Diaziridines

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Reaction of benzylideneaniline (1a) or benzylidene-*p*-toluidine (1b) with hydroxylamine-*O*-sulfonic acid in the presence of aniline or *p*-toluidine did not give the expected diaziridines but benzaldehyde phenyl- (2a) or *p*-tolyl-hydrazone (2b). Under the same conditions, Schiff bases of nonaromatic amines gave diaziridines. The configuration of 1-cyclohexyl-3-(*p*-bromophenyl)diaziridine (7) was established by X-ray crystal structure analysis. The reaction of several 1-cyclohexyl-3-aryldiaziridines with phenyl isocyanate gave 1-cyclohexyl-2-(anilino-formyl)-3-aryldiaziridines. The reaction of these latter compounds with *p*-phenetidine is described.

During the course of a study on the reaction of ethoxycarbonylnitrene with Schiff bases it became desirable to have an authentic sample of a 1,3-diphenyl-diaziridine. Attempts to prepare it by the reaction of benzylideneaniline (1a) with reagents having electrophilic NH groups failed. This led us to investigate the preparation of diaziridines by known methods. This paper deals with the reaction of Schiff bases with hydroxylamine-*O*-sulfonic acid (HAOSA) and the physical and chemical properties of 1-alkyl-3-aryl-diaziridines so obtained.

Diaziridines bearing NH groups have been prepared by the reaction of Schiff bases with reagents having electrophilic NH groups such as HAOSA, chloramine, or oxaziridines.[2] However, the reaction of 1a either with HAOSA in the presence of 2 molar equiv of aniline or with 3-ethyl-3-methyloxaziridine resulted in the formation of benzaldehyde phenylhydrazone (2a). Under the same conditions, benzylidenecyclohexyl-amine gave 1-cyclohexyl-3-phenyldiaziridine as will be shown later. The reaction of benzylidene-*p*-toluidine (1b) with HAOSA and *p*-toluidine gave benzaldehyde *p*-tolylhydrazone (2b). However, the product obtained by the reaction of 1a and HAOSA in the presence of 2 molar equiv of *p*-toluidine was found to be a mixture of 2a and 2b as ascertained by nmr spectroscopy. The mechanism of the hydrazone formation was not pursued since there seemed to be many possible ways to give the hydrazones. Recently, an elegant way to prepare 1-(nitroaryl)diaziridines was reported by Heine, *et al.*[3] They stated that 1-(2,4-dinitrophenyl)- and 1-(2,4,6-trinitrophenyl)diaziridines bearing NH groups rearranged to the corresponding 2,4-dinitrophenyl- or 2,4,6-trinitrophenylhydrazones on heating in refluxing toluene.
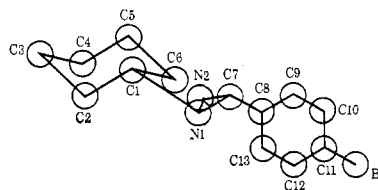
Several 1-alkyldiaziridines (3–7) were prepared from Schiff bases of nonaromatic amines. Results are summarized in Table I. In the case of 5 and 6, a pair of isomers of different melting points was obtained after the chromatography of the reaction mixture. The isomers have very similar ir and mass spectra, but differ markedly in their nmr spectra. The lower melting isomers have their δ_{CH} of the methine hydrogen at 3.2–3.4 while the higher melting ones have theirs at 4.2–4.3. The higher melting isomers were found to be thermally unstable and were transformed into the lower melting ones on heating: 5h and 6h were completely changed to 5l and 6l on heating for 1 hr at 140° (in diphenyl

ether) for the former and at 100° (in CCl4 in a sealed nmr tube) for the latter. Indeed compound 6h was found to change to 6l at an appreciable rate when its nmr spectrum was taken at ambient temperatures. The facts suggest that these pairs of compounds are isomers involving cis and trans orientation of the *N*-cyclohexyl and *C*-phenyl group. Detection of isomers of 3 and 4 by silica gel chromatography was impossible since these compounds are very sensitive to silicic acid. The isomer of 7 was not found after a careful chromatography of the reaction mixture.

In oxaziridines and diaziridines,[4] the existence of stereoisomers due to the slow nitrogen inversion (invertomers) has been discussed. In some oxaziridines,[5] the invertomers were actually isolated and the configuration was established by X-ray crystal structure analysis. With respect to diaziridines, there has been a report[4b] referring to the isolation of the invertomers. However, the stereochemistry was not made clear. Thus, the X-ray crystal structure analysis of an invertomer was undertaken. As a representative of the invertomers with smaller δ_{CH}, 7 was chosen to undergo the heavy atom method.

