-164[d]	77
7		1.5	1.9 (K_2CO_3)	1	164-166	85
8		2	2.5 (K_2CO_3)	1	164-166	88
9		4	5 (K_2CO_3)	0.5	167-168	86
10	CH_2Cl_2	2	3 (DIPEA)[e]	1.5		<15[f]

[a] Lit.[1b,7] mp 167-169 °C. [b] After one recrystallization of the crude reaction product from methanol. All other yields and melting points in the table are for crude reaction products dried under vacuum but not recrystallized. [c] Mainly *p*-toluenesulfonamide with traces of 3 and 4. [d] Contains some unreacted 3. [e] Diisopropylethylamine. [f] Recovered 3; no 4 was isolated.

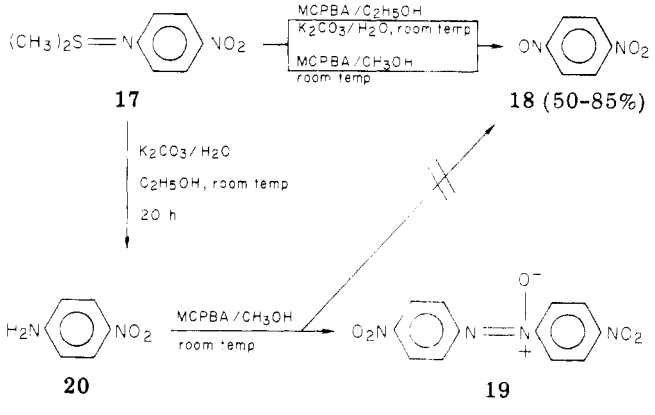
Table II

sulfilimines (5)		sulfoximines (6)		
$R^1 = R^2$	R^3	yield of 6,[a] %	mp, °C	lit. mp, °C
3 CH_3	$CH_3C_6H_4SO_2$[b]	88	164-166	167-169[7]
7 CH_3	$ClC_6H_4SO_2$	94	134-136	136-137.5[8]
8 CH_3	$C_6H_5SO_2$	70[a]	115-117	115[9]
		98[c]	115-117	
9 CH_3	$O_2NC_6H_4SO_2$	97	220-223	224-226[8]
10 CH_3	CH_3SO_2	75[d]	123-125	. . .[10]
		100[d]		
11 C_6H_5	$CH_3C_6H_4SO_2$	91	137-138	135-136[11]
12 $ClCH_2CH_2$	$CH_3C_6H_4SO_2$	0[e]		
13 CH_3	O_2N-C_6H_4C=O	94	181-184	187-189[12]
14 CH_3	Cl_2CH-C=O	97	75-77	76.5-78[1b]
15 C_6H_5	CH_3C=O	69[f]	128-130	127-130[13]
16 CH_3	$O_2NC_6H_5$	90[g]	158-160	160-162[14]

[a] Crude reaction product obtained by filtration and drying of the diluted reaction mixture. The reaction conditions of Table I, experiment 8, were used in all the experiments reported in this table. [b] From Table I for comparison. [c] After separation of crude 6 by filtration (yield, 70%), the filtrate was continuously extracted with CH_2Cl_2; additional 6 was obtained from the aqueous solution making the overall yield virtually quantitative (98%). [d] Sulfoximine 10 is water soluble; several extractions with CH_2Cl_2 gave a 75% yield but continuous extraction resulted in a 100% yield. [e] Sulfilimine was not soluble in the reaction system; it was largely recovered (85%). [f] Reaction temperature 45-50 °C; a large excess of MCPBA anion was required (at least 5:1). [g] Reaction conducted at 0-5 °C with all *m*-chloroperoxybenzoic acid converted to the anion. About 5% of *p*-nitrosonitrobenzene (18) and 4,4 -dinitroazoxybenzene (19) were also formed.

