manganate. The purple color faded rapidly at the beginning of the addition with the formation of a brown precipitate, but remained at the end. After a few minutes of stirring, a small amount of sodium bisulfite was added until the color faded. Ice was added, and the precipitate was filtered and recrystallized from ethanol to give 44 mg (50% yield) of II, mp 178–179°.

Anal. Calcd for $C_{25}H_{24}O_2S$: C, 79.24; H, 5.66. Found: C, 79.21; H, 5.59.

1,2-Diphenyl-2-hydroxyethyl *p*-Tolyl Sulfoxide (III).—The procedure followed resembled that for preparation of I except that benzaldehyde was substituted for benzalaniline. The reaction product was isolated without chromatography by recrystallization of the reaction residue from ether; yield 40%, mp 176.5–178.5°.

Anal. Calcd for $C_{21}H_{20}O_2S$: C, 75.00; H, 5.95. Found: C, 75.15; H, 5.88.

Registry No.—I, 21473-30-3; II, 21473-31-4; III, 21473-32-5.

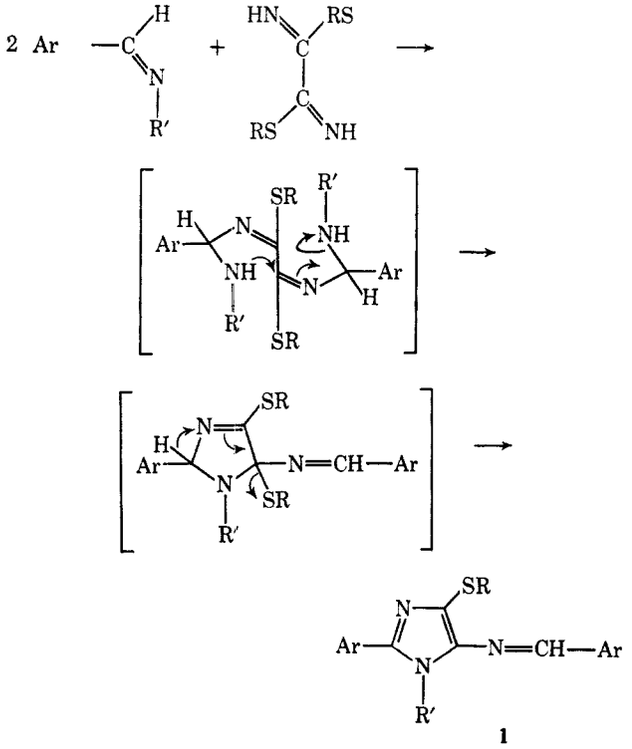
Heterocyclic Ring-Closure Reactions. III. 5-Aminoimidazoles from Azomethines[1a,b]

S. C. MUTHA[1c] AND ROGER KETCHAM[1d]

Department of Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco Medical Center, San Francisco, California 94122

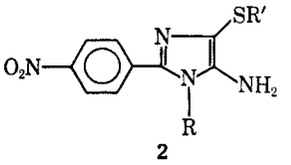
Received May 5, 1969

The thermal condensation of dithiooxamide with aromatic aldehydes has been shown to afford symmetrical, fully aromatized diarylthiazolothiazoles.[2] Aromatic aldehydes react with S,S′-disubstituted dithiooxaldiimidates to give 5-benzalamino-4-aryl- or alkyl-mercapto-2-aryloxazoles.[3] It was of interest to see if azomethines, the nitrogen analogs of aldehydes, would react with S,S′-disubstituted dithiooxaldiimidates in an analogous manner and thereby provide a route to imidazoles (**1**).[4]



1

Reaction of benzalmethylamine with S,S′-dibenzyl dithiooxaldiimidate gave the expected imidazole Schiff base (**1**). The destruction of the original chromophore by acid is similar to that observed in the oxazole series.[3] However, in the imidazole case no characterizable hydrolysis product was isolated. Reaction of Schiff bases of *p*-nitrobenzaldehyde with dialkyl or diaryl dithiooxaldiimidates afforded aminoimidazoles (**2**) in good yields.



2

The reaction between Schiff bases of aromatic aldehydes and S,S′-disubstituted dithiooxaldiimidates seems to be general and to give better yields than obtained in the oxazole synthesis from the aromatic aldehydes.[3]

Experimental Section[5]

Azomethines.—The procedures used for solids were those recommended by Vogel[6] whereas for liquids equimolar amounts of primary amine and aromatic aldehyde were allowed to react in benzene in the presence of Linde molecular sieve No. 3A. The mixture was stirred for 4 hr at room temperature. The reaction mixture was filtered, the solvent removed, and the residue distilled under reduced pressure.