The X-ray structure analysis demonstrated that 7 was a trans isomer with respect to 1-cyclohexyl and 3-(*p*-bromophenyl) groups. Thus, the stereochemistry of the invertomers with smaller δ_{CH} was established to be trans. This result is quite expected from the differences in the thermal stabilities of the pairs of isomers; the more stable isomers, 5l and 6l, have the two large groups in trans orientation. It is interesting to note that, in 2-isopropyl-3-(*p*-nitrophenyl)oxaziridine,[5c] the higher melting invertomer has been established to have cis stereochemistry. It is also the case with 5 and 6 in our study. Chart I shows a molecular conformation

CHART I

MOLECULAR CONFORMATION AND NUMBERING OF ATOMS
IN 1-CYCLOHEXYL-3-(*p*-BROMOPHENYL)DIAZIRIDINE (7)

(1) Tsurumi University, School of Dental Medicine, 2-1-3 Tsurumi, Tsurumi-ku, Yokohama, Japan.

(2) (a) E. Schmitz, *Advan. Heterocycl. Chem.*, **2**, 104 (1966);   (b) E. Schmitz, R. Ohme, and S. Schramm, *Chem. Ber.*, **97**, 2521 (1964).

(3) H. W. Heine, P. G. Williard, and T. R. Hoye, *J. Org. Chem.*, **37**, 2980 (1972).

(4) (a) A. Mannschreck, R. Radeglia, E. Gründemann, and R. Ohme, *Chem. Ber.*, **100**, 1778 (1967);   (b) A. Mannschreck and W. Seitz, *Angew. Chem., Int. Ed. Engl.*, **8**, 212 (1969).

(5) (a) L. Brehm, K. G. Jensen, and B. Jerslev, *Acta Chem. Scand.*, **20**, 915 (1966); (b) B. Jerslev, *Acta Crystallogr.*, **23**, 645 (1967); (c) J. F. Cannon, J. Daly, and J. V. Silverton, *J. Chem. Soc., Perkin Trans. 2*, 1137 (1972).

Ar
\
C——NR¹
/   \
R³   N
        |
        H
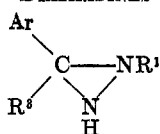
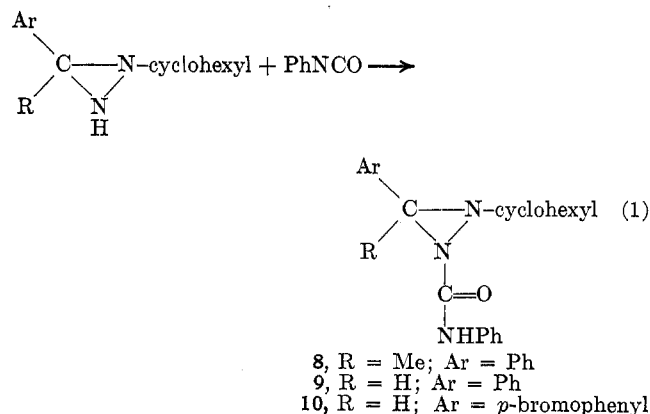| Compd	R¹	Ar	R³	Yield, %	Mp, °C	Nmr data, δ, ppm			Combustion analytical data					
						R³	NH	Solvent	Calcd, %			Found, %		
									C	H	N	C	H	N
3	Cyclohexyl	Ph	Me	35	96–97	1.75^a	Not clear	CDCl₃	77.73	9.32	12.95	77.91	9.01	13.23
4	PhCH₂	Ph	Me	29	60–62	1.68^a	2.00	CCl₄	80.32	7.19	12.49	80.15	7.06	12.65
5h	Cyclohexyl	Ph	H	2	102–104	4.25^b	2.30	CCl₂=CCl₂	77.18	8.97	13.85	77.31	8.72	14.17
5l	Cyclohexyl	Ph	H	23	53–54	3.21^b	2.00	CCl₂=CCl₂	77.18	8.97	13.85	77.18	8.62	13.98
6h	PhCH₂	Ph	H	2	62–63	4.22^b	2.54	CCl₄	79.96	6.71	13.32	79.75	6.75	13.49
6l	PhCH₂	Ph	H	13	38–40	3.36^b	1.82	CCl₄	79.96	6.71	13.32	80.14	6.75	13.46
7	Cyclohexyl	p-Br-phenyl	H	26	74–76	3.33^b	2.05	CDCl₃	55.52	6.09	9.96	55.50	6.08	10.11

^{a} Chemical shift of C³ CH₃. ^{b} Chemical shift of C³ H.

seen from the direction of the *c* axis (hydrogen atoms are excluded). Bond distances and angles are given in Table II with their estimated standard deviations. Chart II is a packing diagram of a unit cell projected