Table II[7-14] reports the results of the oxidation of other sulfilimines (5) using the conditions of Table I, experiment 8. In virtually all cases, excellent yields of sulfoximines (6) are obtained with the exception of that from *S,S*-(2-chloroethyl)-*N*-(*p*-toluenesulfonyl)sulfilimine (12) which failed to oxidize and was recovered. The sulfoximine (16) derived from 12 is a stable compound, mp 53-56 °C, that can be prepared in excellent yield from the sulfilimine by our recently published ruthenium dioxide–sodium periodate cooxidation method.[1b,15]

Scheme I

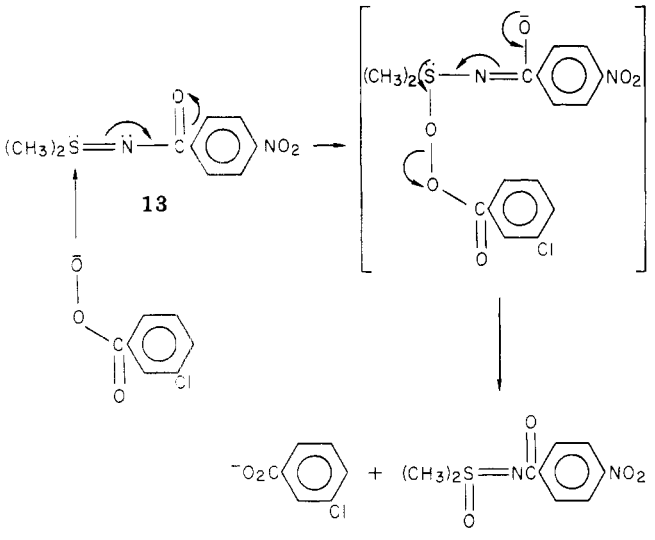


With sulfoximines that have a relatively high solubility in water (Table II, footnotes *c* and *d*), continuous extraction of the aqueous phase with methylene chloride is required to obtain reported yields.

An unexpected result was obtained in the oxidation of *S,S*-dimethyl-*N*-(*p*-nitrophenyl)sulfilimine (17) with MCPBA under the conditions of experiment 8, Table I, or in neutral methanol. Under the former conditions a high yield (85%) of *p*-nitronitrosobenzene (18) was obtained which was converted largely to 4,4′-dinitroazoxybenzene (19) upon attempted recrystallization from refluxing methylene chloride–petroleum ether. *p*-Nitronitrosobenzene (18) was also obtained on oxidation of 17 with MCPBA in neutral dry methanol (base and water absent) but the yield was only about 50%. *p*-Nitroaniline

(7) Bentley, H. R.; Whitehead, J. K. *J. Chem. Soc.* **1950**, 2081.
(8) Heintzelman, R. W.; Swern, D. *Synthesis* **1976**, 731.
(9) Horner, L.; Christman, A. *Chem. Ber.* **1963**, *96*, 388.
(10) The melting points of the sulfilimine and sulfoximine are almost the same; the compounds are readily distinguished and identified by spectral methods and TLC.
(11) Oae, S.; Harada, K.; Tsujihara, K.; Furukawa, N. *Int. J. Sulfur Chem., Part A* **1972**, 49.
(12) Horner, L.; Bauer, G.; Dörges, J. *Chem. Ber.* **1965**, *98*, 2631.
(13) Misani, F.; Fair, T. W.; Reiner, L. *J. Am. Chem. Soc.* **1951**, *73*, 459.
(14) Claus, P. K.; Rieder, W.; Hofbauer, P. *Tetrahedron* **1975**, *31*, 505.
(15) Oxidation was slow, however, and required several hours instead of the usual 15 min.

Scheme II



(20), a hydrolysis product of 17, is presumably not the precursor of 18; 20 yields 19, not 18, on oxidation with MCPBA in neutral methanol. These results are summarized in Scheme I.