S,S′-Dialkyl or Diaryl Dithiooxaldiimidates.—The procedure used was that of Woodburn and Sroog[7] as modified by Martin and Ketcham.[3]

Schiff Bases of Aminoimidazoles.—The following synthetic procedures are representative of the compounds listed in Table I.

Method A. 5-Benzalamino-4-benzylmercapto-1-methyl-2-phenylimidazole (1a).—A solution of 3.8 g (0.032 mol) of benzalmethylamine and 6 g (0.02 mol) of S,S′-dibenzyl dithiooxaldiimidate in 50 ml of absolute ethanol was refluxed for 2 hr. The volume of the resulting solution was reduced to about 25 ml and set aside for crystallization. It afforded yellow needles, mp 140–142°. Two recrystallizations from methanol yielded 5.9 g (80%) of yellow needles: mp 143–144°; λ_{max} 374 (ϵ 12,100) and 252 mμ (18,400) and irreversibly, in acid 273 (11,800) and 224 mμ (17,200); ν 3050 (aromatic CH), 2940 (CH_2), 1600

(1) (a) Paper No. II. Previous paper: S. C. Mutha and R. Ketcham, *J. Org. Chem.*, **34**, 2053 (1969). (b) Supported by National Institute of Mental Health, Grant MH 08787. (c) Abstracted in part from the Ph.D. thesis of S. C. Mutha. (d) To whom inquiries should be sent.

(2) J. R. Johnson and R. G. Ketcham, *J. Amer. Chem. Soc.*, **82**, 2719 (1960).

(3) A. R. Martin and R. Ketcham, *J. Org. Chem.*, **31**, 3612 (1966).

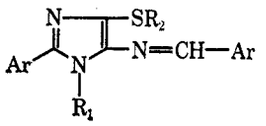
(4) If dithiooxamide were to react with Schiff bases by loss of an amine, then the same diarylthiazolothiazole[2] would be formed. However, there appeared to be the possibility of loss of hydrogen sulfide rather than an amine, thereby affording a tetrasubstituted imidazoimidazole. The only product isolated from Schiff bases of benzaldehyde was the previously described[2] diphenylthiazolothiazole.

(5) Melting points were determined on a Thomas–Hoover capillary melting point apparatus, and are corrected. Elemental analyses were carried out by the microanalytical laboratory of the University of California at Berkeley. The uv spectra were determined in 95% ethanol, using a Cary Model 11 spectrophotometer. Absorptions are reported in millimicrons, intensities as molar extinction coefficient (ϵ). The ir spectra were run on a Perkin-Elmer 337 spectrophotometer. Potassium bromide was used for solids. The nmr spectra were taken in deuteriochloroform, unless otherwise indicated, with tetramethylsilane as the internal standard, using a Varian A-60A spectrometer. Chemical shifts are reported as δ values (parts per million) and coupling constants (J values) are given in cycles per second (hertz).

(6) A. I. Vogel in "A Textbook of Practical Organic Chemistry," Longmans Green and Co., London, 1956, pp 653–654.

(7) H. M. Woodburn and C. E. Sroog, *J. Org. Chem.*, **17**, 371 (1952).