CHART II
PACKING DIAGRAM OF A UNIT CELL
PROJECTED DOWN THE *b* AXIS
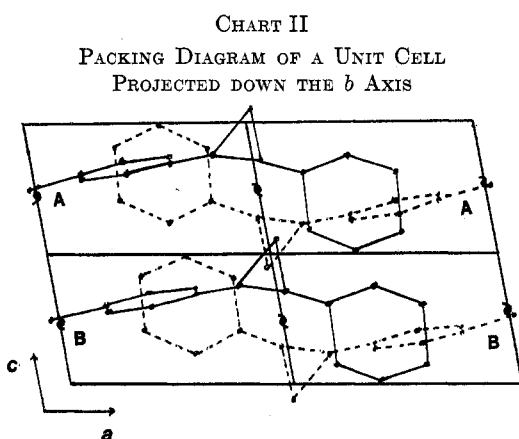
down the *b* axis. The dotted line represents the two molecules in the lower half and the solid line those in the upper half of the cell. A and B are enantiomers of each other. There are no intermolecular contacts significantly less than 3.4 Å for nonhydrogen atoms.

The reaction of **3** and **5** with phenyl isocyanate was investigated. Compound **3** reacted with phenyl isocyanate slowly in refluxing ether, and gave the adduct **8** (eq 1). The reaction of **5l** with phenyl isocyanate in

Ar
\
C——N–cyclohexyl + PhNCO ——→
/   \
R   N
       |
       H

Ar
\
C——N–cyclohexyl   (1)
/   \
R   N
       |
       C=O
       |
       NHPh

8, R = Me; Ar = Ph
9, R = H; Ar = Ph
10, R = H; Ar = p-bromophenyl

ether proceeded at room temperature and a fairly good yield of the adduct **9** was obtained after 3 days. Interestingly, however, **5h** did not react with phenyl isocyanate under the same condition. After several days

TABLE II
BOND LENGTHS AND ANGLES FOR NONHYDROGEN ATOMS WITH
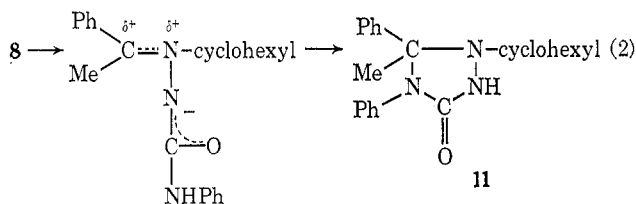ESTIMATED STANDARD DEVIATIONS IN PARENTHESES

A. Lengths

Bond	Å	Bond	Å
Br—C11	1.891 (17)	C7—N1	1.458 (23)
C1—C2	1.496 (21)	C7—N2	1.505 (23)
C1—C6	1.539 (20)	C8—C9	1.415 (19)
C1—N1	1.457 (17)	C8—C13	1.394 (18)
C2—C3	1.532 (25)	C9—C10	1.346 (18)
C3—C4	1.521 (27)	C10—C11	1.391 (22)
C4—C5	1.513 (25)	C11—C12	1.411 (22)
C5—C6	1.493 (23)	C12—C13	1.390 (19)
C7—C8	1.458 (19)	N1—N2	1.506 (17)

B. Angles

Angle	Degree	Angle	Degree
C2-C1-C6	109.5 (12)	C9-C8-C13	117.9 (12)
C2-C1-N1	110.9 (11)	C8-C9-C10	122.2 (13)
C6-C1-N1	109.3 (11)	C9-C10-C11	119.9 (14)
C1-C2-C3	110.3 (13)	Br-C11-C10	121.4 (12)
C2-C3-C4	112.0 (15)	Br-C11-C12	118.6 (12)
C3-C4-C5	110.1 (15)	C10-C11-C12	120.0 (14)
C4-C5-C6	111.8 (14)	C11-C12-C13	119.3 (13)
C1-C6-C5	112.4 (12)	C8-C13-C12	120.8 (12)
C8-C7-N1	120.5 (15)	C1-N1-C7	114.4 (13)
C8-C7-N2	120.4 (15)	C1-N1-N2	109.8 (10)
N1-C7-N2	61.0 (11)	C7-N1-N2	61.1 (11)
C7-C8-C9	120.4 (12)	C7-N2-N1	58.0 (10)
C7-C8-C13	121.7 (12)		

standing of the ethereal solution of **5h** and phenyl isocyanate, a small amount of **9** separated out of the solution. Inspection of the reaction mixture by tlc showed the existence of an appreciable amount of **5h** remaining. When the reaction mixture was heated, the yield of **9** increased. These facts suggest that there exists a great interference in the reaction of **5h** (cis) with phenyl isocyanate, and that the reaction occurs only after **5h** is isomerized to **5l**. The nature of such an interference is not clear now. Compound **7** gave adduct **10** in a high yield by the reaction with phenyl isocyanate.