If the *m*-chloroperoxybenzoic acid is first converted to the anion at 0–5 °C, however, and 17 is then added in ethanol, the sulfoximine *S,S*-dimethyl-*N*-(*p*-nitrophenyl)sulfoximine (21), mp 158–160 °C, is obtained in over 90% yield in 1 h (Table II, last entry). This result suggests that the reaction conditions of experiments 7 and 8, Table I, do not effect complete conversion of MCPBA to its anion instantly and completely in the biphasic system or perhaps MCPBA remains in the alcohol phase for a sufficient length of time to convert 17 to 18 rather than to sulfoximine (21) which requires anion.

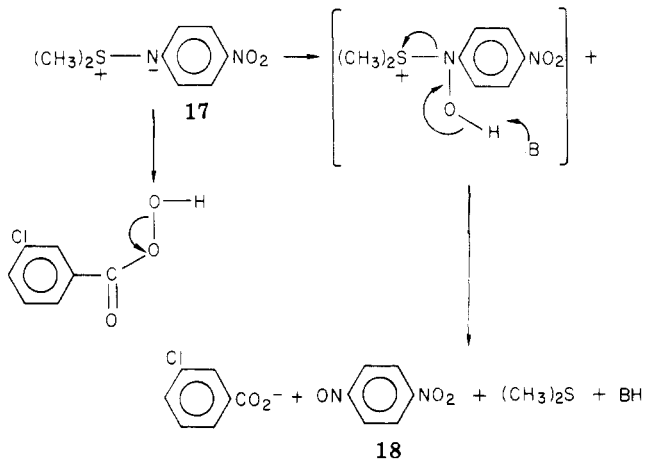
Interestingly, phenanthrene is recovered unchanged when treated for 24 h under the conditions of experiment 8, Table I; GLC analysis shows only phenanthrene present. We repeated Griffin's oxidation procedure by using the weaker base (CH_2Cl_2–water–$NaHCO_3$–MCPBA)[4] with phenanthrene and we were able to separate the hydrocarbon and its epoxide as reported. It seems clear that MCPBA anion is not the reactive species in the Griffin method; the role of sodium bicarbonate must be neutralization of the relatively acidic *m*-chlorobenzoic acid thus avoiding oxirane ring destruction.[4]

Oxidation Pathways

A reasonable pathway for the oxidation of acyl- and sulfonylsulfilimines by MCPBA anion reported in Tables I (3 → 4) and II (5 → 6) is given in Scheme II, using *S,S*-dimethyl-*N*-(*p*-nitrobenzoyl)sulfilimine (13) for illustrative purposes. In the absence of base, 13 undergoes extremely slow oxidation by MCPBA; generation of the anion is essential for facile oxidation at the electrophilic sulfonium sulfur atom. An intriguing alternative pathway requires epoxidation of the S–N double bond, a hitherto unreported reaction, followed by rearrangement of the putative thioxaziridine.

When the sulfonium sulfur is less electrophilic, as in *S,S*-dimethyl-*N*-(*p*-nitrophenyl)sulfilimine (17), the ylide nitrogen is sufficiently nucleophilic to attack the electrophilic MCPBA present as such or in equilibrium with its anion (Scheme III).

Scheme III



Experimental Section

Oxidation of *S,S*-Dimethyl-*N*-(*p*-toluenesulfonyl)-sulfilimine to 4 (Modified Griffin Procedure[4]). A solution of 3 (0.69 g; 3 mmol) and MCPBA (85%) (3 g, 15 mmol) in CH_2Cl_2 (75 mL) was stirred at room temperature for 30 min[22] with saturated aqueous sodium bicarbonate solution (75 mL). Excess MCPBA was destroyed by the addition of sodium thiosulfate (3 g) dissolved in a minimum amount of water followed by cautious acidification with 6 N H_2SO_4. The reaction mixture was neutralized with 6 N NaOH, diluted with CH_2Cl_2 (50 mL), and then washed with water (2 × 100 mL). The organic phase was dried ($MgSO_4$) and filtered, and the solvent was removed by rotary evaporation. The white solid residue was recrystallized from MeOH, yielding pure sulfoximine 4; mp 166–168 °C (0.4–0.5 g, ca. 60%). Its melting point, R_f, and IR were identical with those of authentic 4.[1b]

