(1962).
(13) X-ray data are currently being collected by Dr. F. Fronczek, Louisiana State University.[23]
(14) E. Staude and F. Patat, *Chem. Ether Linkage*, 46–49 (1967); R. E. Lubowicz and P. Reich, *Chem. Eng. Prog.*, **67**, 59 (1971).
(15) T. B. Johnson and G. E. Hilbert, *Science*, **69**, 579 (1929).
(16) T. B. Johnson and G. E. Hilbert, *J. Am. Chem. Soc.*, **52**, 2001 (1930).
(17) M. M. Htay and O. Meth-Cohn, *Tetrahedron Lett.*, 79, 469 (1976).
(18) G. R. Newkome, A. Nayak, and W. H. Benton, *J. Org. Chem.*, to be submitted.
(19) G. R. Newkome, F. Danesh-Khoshboo, A. Nayak, and W. H. Benton, *J. Org. Chem.* **43**, 2685 (1978).
(20) Appropriate chlorothioalkylpyrimidine models were used to further substantiate these spectral assignments.
(21) Methiodide **16** can be isolated (10%) with difficulty only when the reaction is conducted at 0 °C, mp >200 °C dec. Prolonged treatment of **16** with excess methyl iodide affords variable mixtures of insoluble intermediate compounds prior to the generation of **15**.
(22) D. Davidson and O. Baudisch, *J. Am. Chem. Soc.*, **48**, 2379 (1926).
(23) **Note added in proof:**[24] The isomer melting at 171–173 °C has been shown to possess a center of symmetry; therefore, **6a** has the configuration X = N, Y =CH and **6b** has the Y = N, X = CH orientation.
(24) F. Fronczek, A. Nayak, G. R. Newkome, and J. L. Atwood, *Acta Crystallogr.*, submitted for publication.

Studies on Pyrazines. 5.[1] Peracetic and Peroxysulfuric Acid N-Oxidation of Phenyl- and Chlorophenylpyrazines

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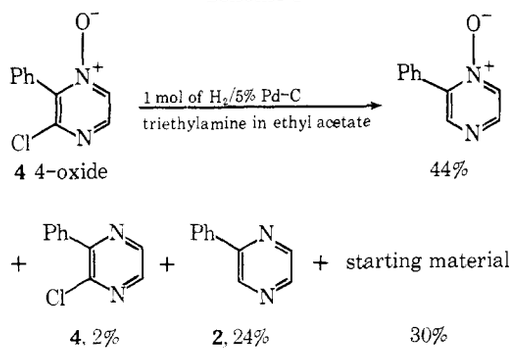
Peracetic and peroxysulfuric acid oxidations of 2-phenyl- (**2**) and 2-chloro-3-, -5-, and -6-phenylpyrazine (**4, 5,** and **6,** respectively) were carried out. On peracetic acid oxidation, **2, 4,** and **6** gave the corresponding 4-oxides and **5** gave a mixture of the 1- and 4-oxides. On the other hand, peroxysulfuric acid oxidation of **4** and **5** afforded the corresponding 1-oxides, but **2** gave a small amount of the 4-oxide and **6** was not oxidized. Structures of these *N*-oxides were determined by NMR spectra and dipole moment measurement. The mechanism of these oxidations is discussed.

N-oxidation of a pyrazine with usual percarboxylic acid reagents takes place on the most basic and least sterically hindered nitrogen.[2–5] The peracetic acid oxidation of a pyrazine bearing an electron-withdrawing substitutent such as halogens occurs in such a manner, e.g., 2-chloropyrazine (**3**) affords exclusively its 4-oxide.[5,6] However, a direct synthesis of 2-chloropyrazine 1-oxides, with the opposite orientation from that in the peracetic acid oxidation of chlorinated pyrazines, was recently reported by Mixan and Pew[7] by treatment of chloropyrazine with peroxysulfuric acid generated in situ from potassium persulfate and concentrated sulfuric acid. On applying these oxidation methods to 2-methyl- (**1**), 2-phenyl- (**2**), 2-chloropyrazine (**3**), and 2-chloro-3-, -5-, and -6-phenylpyrazine (**4, 5,** and **6,** respectively), we have found some interesting observations on the orientation of N-oxidations.