TABLE I
SCHIFF BASES OF AMINOIMIDAZOLES

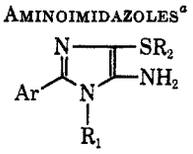


1

Compd	Ar[a]	R_1[a]	R_2	Method	Solvent[b]	Yield, %	Mp, °C	Formula	Analyses: Calcd, % C	H	N	S	Found, % C	H	N	S
a	C_6H_5[c]	CH_3[c]	$CH_2C_6H_5$	A	MeOH	80	143–144	$C_{24}H_{21}N_3S$	75.17	5.52	10.96	8.36	74.89	5.76	10.76	8.09
b	C_6H_5[d]	C_6H_{11}[d]	$CH_2C_6H_5$	A	MeOH	80	140–141	$C_{29}H_{29}N_3S$	77.13	6.47	9.31	7.09	77.31	6.23	9.12	6.96
c	C_6H_5[e]	C_6H_5[e]	$CH_2C_6H_5$	A	MeOH	60	164–165	$C_{29}H_{23}N_3S$	78.18	5.20	9.43	7.18	78.22	5.52	8.96	6.90
d	p-$CH_3OC_6H_4$[f]	C_6H_5[f]	$CH_2C_6H_5$	B	MeOH	56	154–155	$C_{31}H_{27}N_3SO_2$	73.65	5.38	8.31	6.33	73.61	5.25	8.26	6.31
e	p-$CH_3OC_6H_4$[g]	C_6H_{11}[g]	$CH_2C_6H_5$	B	EtOH	68	174–176	$C_{31}H_{33}N_3SO_2$	72.78	6.50	8.21	6.26	72.65	6.48	8.20	6.18
f	C_6H_5	C_6H_5	C_6H_5	B	MeOH	50	149–151	$C_{28}H_{21}N_3S$	77.94	4.91	9.74	7.42	77.68	4.71	9.68	7.30
g	C_6H_5[e]	C_6H_5[e]	CH_3	B	MeOH	70	184–186	$C_{23}H_{19}N_3S$	74.78	5.18	11.37	8.66	74.91	5.01	11.21	8.51
h	p-$CH_3OC_6H_4$[f]	C_6H_5[f]	CH_3	A	MeOH	44	179–180	$C_{25}H_{23}N_3SO_2$	69.92	5.40	9.78	7.45	69.76	5.31	9.71	7.38
i	p-$CH_3OC_6H_4$[g]	C_6H_{11}[g]	CH_3	A	MeOH	40	167–169	$C_{25}H_{29}N_3SO_2$	68.95	6.71	9.65	7.34	68.89	6.54	9.61	7.10

[a] Footnotes in these columns refer to the preparations of the azomethines. [b] Crystallization solvent; MeOH, methanol; EtOH, absolute ethanol. [c] Benzalmethylamine, bp 178–180° [lit. 180°, H. Zaunschirm, *Ann. Chem.*, **245**, 279 (1888)]. [d] Benzalcyclohexylamine, bp 94–95° (1 mm) [lit. 136° (16 mm): A. Skita and C. Wulff, *Ber.*, **59**, 2683 (1926)]. [e] Benzalaniline, mp 46–47° [lit. 52°: L. A. Bigelow and H. Eatough, "Organic Syntheses," Coll. Vol. I, John Wiley & Sons, Inc., New York, N. Y., 1941]. [f] p-Methoxybenzalaniline, mp 61–62° [lit. 63°: O. Anselmino, *Ber.*, **40**, 3465 (1907)]. [g] p-Methoxybenzalcyclohexylamine, bp 158–161° (5 mm) [lit 319°: D. Collins and J. Graymore, *J. Chem. Soc.*, 9 (1957)].

TABLE II
AMINOIMIDAZOLES[a]



2

Compd	R_1[b]	R_2	Solvent[c]	Yield, %	Mp, °C	Formula	Analyses: Calcd, % C	H	N	S	Found, % C	H	N	S
a	C_6H_5[d]	$CH_2C_6H_5$	MeOH	67	148–150	$C_{22}H_{18}N_4SO_2$	65.67	4.51	13.92	7.95	65.41	4.38	13.85	7.86
b	C_6H_{11}[e]	$CH_2C_6H_5$	MeOH	63	173–175[f]	$C_{22}H_{24}N_4SO_2$	64.69	5.92	13.72	7.83	64.57	5.81	13.61	7.92
c	C_6H_5	C_6H_5	MeOH	38	186–188	$C_{21}H_{16}N_4SO_2$	64.94	4.15	14.93	8.24	64.98	4.07	14.09	8.07
d	C_6H_{11}	C_6H_5	MeOH	50	186–187	$C_{21}H_{22}N_4SO_2$	63.95	5.62	14.20	8.12	63.72	5.48	14.01	8.30
e	C_6H_5	CH_3	MeOH	54	151–153	$C_{16}H_{14}N_4SO_2$	58.89	4.32	17.17	9.00	58.72	4.09	17.23	9.17
f	C_6H_{11}	CH_3	C_6H_6	50	188–190	$C_{16}H_{20}N_4SO_2$	57.82	6.07	16.86	9.63	57.63	5.82	16.74	9.39

[a] Ar = p-$O_2NC_6H_4$. [b] Footnotes to this column refer to the preparations of the azomethine. [c] Crystallization solvent. [d] p-Nitrobenzalaniline, mp 92–93° [lit. 93°: O. Fischer, *Ber.*, **14**, 2520 (1881)]. [e] p-Nitrobenzalcyclohexylamine, mp 84–86° [lit. 85.6–86°: G. Baddar, *J. Chem. Soc.*, **136** (1950)]. [f] With decomposition.