Oxidation of 3 to 4 (Preferred Procedure: Experiment 8, Table I). To a stirring biphasic mixture of 3 (1.16 g, 5 mmol) dissolved in 95% C_2H_5OH (30 mL) and a solution of K_2CO_3 (1.8 g, 13 mmol) in water (4 mL) at room temperature (20–25 °C) a solution of MCPBA (85%) (2 g, 10 mmol) in 95% C_2H_5OH (10 mL) was added dropwise in 15–20 min. After 1 h, excess MCPBA was destroyed by addition of excess sodium thiosulfate solution (negative starch–iodide test). The reaction mixture was then poured into water (100 mL) and cooled in a refrigerator to 0 °C (7 h). The white precipitate of 4 was filtered, washed several times with cold water, and dried under vacuum; mp 164–166 °C (1.09 g, 88%). It was identical with an authentic specimen.[1b]

Table I summarizes the oxidation of 3 to 4 under a variety of reaction conditions.

Oxidation of Other Sulfonyl- and Acylsulfilimines. Table II summarizes the oxidation of other sulfilimines using the oxidation conditions of experiment 8, Table I, just described. In several cases noted in the table, continuous extraction of the diluted reaction mixture with CH_2Cl_2 is required to obtain the reported yields. The products were virtually identical with authentic specimens of sulfoximines (R_f, IR, NMR, mp); occasionally small quantities of unoxidized sulfilimines were present as contaminants (TLC).

Oxidation of *S,S*-Dimethyl-*N*-(*p*-nitrophenyl)sulfilimine (17) to *p*-Nitronitrosobenzene (18). Oxidation of 17 under the conditions of experiment 8, Table I, produced a variety of color changes (orange → yellow → greenish yellow). After the usual workup, a greenish yellow solid, impure 18, mp 110 °C, was obtained in 80% yield (from 0.5 g of 17, 0.32 g of 18 was obtained). Attempted recrystallization of 18 from boiling CH_2Cl_2–petroleum ether yielded a yellow solid, mp 188–190 °C, which was further recrystallized from CH_2Cl_2 to give analytically pure 4,4′-dinitroazoxybenzene (19); mp 199–200 °C (lit. mp 190–193 °C). Anal. Calcd for $C_{12}H_8N_4O_5$: C, 50.0; H, 2.80; N, 19.4. Found: C, 50.3; H, 2.74; N, 18.6.

An alternate procedure for the conversion of 17 to 18 of better purity is the following: To a stirring solution of 17 (0.5 g, 2.5 mmol)

(16) Sulfilimines were prepared by previously reported methods.[6,17–21] Apparatus, techniques, and chemicals used have also been described.[6,17–21] MCPBA (85%) was obtained from Aldrich. All other reagents were the best commercial grades.

(17) Dawson, A. D.; Swern, D. *J. Org. Chem.* 1977, *42*, 592.

in CH_3OH (15 mL) a solution of MCPBA (1.0 g, 5 mmol) in methanol was added in 15 min at 22–25 °C. After 1 h at room temperature, the reaction mixture was cooled to 0–10 °C and filtered. The greenish yellow precipitate was washed with cold CH_3OH and dried (0.20 g, 53%); mp 118–120 °C (lit.[18] mp 118.5–119 °C). Anal. Calcd for $C_6H_4N_2O_3$: C, 47.4; H, 2.65; N, 18.4. Found: C, 47.2; H, 2.91; N, 19.2.