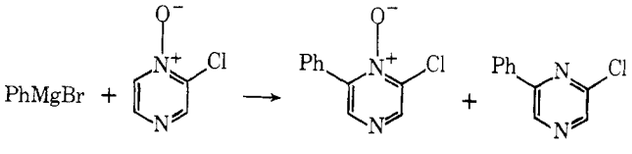
Results

As shown in Table I, methylpyrazine (**1**) was converted to the corresponding 1- and 4-oxides in the relative ratio of about 3:2[8] on treatment with peracetic acid by the procedure of the literature,[9,10] whereas the peroxysulfuric acid oxidation gave no *N*-oxide. The peracetic acid oxidation of phenylpyrazine (**2**) provided only the 4-oxide in the same manner as oxidation of 2-phenylquinoxaline with percarboxylic acids.[11,12] The peroxysulfuric acid oxidation of **2** gave a small amount (2.5%) of the 4-oxide, and the expected 1-oxide was not detected. The preparation of this 1-oxide was eventually achieved by catalytic hydrogenation of 2-chloro-3-phenylpyrazine (**4**) 4-oxide in the presence of 5% palladium on carbon and triethylamine together with other reduced products **2** and **4** as shown in Scheme I. When 10% palladium on carbon was used as the catalyst in this hydrogenation, the reaction proceeded so that it had to be controlled. Other catalysts, 5% palladium on $BaSO_4$ or Raney nickel, were also unappropriate for increasing the proportion of the desired product.

Scheme I



The peracetic acid oxidation of 2-chloro-3-phenylpyrazine (**4**) gave the 4-oxide, and the persulfate oxidation provided the 1-oxide. Thus orientation of N-oxidation of **4** is governed by an effect of the chloro substituent in the same way as that of 2-chloropyrazine (**3**), indicating no effect of the phenyl group. In contrast, oxidation of 2-chloro-5-phenylpyrazine (**5**) with peracetic acid provided equal amounts (by NMR) of the 1- and 4-oxides, and the persulfate oxidation gave only the 1-oxide. Since the 4-nitrogen atom of 2-chloro-6-phenylpyrazine (**6**) is the least sterically hindered among three chlorophenylpyrazines **4, 5,** and **6,** peracetic acid oxidation of **6** provided, as expected, the 4-oxide in excellent yield. However, the persulfate oxidation of **6** afforded no *N*-oxide because the 1-nitrogen is sterically hindered by two substituents. The 1-oxide of **6** was prepared in minor component (2%) by treatment of 2-chloropyrazine 1-oxide with phenylmagesium bromide.



Determination of the position of the N–O group in these *N*-oxides was conveniently accomplished by comparison of

0022-3263/78/1943-3367$01.00/0

Table I. Preparation of Pyrazine *N*-Oxides[e]

	substituents	method[a]	products	yield, %	mp, °C (lit., °C)
1	2-methyl	A	{1-oxide}[b] {4-oxide}	64	93–95 (90–91)[10] 69–71 (69–70)[10]
		B		0	
2	2-phenyl	A	4-oxide	28	141–142
		B	4-oxide	2.5	
		C	1-oxide	44	132–133
3	2-chloro	A	4-oxide	61	97 (95–96)[5]
		B	1-oxide	22[d]	135–136 (133–134)[6]
4	2-chloro-3-phenyl[15]	A	4-oxide	55	151–152
		B	1-oxide	21	188–189
5	2-chloro-5-phenyl[1,16,17]	A	{1-oxide}[c] {4-oxide}	33	146 151
		B	1-oxide	26	
6	2-chloro-6-phenyl[1,17]	A	4-oxide	89	121–122
		B		0	
		D	1-oxide	2	128

[a] A: Acetic acid–30% hydrogen peroxide; B; sulfuric acid–potassium persulfate. C: Hydrogenation of 2-chloro-3-phenylpyrazine 4-oxide. D: Reaction of 2-chloropyrazine 1-oxide with phenylmagnesium bromide. [b] Relative ratio, 1-oxide:4-oxide 3:2. [c] Relative ratio, 1-oxide:4-oxide 1:1. [d] Lit.[7] yield 55%. We have a suspicion on this yield because our several attempts to increase the yield failed. [e] Satisfactory analytical values (±0.3% for C, H, N) were submitted with the manuscript for all oxides of **2**, **4**, **5**, and **6**.