That the adducts **8–10** have the diaziridine ring intact is apparent from their physical and chemical properties. In their nmr spectra, the cyclohexyl hydrogens appear as a broad multiplet extending from δ 1 to 2 like they do in the spectra of **3**, **5**, and **7**. This is in contrast to many other cases where the α-CH absorption of the negatively substituted cyclohexyl group appears at a lower field separated from the rest of the

methylene hydrogens of the cyclohexane ring. The nmr spectra of these adducts suggest that only one invertomer has been obtained in each adduct. From the behavior of **5h** and **5l** toward phenyl isocyanate mentioned above, the orientation of 1-cyclohexyl and 3-aryl groups in **9** and **10** are considered to be trans. However, no information has been given concerning the stereochemistry of the 2-anilinoformyl group.
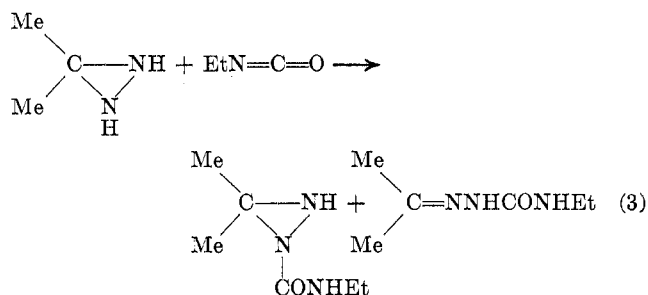
The reaction of **8** and **9** with *p*-phenetidine was carried out at 100° in an atmosphere of nitrogen. The adduct **9** and *p*-phenetidine gave a mixture of 1-cyclohexyl-4-phenylsemicarbazide and benzylidene-*p*-phenetidine along with a small amount of 1-(*p*-ethoxyphenyl)-3-phenylurea. 1-Cyclohexyl-4-phenylsemicarbazide is reported by Schmitz and Habisch.[6] The structure of the semicarbazide was established by the elemental analysis and nmr spectroscopy and by its conversion to the 1-anilinoformyl derivative, 1,2-bis(anilinoformyl)cyclohexylhydrazine.[7] Benzylidene-*p*-phenetidine was confirmed by a comparison with an authentic sample.[8] In the same manner, **8** and *p*-phenetidine gave the same semicarbazide and α-methylbenzylidene-*p*-phenetidine.[9] In this case, however, an appreciable amount of unknown compound, **11**, was obtained at the same time. The same compound was also obtained (in 65% yield) when **8** was heated at 100° for 1 hr. Combustion analysis and mass spectroscopy revealed that compounds **11** and **8** were isomeric. Significant differences are observed in the intensities of peaks at 216 (loss of PhNCO) and 243 (loss of Ph-NH). Both peaks are more intense in **8** than in **11**, and the difference is more pronounced in those at 243. The nmr spectrum of **11** has the absorption of cyclohexyl α-CH at δ 2.90 separated from the other methylene hydrogens of the cyclohexane ring. These facts strongly suggest that **11** does not hold the diaziridine ring any more. It has an absorption at 1700 cm^{-1} attributable to $\nu_{C=O}$ in the ir.[10] We have tentatively proposed 1-cyclohexyl-4,5-diphenyl-5-methyl-1,2,4-triazolidin-3-one for the structure of **11**, which would be formed finally after the cleavage of the C–N bond of the diaziridine ring in **8**, possibly through the intermediacy of a stabilized 1,3 dipole as depicted in eq 2.[11] No

$$8 \rightarrow \underset{Me}{\overset{Ph}{>}}C\overset{\delta^+}{\cdots}\overset{\delta^+}{N}\text{-cyclohexyl} \rightarrow \underset{Me}{\overset{Ph}{>}}C\text{---}N\text{-cyclohexyl} \quad (2)$$
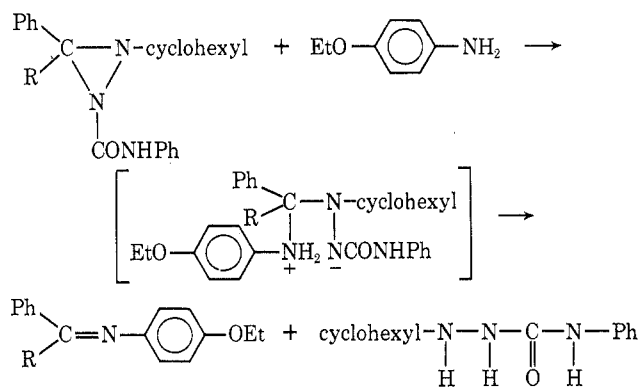
11

contradictory facts have been found to the proposed structure so far. However, we have not succeeded in the preparation of the corresponding isomer of **9**. Compound **9** seems fairly unstable thermally.