Oxidation of *S,S*-Dimethyl-*N*-(*p*-nitrophenyl)sulfilimine (17) to Sulfoximine (21) by Preformed MCPBA Anion. To a stirring solution of MCPBA (1.0 g, 5 mmol) in ethanol (6 mL) at 0 °C a solution of K_2CO_3 (1.8 g, 13 mmol) in water (6 mL) was added. After 20 min at 0 °C, **17** (0.5 g, 2.5 mmol) in ethanol (30 mL) was added in one portion, the cooling bath was then removed, and stirring was continued at room temperature for 1 h. The reaction mixture was concentrated under vacuum (to about 5 mL) and water was added (20 mL) followed by extraction with CH_2Cl_2 (2 × 30 mL). The organic phase was washed successively with concentrated NaCl solution (20 mL), dried over anhydrous $MgSO_4$, and filtered. Evaporation of solvent yielded an orange solid consisting (TLC) largely of sulfoximine (**21**) contaminated with **18** and **19**. Recrystallization from methanol yielded pure **21**; mp 158–160 °C (0.48 g, 90%) (lit.[14] mp 160–162 °C).

Hydrolysis of 17 to 20. A solution of sulfilimine **17** (0.25 g, 1.25 mmol) in 95% C_2H_5OH (10 mL) was stirred with a solution of K_2CO_3 (0.5 g) in water (2 mL) at room temperature for 20 h. The reaction mixture was diluted with H_2O (10 mL), cooled, and filtered. The dried yellow solid (0.13 g, mp 145–147 °C, 75% yield) was identical wiith authentic *p*-nitroaniline (**20**).

MCPBA Oxidation of *p*-Nitroaniline (20). A solution of **20** (1.38 g, 10 mmol) and MCPBA (85%) (2.2 g, 11 mmol) in CH_3OH was stirred at room temperature for 90 min (a yellow precipitate formed after 5 min). The reaction mixture was cooled to ca. 0 °C and filtered. The light brown solid obtained (0.83 g) was mainly **19** with a trace of **20** (TLC). No evidence of **18** was found.

Acknowledgment.[22] This research was supported by Grant CA12227 awarded by the National Cancer Institute, DHEW, Instrument Grant CHE 76-05757 from the National Science Foundation, Grant IN88J from the American Cancer Society, and the Samuel S. Fels Fund.

Registry No. 3, 13150-75-9; **4**, 22236-45-9; **6** ($R^1 = R^2 = CH_3$, R^3 = Cl-*p*-$C_6H_4SO_2$), 61706-01-2; **6** ($R^1 = R^2 = CH_3$, $R^3 = C_6H_5SO_2$), 22236-46-0; **6** ($R^1 = R^2 = CH_3$, $R^3 = O_2N$-*p*-$C_6H_4SO_2$), 61706-02-3; **6** ($R^1 = R^2 = CH_3$, $R^3 = CH_3SO_2$), 70355-69-0; **6** ($R^1 = R^2 = C_6H_5$, R^3 = CH_3-*p*-$C_6H_4SO_2$), 38764-58-8; **6** ($R^1 = R^2 = CH_3$, $R^3 = O_2N$-*p*-$C_6H_4C{=}O$), 3532-29-4; **6** ($R^1 = R^2 = CH_3$, $R^3 = Cl_2CHC{=}O$), 66406-35-7; **6** ($R^1 = R^2 = C_6H_5$, $R^3 = CH_3C{=}O$), 70355-70-3; **6** ($R^1 = R^2 = CH_3$, $R^3 = O_2N$-*p*-C_6H_4), 56158-00-0; **7**, 52259-84-4; **8**, 19871-30-8; **9**, 18922-58-2; **10**, 13553-68-9; **11**, 13150-76-0; **12**, 70355-71-4; **13**, 52259-85-5; **14**, 6026-68-2; **15**, 42397-41-1; **17**, 27691-52-7; **18**, 4485-08-9; **19**, 614-25-5; **20**, 100-01-6.