Table II. Chemical Shift and Coupling Constant Data for Protons of the Pyrazine Ring in $CDCl_3$

compd	registry no.	chemical shift, δ			coupling constant, Hz		
		3	5	6	$J_{3,5}$	$J_{3,6}$	$J_{5,6}$
1		8.47	8.39	8.44	0	1.4	2.4
1-oxide	31396-35-7	8.49	8.36	8.27	0	0.5	4.2
4-oxide	25594-37-0	8.09	8.40	8.04	1.2	0.7	4.2
2		9.05	8.53	8.66	0	1.7	2.5
1-oxide	58861-89-5	8.59	8.33	8.17	0	0.7	4.1
4-oxide	58861-94-2	8.55	8.06	8.49	1.6	0.8	4.0
3		8.66	8.55	8.44	0	1.3	2.5
1-oxide	16025-16-4	8.69	8.41	8.30	0	0.7	4.3
4-oxide	6863-76-9	8.22	8.09	8.30	1.6	0.7	4.2
4			8.56	8.31			2.5
1-oxide	66769-58-2		8.39	8.23			4.0
4-oxide	58861-87-3		8.18	8.20			4.0
5		8.66		8.81		1.3	
1-oxide	61578-11-8	8.65		8.65		0.8	
4-oxide	61578-12-9	8.26		8.41		0	
6		8.49	8.89		0.6		
1-oxide	66769-59-3	8.56	8.46		0		
4-oxide	66769-60-6	8.08	8.45		1.2		

IR or NMR spectra of each pair of isomers. An N–O stretching frequency in the region of 1350–1260 cm^{-1} is an indication to identify the isomeric *N*-oxides of monosubstituted pyrazines **1**, **2**,[13] and **3** (1-oxides exhibit a deviation to lower frequencies than the corresponding 4-oxides).[6,14] However, *N*-oxides of disubstituted pyrazines **4**, **5**, and **6** do not show such a tendency. The NMR spectra are more informative, e.g., each pair of isomers, except for *N*-oxides of **1** and **2**, conforms to the rule that the ring protons of 2-substituted pyrazine 4-oxides generally resonate at higher field than those of the corresponding 1-oxide isomers.[6,7] The coupling constants for the ring protons in pyrazine *N*-oxides were also found to be useful for the elucidation of *N*-oxide position (1-oxides: $J_{3,5}$ = 0 Hz, $J_{3,6}$ = 0.5–0.8 Hz, $J_{5,6}$ = 4.0–4.3 Hz; 4-oxides: $J_{3,5}$ = 1.2–1.6 Hz, $J_{3,6}$ = 0–0.8 Hz, $J_{5,6}$ = 4.0–4.2 Hz, respectively). A more reliable identification, however, is achieved by comparison of dipole moments of each pair of isomers. Particularly, the observed dipole moments of pyrazine 4-oxides and 2-phenylpyrazine 1-oxide are in good agreement with a vectorial sum calculated from the empirical group moments (C–Cl: 1.38 D, C–Ph: 0.84 D, and N–O: 1.62 D; see Table III). A considerable deviation (0.48–0.57 D) lower than the calculated value in 1-oxides of **3**, **4**, and **5** may be ascribed to the inductive replusion with the electron-withdrawing chlorine and oxygen atoms.

Discussion

With the results obtained, the mechanisms of the peracetic and peroxysulfuric acid oxidations were considered. In general, the N-oxidation reaction depends on a combination of an electronic and a steric effect.[2,3] On peracetic acid oxidations of **2**, **3**, and **6**, which have phenyl, chloro, or both the substituents in the 2 or 2,6 positions, the yields of their 4-oxides were 28, 61, and 89%, respectively. The extent of these N-oxidations presumably depends on electronic effects since the N-oxidation reactions are not sterically inhibited at all. The yields of *N*-oxides are likewise subject to a steric effect by the pyrazine substituents. In the peracetic acid oxidation of **5**, the steric hindrance by the phenyl group is evident from the low yield of the 4-oxide while the oxidation on the 1-nitrogen adjacent to the chloro substituent was suppressed. An extreme case for the steric inhibition by the phenyl group is a failure of persulfate oxidation on the 1-nitrogen of **6** whereas 2,6-dichloropyrazine forms the 1-oxide in good yield under the same conditions.[7] In the case of **4**, however, the steric effect of the phenyl group could be hardly recognized on oxidation of the 4-nitrogen adjacent to this substituent because the yield of the 4-oxide was close to that of 2-chloropyrazine 4-oxide.