The triazolidinone formation from diaziridines and phenyl isocyanate was once reported by Schmitz and

Habisch.[6] According to them, 3,3-dialkyldiaziridines (including 1-cyclohexyl-3,3-dimethyldiaziridine) and phenyl isocyanate gave 1,2,4-triazolidin-3-ones in ether instead of the diaziridine derivatives. The structural assignment was based on the fact that the products did not liberate iodine from acidic KI solution as many diaziridines did. Later,[12] however, they found that some of the diaziridine derivatives failed to oxidize iodide owing to the greater liability of the ring to acidic hydrolysis. After alkaline hydrolysis of the reaction product of 1-cyclohexyl-3,3-dimethyldiaziridine and phenyl isocyanate, they actually obtained the starting diaziridine and thus established the structure of the adduct as 1-cyclohexyl-2-(anilinoformyl)-3,3-dimethyldiaziridine. Thus far, there has been no report which clearly characterizes the reaction product of a diaziridine and phenyl isocyanate or the rearranged product as 1,2,4-triazolidin-3-one. Abendroth[13] reported that the reaction of 3,3-dimethyldiaziridine and ethyl isocyanate gave both the corresponding diaziridine derivative as well as the rearranged hydrazone (eq 3).

$$\underset{Me}{\overset{Me}{>}}C\text{---}NH + EtN{=}C{=}O \longrightarrow$$

$$\underset{Me}{\overset{Me}{>}}C\text{---}NH + \underset{Me}{\overset{Me}{>}}C{=}NNHCONHEt \quad (3)$$

The formation of benzylidene-*p*-phenetidines and 1-cyclohexyl-4-phenylsemicarbazide by the reaction of **8** or **9** with *p*-phenetidine may be considered to proceed *via* the ring-opened addition product as shown in eq 4. No appreciable amount of α-methylbenzyl-

idene-*p*-phenetidine was obtained on heating a mixture of *p*-phenetidine and acetophenone at 100° for 2 hr.

(6) E. Schmitz and D. Habisch, *Rev. Chim. Acad. Rep. Populaire Roumaine*, **7**, 1281 (1962); *Chem. Abstr.*, **61**, 4331 (1964).
(7) M. Busch and K. Linsenmeier, *J. Prakt. Chem.*, [2] **115**, 232 (1927).
(8) Beilstein's "Handbuch der Organischen Chemie," Vol. 13, 1930, p 453.
(9) Beilstein's "Handbuch der Organischen Chemie," Vol. 13, 1930, p 454.
(10) It has been reported recently that 1-*tert*-butyl-2,4,5-triphenyl-1,2,4-triazolidin-3-one has an absorption at 1715 (C=O) and 1,2,4,5-tetraphenyl-1,2,4-triazolidinon-3-one has one at 1710 cm^{-1} in the ir [M. Komatsu, Y. Ohshiro, and T. Agawa, *J. Org. Chem.*, **37**, 3192 (1972)].
(11) We thank one of the reviewers for the suggestion.

(12) E. Schmitz, D. Habisch, and C. Gründemann, *Chem. Ber.*, **100**, 142 (1967).
(13) H. J. Abendroth, *Angew. Chem.*, **73**, 67 (1961).
(14) Melting points are uncorrected.
(15) H. J. Matsuguma and L. F. Audrieth, "Inorganic Syntheses," Vol. V, T. Moeller Ed., McGraw-Hill, New York, Toronto, London, 1957.

Experimental Section[14]

Reaction of Benzylideneaniline (1a) with Hydroxylamine-*O*-sulfonic Acid.—Hydroxylamine-*O*-sulfonic acid was prepared, and the purity was determined according to the literature.[15] In a 100-ml, three-necked, round-bottomed flask equipped with

a stirrer, an addition funnel, and a calcium chloride tube was added 15 ml of dry methanol. After the methanol was cooled with a Dry Ice–acetone bath, 1.25 g of HAOSA (90% purity) was added. To the methanolic suspension was added a solution of 1.81 g (0.01 mol) of **1a** and 2.07 g (0.022 mol) of aniline in 5 ml of methanol dropwise. After the addition was complete, the cooling bath was removed, and the reaction mixture was stirred overnight at room temperature. Ether was added to the mixture to promote the precipitation of aniline sulfate. The sulfate was filtered, and the filtrate was concentrated by rotary evaporation. To the concentrate, ether was added, and the organic solution was washed (H_2O) and dried (Na_2SO_4). Evaporation of ether gave 600 mg (30%) of **2a** melting at 150°. The structure of **2a** was confirmed by a comparison with an authentic sample[16] (lit.[16] mp 152.5°).

The reaction of **1b** with HAOSA and p-toluidine and the reaction of **1a** with HAOSA and p-toludine were carried out in the same way. The nmr spectrum ($CDCl_3$) of the latter reaction product had a peak at δ 2.25 (CH_3). Comparison of the spectrum with those of authentic **2a** and **2b**[17] indicated that the product was a 1:1 mixture of **2a** and **2b**.

Reaction of 1a with 3-Ethyl-3-methyloxaziridine.—3-Ethyl-3-methyloxaziridine was prepared from ethyl methyl ketone and HAOSA[2b], and was obtained as a mixture with the ketone by distillation under 0.6 mm. The ir (neat) had a characteristic absorption of NH at 3200 cm^{-1}.