cm^{-1} (C=C); δ 8.66 (N=CH), 7.50 (Ar), 3.73 (CH_3), 4.28 (CH_2).[8]

5-Benzalamino-4-benzylmercapto-1-cyclohexyl-2-phenylimidazole (1b), 5-benzalamino-4-benzylmercapto-1,2-diphenylimidazole (1c), 5-p-methoxybenzalamino-2-p-methoxyphenyl-4-methylmercapto-1-phenylimidazole (1h), and 1-cyclohexyl-5-p-methoxybenzalamino-2-p-methoxyphenyl-4-methylmercaptoimidazole (1i) were synthesized by the above procedure using appropriate azomethines and dithiooxaldiimidates.

Method B. 4-Benzylmercapto-5-p-methoxybenzalamino-2-p-methoxyphenyl-1-phenylimidazole (1d).—S,S'-Dibenzyl dithiooxaldiimidate (3 g, 0.01 mol) and 4.5 g (0.021 mol) of p-methoxybenzalaniline were heated on a steam cone for 30 min. The reaction mixture was cooled and 50 ml of absolute alcohol added and allowed to crystallize. Cotton greenish yellow needles (3 g, 56%) were obtained. Recrystallization from methanol gave yellow cottony needles, mp 154–155°. **1-Cyclohexyl-4-benzylmercapto-5-p-methoxybenzalamino-2-p-methoxyphenylimidazole (1e)** and **5-benzalamino-1,2-diphenyl-4-phenylmercaptoimidazole (1f)** were synthesized by the above procedure using appropriate starting materials.

5-Benzalamino-1,2-diphenyl-4-methylmercaptoimidazole (1g).—Three grams (0.02 mol) of S,S'-dimethyl dithiooxaldiimidate and 6.9 g (0.04 mol) of benzalaniline were mixed; the reaction starts immediately and heating on the steam cone for 1 min completes the reaction. Cooling the resultant mixture results in yellow cottony needles, mp 183–185°.

(8) Other compounds gave appropriate spectroscopic data. Integration values and coupling constants for nmr spectra were in accord with the structures assigned.

Aminoimidazoles.—The following synthetic procedures are representative of compounds listed in Table II.

5-Amino-4-benzylmercapto-2-p-nitrophenyl-1-phenylimidazole (2a).—S,S'-Dibenzyl dithiooxaldiimidate (6 g, 0.02 mol) and 4.2 g (0.02 mol) of p-nitrobenzalaniline were heated on a steam cone for 30 min. When the reaction mixture was diluted with 50 ml of absolute ethanol and cooled to 5°, it afforded 5.2 g (67%) of dark, reddish brown needles, mp 148–150°. Recrystallization from methanol afforded orange-red needles: mp 151–152°; λ_{max} 420 mμ (ε47,100); ν 3350 and 3150 (NH_2), 1512 and 1360 cm^{-1} (NO_2); δ 7.92 ($ArNO_2$), 7.3 (C_6H_5), 3.90 (CH_3), 3.15 (NH_2).[8] **5-Amino-4-benzylmercapto-1-cyclohexyl-2-p-nitrophenylimidazole (2b), 5-amino-2-p-nitrophenyl-1-phenyl-4-phenylmercaptoimidazole (2c), 5-amino-1-cyclohexyl-2-p-nitrophenyl-4-phenylmercaptoimidazole (2d), 5-amino-4-methylmercapto-1-phenyl-2-p-nitrophenylimidazole (2e),** and **5-amino-1-cyclohexyl-4-methylmercapto-2-p-nitrophenylimidazole (2f)** were synthesized using the above procedure starting from appropriate Schiff bases of p-nitrobenzaldehyde and disubstituted dithiooxaldiimidates.

Registry No.—**1a**, 21643-90-3; **1b**, 21643-91-4; **1c**, 21643-92-5; **1d**, 21643-93-6; **1e**, 21643-94-7; **1f**, 21643-95-8; **1g**, 21681-52-7; **1h**, 21643-96-9; **1i**, 21643-97-0; **2a**, 21643-98-1; **2b**, 21643-99-2; **2c**, 21644-00-8; **2d**, 21644-01-9; **2e**, 21644-02-0; **2f**, 21644-03-1.

Acknowlegment.—We wish to thank Miss Elizabeth Bertram and Mr. James Roossien for technical assistance.