The generally accepted mechanism of N-oxidation involves nucleophilic attack of the lone pair of electrons on nitrogen

Table III.[a] Dipole Moments of Substituted Pyrazines in Benzene at 25 °C

compd	dε/dω	dρ/dω	$T^{P_{2\infty}}$	P	μ, D	calcd value, D	Δμ[f]
2	0.717 ± 0.001	0.2162 ± 0.0003	61.2 ± 0.1	46.8	0.84 ± 0.003		
1-oxide	1.63 ± 0.09	0.298 ± 0.001	91.5 ± 0.5	51.8	1.39 ± 0.01	1.40	0.01
4-oxide	3.0 ± 0.2	0.299 ± 0.002	135.8 ± 1.4	51.8	2.03 ± 0.02	2.09	0.06
3	1.88 ± 0.02	0.2933 ± 0.0002	66.5 ± 0.7	27.5	1.38 ± 0.01[b]		
1-oxide	3.90 ± 0.09	0.395 ± 0.002	120.1 ± 1.2	32.5	2.07 ± 0.02	2.60	0.53
4-oxide	2.24 ± 0.07	0.389 ± 0.002	79.7 ± 0.8	32.5	1.52 ± 0.01[d]	1.51	0.01
4	1.325 ± 0.004	0.290 ± 0.001	91.0 ± 0.4	51.6	1.39 ± 0.01	1.20	−0.19
1-oxide	2.912 ± 0.008	0.346 ± 0.006	155.8 ± 0.7	56.6	2.20 ± 0.01	2.68	0.48
4-oxide	0.55 ± 0.02	0.3395 ± 0.0004	64.5 ± 2.3	56.6	0.62 ± 0.09	0.70	0.08
5	2.762 ± 0.007	0.279 ± 0.001	143.3 ± 0.6	51.6	2.12 ± 0.01	2.22	0.10
1-oxide	4.431 ± 0.003	0.354 ± 0.001	214.1 ± 0.6	56.6	2.77 ± 0.01	3.34	0.57
4-oxide	2.325 ± 0.003	0.3397 ± 0.007	133.5 ± 0.3	56.6	1.94 ± 0.004	1.99	0.05
6	2.56 ± 0.05	0.2904 ± 0.0002	135.2 ± 1.8	51.6	2.02 ± 0.03	1.94	0.08
4-oxide	3.20 ± 0.02	0.3294 ± 0.0006	168.3 ± 1.1	56.6	2.33 ± 0.03	2.34	0.01
pyrazine 1-oxide	3.36 ± 0.03	0.329 ± 0.001	81.2 ± 0.7	27.6	1.62 ± 0.01[c,e]		

[a] The dipole moment of the 1-oxide of **6** could not be measured because of insufficient amount of the sample. [b] Lit.[18] 1.42 D. [c] Lit.[18] 1.62 D. [d] Lit. 1.46 D: H. Lumbroso and G. Palamidessi, *Bull. Soc. Chim. Fr.*, 3150 (1965). [e] Lit. 1.66 D: H. Lumbroso and G. Palamidessi, *Bull. Soc. Chim. Fr.*, 3150 (1965). [f] $\Delta\mu = \mu_{calcd} - \mu_{found}$.

Table IV. UV Spectra of 4, 5, and 6[a]

compd	nm (log ε)
4	237 (3.89), 249 (3.86), 287 (3.89)
5	254 (4.23), 291 (3.99), 311 (4.03)
6	252 (4.03), 290 (3.98), 310 (4.03)

[a] In 95% C_2H_5OH.

on the outermost oxygen of the peracid.[2-4,7] The orientation of substituent pyrazines is governed by the relative basicities of the ring nitrogen.[2-5,7] The inductive effect of the substituent is assumed to be one factor in the difference in basicities of the ring nitrogens; e.g., peracetic acid oxidation of methylpyrazine **1**, having an electron-donating methyl group, leads to the formation of the 1-oxide rather than the 4-oxide in spite of the steric hindrance of the methyl group. In the same manner, the orientation of peracetic acid oxidation of chloropyrazines **3**, **4**, and **6** can be explained by the reduction of basicity of the 1-nitrogen by the electron-withdrawing inductive effect of the 2-chloro substituent. However, the 1:1 formation of the 1- and 4-oxides of **5** on peracetic acid oxidation cannot be elucidated by the inductive effect alone.