The oxaziridine mixture (3.5 g) was dissolved in 200 ml of dry ether. To the solution was added 5 g of **1a** and 0.6 ml of acetic acid. After standing at room temperature overnight, the solution was washed (H_2O), dried (Na_2SO_4), and concentrated. The concentrate was chromatographed (silica gel, benzene) to give 250 mg of **2a** melting at 150°.

1-Cyclohexyl-3-methyl-3-phenyldiaziridine (3).—The procedure for the preparation of **3** and other diaziridines was almost the same as in the reaction of **1a** with HAOSA mentioned above. From 8.0 g (0.04 mol) of α-methylbenzylidenecyclohexylamine, 5.0 g (90% purity) of HAOSA, and 8.8 g (an equivalent amount to HAOSA) of cyclohexylamine, 3.0 g (35%) of almost pure **3** was obtained. Recrystallization from low boiling petroleum ether (bp 35–80°) gave a pure sample of **3** melting at 96–97°. Column chromatography of the reaction mixture (silica gel, benzene) did not give any diaziridine in this case.

Compounds **4** and **7** were obtained in the same manner. Compounds **5** and **6** were not obtained in crystalline form after workup. The concentrate was chromatographed (silica gel, benzene with increasing amount of chloroform). Lower melting isomers **5l** and **6l** eluted first and then did the higher melting **5h** and **6h**.

All diaziridines obtained above had a characteristic band of NH in the vicinity of 3200 cm^{-1} in the ir (KBr).

X-Ray Crystal Structure Analysis of 1-Cyclohexyl-3-(p-bromophenyl)diaziridine (7).—Colorless single crystals of **7** were obtained by recrystallization of purified **7** from n-hexane. Weissenberg photographs showed that these crystals belonged to the monoclinic system. The systematic absences, $h0l$, when l is odd, and $0k0$, when k is odd, are consistent with the space group C_{2h}^5-$P2_1/c$.[18] Precision lattice constants were obtained by least-squares refinement using 2θ angles measured with a Rigaku Denki four-circle diffractometer. The crystal data are as follows: $C_{13}H_{17}BrN_2$, mol wt 281.211; $a = 12.464$ (7), $b = 14.715$ (8), $c = 7.143$ (4) Å, and $\beta = 98.99$ (1)°; $V = 1293.9$ (1.2) Å^3. The density of the crystals (d_{obsd}) was found to be 1.4 g cm^{-3} by flotation in potassium iodide solution at room temperature. Assuming that each unit cell contains four formula units of **7**, the calculated density (d_{calcd}) is 1.442 g cm^{-3} which agrees with d_{obsd}.

A crystal with dimensions $0.5 \times 0.2 \times 0.1$ mm was mounted with its c axis parallel with the rotation axis of the goniometer of the diffractometer. X-Ray intensity data were collected in the θ–2θ scanning mode using Mo $K\alpha$ radiation ($\lambda = 0.7101$ Å), and obtained 4056 independent reflections in the range of $2\theta >$ 60°; 1676 reflections with $F_o > 3$ (ΔF_o) were used for the structure determinations. Lorentz and polarization corrections were made in a usual manner, but the absorption correction was neglected ($\mu = 33.42$ cm^{-1}).

The structure of **7** was solved by the heavy atom method. The bromine atom coordinates were assumed from three-dimensional Patterson functions. Fourier synthesis, with contribution of bromine atoms, found positions of the other atoms except for hydrogens. Further refinement was performed by block-diagonal least squares.[19] First ten cycles using isotropic temperature factors yielded an R value of 0.20. Nine successive cycles of anisotropic refinements gave an R index of 0.16 for 1653 reflections. The minimized quantity was $\Sigma w(|F_o| - k|F_c|)^2$, where weighting the scheme was as follows: $w = 0.5$ when $F_o <$ 7.90, $w = 1.0$ when $7.90 \le F_0 \le 29.86$, and $w = 29.86/F_0$ when $F_0 > 29.86$.

The positions of the hydrogen atoms were calculated assuming 1.08 Å for both C–H and N–H bond distances, since they were not clearly found from difference Fourier synthesis. A final R value was 0.125 after five cycles of least-squares refinement including all hydrogen atoms using anisotropic temperature factors for nonhydrogen atoms and isotropic temperature factors for hydrogens. A final difference Fourier synthesis seemed free of any significant features. All of the computations were performed on a Hitac 5020E computer at the University of Tokyo. UNICS program system[20] was used for structure refinements. Final atomic parameters are given in Table III, and final structure factors are in Table IV.[21]

Reaction of 3 with Phenyl Isocyanate.—A mixture of 1.08 g (5 mmol) of **3**, 0.60 g (5 mmol) of phenyl isocyanate, and 8 ml of dry ether was refluxed for 20 hr. Concentration of the solution and the subsequent addition of low boiling petroleum ether to the concentrate gave 1.0 g (60%) of the adduct **8** melting at 100–105°. Recrystallization from ether gave a pure sample of **8**: mp 106–106.5°; ν^{KBr} 3350, 1680 cm^{-1}; δ^{CDCl_3} 0.5–2.0 (m, 14, all cyclohexyl protons and CH_3), 6.8–7.7 (m, 10), 8.05 (s, 1).