(18) Huang, S. L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 4537.
(19) Mann, F. G.; Pope, W. J. *J. Chem. Soc.* **1922**, *121*, 1052.
(20) Atkins, R. C.; Lentz, C. M. *J. Org. Chem.* **1978**, *43*, 773.
(21) Tamura, Y.; Sumoto, K.; Matsushima, H.; Taniguchi, H.; Ikeda, M. *J. Org. Chem.* **1973**, *38*, 4324.
(22) Certain sulfilimines are oxidized to sulfoximines in high yields by alkaline hydrogen peroxide; a sulfurane is suggested as an intermediate (Johnson, C. R.; Kirchhoff, R. A. *J. Org. Chem.* in press.

Orientation of the Sulfoxide Bond as a Stereochemical Probe. Synthesis and ^1H and ^{13}C NMR of Substituted Thiopyrano[4,3-*c*]pyrazoles

Mohindar S. Puar,*[1] George C. Rovnyak,* Allen I. Cohen, and B. Toeplitz

The Squibb Institute for Medical Research, Princeton, New Jersey 08540

J. Z. Gougoutas

Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455

Received February 9, 1979

The synthesis of the novel substituted thiopyrano[4,3-*c*]pyrazole ring system is reported. Proton (^1H NMR) and carbon-13 (^{13}C NMR) magnetic resonance studies, utilizing shift reagents, were used to make conformational assignments in this bicyclic system, taking advantage of the chemical shift sensitivity to the orientation of the exocyclic sulfur oxygen observed in **8a** and **8b**. Single-crystal X-ray results and NMR evidence are presented to show that the thiopyran ring of **7–9** exists in the chair conformation and that the S→O bond in **8a** is α-axial, while in **8b** the S→O bond is β-equatorial.

From earlier ^1H NMR studies, empirical correlations for the determination of configurations and conformations in cyclic sulfoxides have been proposed; these correlations have been subsequently strengthened by solvent-effect and shift-reagent studies.[2] More recently, the analysis of the ^{13}C NMR data of cyclic sulfides, sulfoxides, and sulfones has provided stronger evidence of axial–equatorial orientation of the S→O bond.[3,4] Most of the reported data pertains to simple four-, five-, or six-membered cyclic compounds. The objective of this study was to utilize the orientation of the S→O bond for conformational assignments in a new bicyclic system (thiopyrano[4,3-*c*]pyrazole), employing ^1H NMR spectrometry, shift reagents, and ^{13}C NMR spectrometry. Few studies are available wherein all three techniques are utilized on the same sulfoxide system.

Chemistry

Tetrahydro-4*H*-thiopyran-4-one (**1**),[5] the 1-oxide **2**,[6] and the 1,1-dioxide **3**[7] were prepared by literature methods. Tetrahydro-3,5-bis(phenylmethylene)-4*H*-thiopyran-4-one (**4**) was prepared by the condensation of benzaldehyde and ketone **1** with concentrated hydrochloric acid in ethanol, which in our hands was preferred over the method of Leonard.[8] The bis-aldol sulfoxide **5** could not be obtained

(1) Present address: Schering Corporation, 60 Orange St., Bloomfield, N.J. 07003.
(2) R. R. Fraser, T. Durst, M. R. McClory, R. Viau, and Y. Y. Wigfield, *Int. J. Sulfur Chem., Part A*, 1, 133 (1971), and references cited therein.
(3) J. A. Hirsch and E. Havinga, *J. Org. Chem.*, **41**, 455 (1976).
(4) G. W. Buchanan and T. Durst, *Tetrahedron Lett.*, 1683 (1975).
(5) P. Y. Johnson and G. A. Berchtold, *J. Org. Chem.*, **35**, 584 (1970).
(6) N. J. Leonard and C. R. Johnson, *J. Org. Chem.*, **27**, 282 (1962).
(7) E. A. Fehnel and M. Carmack, *J. Am. Chem. Soc.*, **70**, 1813 (1948).

0022-3263/79/1944-2515$01.00/0