Another factor in the direction of peracetic acid oxidation is suggested to be the mesomeric interaction of the substituent with the pyrazine ring. It is particularly useful in elucidation of the effect of the phenyl group on the regiospecificity in which the nitrogen furthest removed from this substituent is exclusively oxidized. Namely, in peracetic acid oxidations of phenylchloropyrazines **5** and **6**, each phenyl group of which is conjugated with the pyrazine ring, the site of N-oxidation is controlled by the phenyl as well as by the chloro substituents. This behavior is significantly illustrated by the peracetic acid oxidation of **5**, in which the phenyl and chloro substituents lead the competitive formations of the 1- and 4-oxides, respectively. On the other hand, the excellent reactivity on the 4-nitrogen of **6** can be attributed to the combined influence of both the substituents. However, unlike the phenyl group of **5** and **6**, that of **4** is interfered in resonance conjugation with the pyrazine ring by the steric hindrance of the adjacent chloro substituent,[19,20] accordingly the influence of the phenyl group on the N-oxidation vanishes, thus the peracetic acid oxidation of **4** is governed only by the chloro substituent. This exclusive oxidation on the 4-nitrogen is seen in **4** but not in 2-methoxy-3-phenylpyrazine which gives only the 4-oxide under the same conditions.[15]

The difference between persulfate and peracetic acid oxidations may be mainly acidic strength of the solvents. In concentrated sulfuric acid, the ring nitrogens of pyrazine and 2-methylpyrazine (**1**) were strongly diprotonated resulting in no formation of any N-oxide by the persulfate oxidation. Similarly, 2-phenylpyrazine (**2**) gave a low yield of the 4-oxide by treatment with peroxysulfuric acid. In contrast, the equilibrium of chloropyrazines favors protonation on the nitrogen furthest removed from the chloro substituent[7] as a result of reduction of basicity on the 1-nitrogen by the electron-withdrawing chlorine atom. In persulfate oxidation of **4** and **5**, the phenyl group has no effect on the direction and the ease of oxidation. Thus, they provided the corresponding 2-chloropyrazine 1-oxides in the same ratio as **3**.

Experimental Section

All melting points were determined in capillary tubes and are corrected. Satisfactory analytical data (±0.3% for C, H, N, Cl) were reported for all new compounds listed in Table I. Infrared spectra were recorded on a Hitachi Model EPI-G_3 spectrometer, the UV spectra on a Shimazu Model UV-220 spectrometer, and the NMR spectra on a JEOL Model JNM-MH-100 instrument with tetramethylsilane as an internal standard.

Dipole Moment Measurements. Dipole moments were calculated by the method of Halverstadt and Kumler[21] from measurements of the dielectric constant (ε) and the specific gravity (ρ) of the solvent (benzene) and four different solutions of each compound. The specific gravities were measured with a 5-mL Lipkin-Davison's pyknometer. Dielectric constants at 25 °C were derived from measurements with a Yamato FAM-3A capacitance bridge and a glass cell. The electronic polarization was obtained by summation of bond electronic polarizabilities which were taken for C_{Ar}–C_{Ar}, C_{Ar}–N_{Ar}, C–C, C–H, C–Cl, and N–O as 2.69, 2.64, 1.30, 1.68, 6.51,[22] and 5.00,[18] respectively. No allowance was made for atomic polarization. The dielectric constant and specific gravity of benzene were taken as 2.2741 and 0.8732, respectively, at 25 °C.

2-Phenylpyrazine (2). A mixture of 5-phenylpyrazinedicarboxylic acid[23] (mp 193 °C, 17.5 g, 0.072 mol), which was prepared by potassium permanganate oxidation of 2-phenylquinoxaline, and powdered copper (II) oxide (0.7 g) was heated and distilled at 200–236 °C to give 12.7 g of colorless solid. Redistillation at 80 °C (5 mm) afforded 9.5 g (85%) of **2**,[24] which was recrystallized from ethanol to provide colorless needles, mp 72–73 °C.

This pyrazine **2** was also prepared by hydrogenolysis of chlorophenylpyrazine. A solution of **3** (5.52 g, 0.029 mol) in a mixture of ethyl acetate and triethylamine (9:1 v/v, 100 mL) was hydrogenated in the presence of 10% palladium on carbon (2.0 g) under atmospheric

pressure until the uptake of hydrogen ceased (720 mL of hydrogen at 20 °C for ca. 2 h). Then the resulting mixture was filtered and evaporated under reduced pressure. The residue was washed with cold water, dried in air, and recrystallized from ethanol to give 4.10 g (91%) of **2**.