Anal. Calcd for $C_{21}H_{25}N_3O$: C, 75.19; H, 7.51; N, 12.53. Found: C, 75.13; H, 7.52; N, 12.59.

1-Cyclohexyl-2-(anilinoformyl)-3-phenyldiaziridine (9).—Phenyl isocyanate (60 mg, 0.5 mmol) was dissolved in 2 ml of dry ether. To the solution was added 100 mg (0.5 mmol) of **5l**, and the mixture was left standing at room temperature. White crystals began to separate in a few hours. After 3 days' standing of the mixture, low boiling petroleum ether was added, and the crystals were collected to give 145 mg (90%) of **9** melting at 145–146°. Recrystallization from an ethanol–ether mixture gave a sample for analysis: mp 145–146°; ν^{KBr} 3380, 1700 cm^{-1}; δ^{CDCl_3} 1.0–2.3 (m, 11), 4.15 (s, 1), 6.9–7.6 (m, 10), 7.95 (s, 1).

Anal. Calcd for $C_{20}H_{23}N_3O$: C, 74.74; H, 7.21; N, 13.07. Found: C, 74.36; H, 7.21; N, 13.31.

Reaction of **7** (1.98 g, 7 mmol) with phenyl isocyanate (0.84 g, 7 mmol) was carried out in the same way and gave 2.6 g (93%) of the adduct **10**, mp 144–145°, after 3 days. Recrystallization from ethanol gave white crystals of **10**: mp 145–146°; ν^{KBr} 3350, 1700 cm^{-1}; δ^{CDCl_3} 1.0–2.3 (m, 11), 4.08 (s, 1), 6.8–7.7 (m, 9), 7.87 (s, 1).

Anal. Calcd for $C_{20}H_{22}BrN_3O$: C, 59.98; H, 5.55; N, 10.50. Found: C, 60.07; H, 5.53; N, 10.95.

Reaction of 9 with p-Phenetidine.—A mixture of 214 mg (0.67 mmol) of **9** and 88 mg (0.67 mmol) of p-phenetidine was heated at 100° for 2 hr in an atmosphere of nitrogen. Low boiling petroleum ether was added to the reaction mixture, and the white crystals were collected on a filter. From the filtrate, 50 mg (33%) of pale yellow crystals of benzylidene-p-phenetidine, mp 67–69° (lit.[8] mp 71°), was obtained.

The white crystals on the filter weighed 140 mg and were recrystallized from ethanol. After the removal of a small amount of 1-(p-ethoxyphenyl)-3-phenylurea,[22] 1-cyclohexyl-4-phenylsemicarbazide was obtained. The semicarbazide obtained here still seemed to contain some urea from the melting point (130–135°). Careful crystallizations from ethanol gave a pure sample of 1-cyclohexyl-4-phenylsemicarbazide: mp 136–137° (lit.[6] mp 140.5–141°); ν^{KBr} 1665 cm^{-1}; δ^{CDCl_3} 0.9–2.1 (m, 10), 2.65 (br, 1, cyclohexyl α-CH), 3.76 (br, 1, 1-NH), 6.75 (br, 1, 2-NH), 6.8–7.6 (m, 5), 8.25 (s, 1, 4-NH).

Anal. Calcd for $C_{13}H_{19}N_3O$: C, 66.92; H, 8.21; N, 18.01. Found: C, 66.65; H, 8.15; N, 17.96.

(16) (a) E. Fischer, *Chem. Ber.*, **9**, 887 (1876); (b) Beilstein's "Handbuch der Organischen Chemie," Vol 15, 1932, p 134.

(17) O. Schlenk, *J. Prak. Chem.*, [2] **78**, 56 (1908); ref 16b, p 513.

(18) "International Tables for X-Ray Crystallography," Vol I–III, K. Lonsdale, *et al.*, Ed., Kynoch Press, Birmingham, 1969.

(19) Program HBLS written by Dr. T. Ashida.

(20) "Universal Crystallographic Computation Program System," T. Sakurai Ed., Vol. I, II, The Crystallographic Society of Japan, 1967.

(21) See paragraph at the end of the paper regarding supplementary material.

(22) Reference 9, p 481.

On addition of phenyl isocyanate to the ethereal solution of the semicarbazide, 1,2-bis(anilinoformyl)cyclohexylhydrazine was obtained, which was recrystallized from ethanol to give a pure sample: mp 200–202° (lit.[7] mp 202°); ν^{KBr} 1660 cm^{-1}.