General Preparation of Pyrazine *N*-Oxides. The peracetic acid oxidations were accomplished according to the procedure of the literature,[5,6,9,10,15] and the peroxysulfuric acid oxidation followed a procedure by Mixan and Pew.[7] The ratio of the 1- and 4-oxides of **1** in the reaction mixture was determined by GC (5% PEG succinate on Chromosorb WAW DMCS, 1 m glass column at 135 °C), and the separation was achieved by the procedure of Gumprecht and coworkers.[10] As the *N*-oxides of **4** and **5** were contaminated with a considerable amount of the starting pyrazines, the *N*-oxides were purified by column chromatography on silica gel (1 g/10 g). The first elution with benzene gave the starting pyrazine, and the second elution with benzene–chloroform or chloroform provided the *N*-oxide. The separation of the 1- and 4-oxides of **5** was carried out on a Merck PLC plate (silica gel 60 F_{254}) eluted with benzene.

2-Phenylpyrazine 1-Oxide. A solution of 2-chloro-3-phenylpyrazine (**4**) 4-oxide (1.652 g, 8.0 mmol) in 40 mL of ethyl acetate containing triethylamine (0.81 g, 8.0 mmol) was stirred with hydrogen (198 mL at 29 °C) in the presence of 5% palladium on carbon (0.5 g) under atmospheric pressure. The mixture was filtered and evaporated under reduced pressure. The residue was washed with cold water, dried in air, and dissolved in benzene, which was passed through a column of silica gel (30 g). The chromatogram was developed with benzene and successively benzene–chloroform (3:1), to afford **2**, **4**, and the starting *N*-oxide. Further elution with chloroform gave 0.605 g (44%) of 2-phenylpyrazine 1-oxide, which was recrystallized from ethanol to give colorless prisms.

2-Chloro-6-phenylpyrazine 1-Oxide (6). A solution of phenylmagnesium bromide in dry tetrahydrofuran (THF) (2.2 mol/L, 20.0 mL, 0.044 mol) was added dropwise to a stirred solution of 2-chloropyrazine 1-oxide (2.512 g, 0.019 mol) in 80 mL of THF and refluxed for 5 h. The mixture was washed with saturated aqueous ammonium chloride, dried over magnesium sulfate, and evaporated under reduced pressure. The residue (ca. 5 g) was dissolved in benzene and the solution was passed through a column of silica gel (80 g). The first elution with petroleum ether–benzene (1:1) gave biphenyl, and the second elution with benzene afforded 2.934 g of **6**. Further development with chloroform gave 0.080 g (2%) of the *N*-oxide, which was recrystallized from ethanol to give colorless crystals.

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Registry No.—**1**, 109-08-0; **2**, 29460-97-7; **3**, 14508-49-7; **4**, 41270-65-9; **5**, 25844-73-9; **6**, 41270-62-6; peracetic acid, 79-21-0; peroxysulfuric acid, 7722-86-3; 5-phenylpyrazinedicarboxylic acid, 39784-64-0.

References and Notes

(1) N. Sato, *J. Heterocycl. Chem.*, **15**, 665 (1978).
(2) E. Ochiai, "Aromatic Amine Oxides", Elsevier, Amsterdam, 1967.
(3) A. R. Katritzky and J. M. Lagowski, "Chemistry of the Heterocyclic *N*-Oxides", Academic Press, New York, N.Y., 1971, Chapter 2.
(4) G. W. H. Cheeseman and E. S. G. Werstiuk, *Adv. Heterocycl. Chem.*, **14**, 99 (1972).
(5) B. Klein, N. E. Heltman, and M. E. O'Donnell, *J. Org. Chem.*, **28**, 1682 (1963).
(6) S. Okada, A. Kosasayama, T. Konno, and F. Uchimaru, *Chem. Pharm. Bull.*, **19**, 1344 (1971).
(7) C. E. Mixan and R. G. Pew, *J. Org. Chem.*, **42**, 1869 (1977).
(8) Similar observation has emerged in monoperphthalic acid oxidation of 2-methylquinoxaline: E. Hayashi, Ch. Iijima, and Y. Nagasawa, *Yakugaku Zasshi*, **84**, 163 (1964); see also ref 2, p 44.
(9) M. Asai, *Yakugaku Zasshi*, **79**, 1273 (1959); *Chem. Abstr.*, **54**, 4607 (1960).
(10) W. H. Gumprecht, T. E. Beukelman, and R. Paju, *J. Org. Chem.*, **29**, 2477 (1964).
(11) J. K. Landquist and G. T. Stacy, *J. Chem. Soc.*, 2822 (1953).
(12) E. Hayashi and Ch. Iijima, *Yakugaku Zasshi*, **82**, 1093 (1962); see also ref 2, p 45.
(13) IR (KBr) 1-oxide, 1332 and 4-oxide, 1340 cm^{-1}.
(14) H. Shindo, *Chem. Pharm. Bull.*, **8**, 33 (1960).
(15) G. Karmas and P. E. Spoerri, *J. Am. Chem. Soc.*, **78**, 4071 (1956).
(16) S. Sugiura, S. Inoue, Y. Kishi, and T. Goto, *Yakugaku Zasshi*, **89**, 1646 (1969); *Chem. Abstr.*, **72**, 90404 (1970).
(17) P. J. Lont and H. C. van der Plas, *Recl. Trav. Chim. Pays-Bas*, **92**, 449 (1973).
(18) R. P. Duke, R. A. Y. Jones, A. R. Katritzky, J. M. Lagowski, and Yu. Sheinker, *J. Chem. Soc., Perkin Trans. 2*, 668 (1972).
(19) This interference of resonance conjugation is distinctly established by comparision of UV spectra of **4** with that of **5** and **6** (Table IV). Namely, **4** absorbs in the considerable shorter wavelength region than **5** or **6**, while the absorbances of **4** are smaller than those of **5** or **6**.
(20) Similar phenomena have emerged in percarboxylic acid oxidation of 2-methoxy- and 2-isopropyl-3-phenylquinoxaline: E. Hayashi, Ch. Iijima, and Y. Nagasawa, *Yakugaku Zasshi*, **84**, 163 (1964); see also ref 2, pp 46 and 47.
(21) I. F. Halverstadt and W. D. Kumler, *J. Am. Chem. Soc.*, **64**, 2988 (1942).
(22) C. P. Smyth, "Dielectric Behavior and Structure", McGraw-Hill, New York, N.Y., 1955.
(23) S. Yurugi and M. Hieda, *Yakugaku Zasshi*, **92**, 1322 (1972); *Chem. Abstr.*, **78**, 58353 (1973).
(24) S. Yasuda, T. Niwa, and N. Asegawa, Japanese Patent 74 117 480; *Chem. Abstr.*, **82**, 171053 (1975).

Novel Rearrangement of Ketazine Dianion: New Synthetic Route to Pyrrole, Tetrahydropyridazine, and Pyrazole

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The dianions of alkyl aryl ketazines, generated by treating alkyl aryl ketazines with 2 equiv of lithium diisopropylamide, rearranged selectively to pyrrole, tetrahydropyridazine, or pyrazole depending on the nature of the ketazine. The main factor governing the course of the reaction is the electron density on the carbon termini. Ketazine dianions bearing electron-releasing groups (i.e., propiophenone, butyrophenone, and tetralone azines) on their carbon termini rearrange to pyrroles, while ketazine dianions without substituents (i.e., acetophenone and acetonaphthone azines) and with electron-withdrawing substituents rearrange to tetrahydropyridazines and pyrazoles, respectively.

Coupled with the development of versatile methods for preparing systems suitable for rearrangement, various modifications of the Cope and Claisen rearrangements have been exploited in recent years[1] and the high stereoselectivity has prompted several applications of these rearrangements in the syntheses of natural products.[2] One of the current topics in this field is the hetero-Claisen rearrangement[3] (especially thio-Claisen rearrangement[4]), which generally proceeds highly stereoselectively at relatively low temperatures. Further, interesting anion-assisted oxy-Cope and Claisen rearrangements have been reported; i.e., R. E. Ireland et al.[5] have reported that the rearrangement of the enolate anion of allyl esters proceeds easily at room temperature. The oxy-Cope rearrangement was also accelerated enormously by the metalation of the hydroxyl group.[6]

In this context, we have been interested in the possibility

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