Anal. Calcd for $C_{20}H_{24}N_4O_2$: C, 68.16; H, 6.86; N, 15.90. Found: C, 68.10; H, 6.90; N, 15.96.

Reaction of 8 with *p*-Phenetidine.—An equimolar mixture of **8** (224 mg, 0.67 mmol) and *p*-phenetidine (88 mg, 0.67 mmol) was heated at 100° for 2 hr, and the reaction mixture was treated with low boiling petroleum ether as in the preceding example. From the petroleum ether soluble part, 50 mg (31%) of pale yellow crystals of α-methylbenzylidene-*p*-phenetidine was obtained, mp 85–87° (lit.[9] mp 88°).

The product remaining on the filter (130 mg) was a mixture of 1-cyclohexyl-4-phenylsemicarbazide and **11**. Recrystallization of the mixture from ethanol gave 30 mg of **11**, mp 155°. However, a quantitative separation of **11** and the semicarbazide was impossible. Crystallization of crude **11** from ethanol gave a pure sample: mp 156–157°; ν^{KBr} 3200, 1700 cm^{-1}; δ^{CDCl_3} 0.7–2.2 (m, 13), 2.90 (br, 1, cyclohexyl α-CH), 6.30 (s, 1), 6.8–7.2 (m, 10).

Anal. Calcd for $C_{21}H_{25}N_3O$: C, 75.19; H, 7.51; N, 12.53. Found: C, 75.05; H, 7.51; N, 12.60.

Compound **11** was also obtained on heating of **8** (100 mg) at 100° for 1 hr. Treatment of the reaction product with low boiling petroleum ether gave 65 mg of **11** melting at 155°. The tlc of the reaction mixture showed the existence of remaining **8**.

Heating of **9** in the same way resulted in an extensive decomposition as judged from the tlc.

Transmission of Substituent Effects in Heterocyclic Systems. Rates of Solvolysis of Substituted 1-(1-Methylimidazolyl)ethyl *p*-Nitrobenzoates[1]

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Reactivities of 1-(1-methyl-2-imidazolyl)ethyl *p*-nitrobenzoate (**2**), 1-(1-methyl-4-imidazolyl)ethyl *p*-nitrobenzoate (**4**), and 1-(1-methyl-5-imidazolyl)ethyl *p*-nitrobenzoate (**5**) are in the order 1:13:15. By comparison with other heteroarylethyl *p*-nitrobenzoates, effective replacement substituent constants, σ^+_{Ar}, are determined as $\sigma^+_{2-Im} = -0.82$, $\sigma^+_{4-Im} = -1.01$, and $\sigma^+_{5-Im} = -1.02$. Substituent effects on the rates of solvolysis of substituted 1-(1-methyl-2-imidazolyl)ethyl *p*-nitrobenzoates were examined, including the following substituents: 5-methyl, 5-chloro, 4-methyl, 4-phenyl, 4-chloro, 4-bromo, and 4,5-dimethyl. Though the rates for 5-substituents were satisfactorily represented by σ_p^+, σ_m^+ failed to account properly for the observed reactivities of 4-substituents. Various methods allowing greater proportions of resonance interaction were explored to seek an explanation for the latter fact and to provide a satisfactory basis for correlation of the observed relative reactivities.

Recent papers from these laboratories have examined the transmission of substituent effects in furan,[2–4] thiophene,[5,6] and thiazole[7] systems. These previous studies have shown that σ_p^+ gives a high quality representation of the influence of substituents when the substituent is located in a position capable of direct conjugation with the reacting side chain. Furthermore, the magnitude of ρ, which is found from the Hammett equation, is directly related to the changes in regional charges associated with the change $ArCH_3 \rightarrow ArCH_2^+$.[5,8] In the present study we examine the heterocyclic nucleus, imidazole.

The reactivity of imidazole in electrophilic substitu-

tion has received substantial attention[9] with substitution at the 4(5) position being most facile. 1-Methylimidazole gives substantial amounts of both 1-methyl-4-nitroimidazole and 1-methyl-5-nitroimidazole on nitration. The solvolysis reaction is a useful probe for the susceptibility of an aromatic moiety to electrophilic substitution[2,6,10] and is particularly useful in the present case because of the marked basicity of imidazoles.

The rates of solvolysis of the three isomeric 1-(1-methylimidazolyl)ethyl *p*-nitrobenzoates, **2**, **4**, and **5**, are given in Table I.

The isomeric imidazoles bracket the reactivity of 1-(2-furyl)ethyl *p*-nitrobenzoate; all are somewhat more reactive than the related thiophene. It is of interest that the spread in reactivity of **2**, **4**, and **5** is substantially less than for the analogous set of isomers of

(1) Supported in part by a grant from the National Science Foundation, GP-6133X.

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