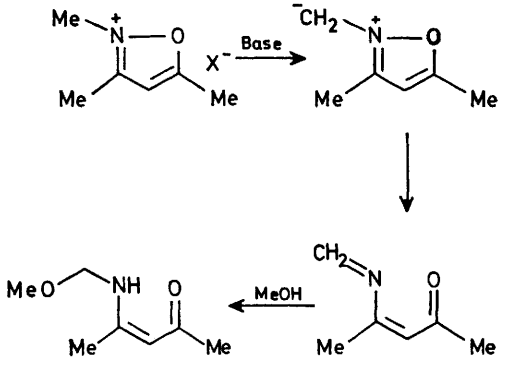
Preparation of 3-Imino-2-en-1-ones from 2-Aralkylisoxazolium Salts

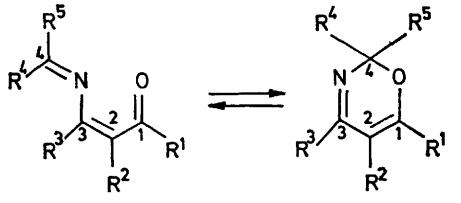
By **Choji Kashima,* Yoshihiko Tsuda, Satoshi Imada,** and **Takehiko Nishio,** Department of Chemistry, University of Tsukuba, Sakura-mura, Niiharigun, Ibaraki 305, Japan

Isoxazolium salts having an aralkyl group on the nitrogen atom, such as 2-benzhydryl- and 2-fluoren-9-yl-isoxazolium salts, are decomposed by base to give the corresponding 3-imino-2-en-1-ones, while 2-methyl-3,5-diphenylisoxazolium perchlorate gives 4,6-diphenyl-2*H*-1,3-oxazine. The chemical behaviour of these 3-imino-2-en-1-ones and the mechanism of their formation are also discussed.

RECENTLY we reported the reactions of 3,5-disubstituted isoxazoles and isoxazolium salts.[1,2] In these papers, we proposed 3-imino-2-en-1-ones as the intermediates in the reaction of 2-methylisoxazolium salts with sodium methoxide to give 3-(methoxymethyl)amino-2-en-1-ones.[3] Therefore, we wished to prepare the 3-imino-2-en-1-ones and to investigate their chemical behaviour. In the literature, there are only two publications concerning 3-imino-2-en-1-ones (2). In one, Barluenga



and his co-workers reported [4] that the reaction products from acetophenone and nitriles in the presence of aluminium chloride were 3-substituted 3-(1-phenylethylideneamino)-1-phenylprop-2-en-1-ones. However, the structures of these compounds were later corrected to 4*H*-1,3-oxazines from their ^{13}C n.m.r. spectra and their



chemical reactivity.[5,6] In the other, Kohler and Blatt tentatively proposed the 3-methylideneamino-1,2,3-triphenylprop-2-en-1-one structure (2a) for the product of the reaction of the 2-methyl-3,4,5-triphenylisoxazolium salt (1a) with alkali.[7] However, King and Durst revised the structure of this compound to 4,5,6-triphenyl-2*H*-1,3-oxazine (3a) on the basis of ^1H n.m.r. spectrum and chemical behaviour.[8]

RESULTS AND DISCUSSION

The structures (2a) and (3a) are tautomeric, so we wished to check in which form the product from compound (1a) existed. In structure (2a), there is no sp^3 carbon, while (3a) has one sp^3 carbon. The ^{13}C n.m.r. of the compound, which was prepared from (1a) according to Kohler's procedure (m.p. 141 °C), shows one sp^3 carbon signal at δ 79.6. From this fact, the structure was shown to be (3a) coinciding with King's structure. Similarly, 2-methyl-3,5-diphenylisoxazolium perchlorate (1b) was decomposed to 4,6-diphenyl-2*H*-1,3-oxazin- (3b) by treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).

Since the benzylideneamino-group is more stable than the methylideneamino-group as a result of conjugation, the introduction of a phenyl group onto the imino-carbon was expected to increase the stability of the 3-imino-2-en-1-ones (2) over their cyclic tautomers, the 2-phenyl-2*H*-1,3-oxazines (3). Therefore, 2-benzhydryl-3,5-dimethylisoxazolium perchlorate (1c) was treated with DBU in ether. The product showed the different i.r. absorption pattern listed in Table 1. The sp^3 carbon signal could not be observed in the ^{13}C n.m.r. spectrum. The product was hydrogenated to 4-benzyhydrylaminopent-3-en-2-one (4c) over a platinum catalyst and was hydrolysed to pentane-2,4-dione (5). From these facts, this product was shown to be 4-(diphenylmethylideneamino)pent-3-en-2-one (2c). Treatment of (1c) with potassium methoxide instead of DBU also gave (2c).

For further confirmation of these structures, 2-bis-*p*-tolylmethyl-3,5-dimethylisoxazolium perchlorate (1d) was treated with DBU to afford 4-(bis-*p*-tolylmethylideneamino)pent-3-en-2-one (2d). From the ^1H n.m.r. spectrum in the presence of an europium shift reagent, the acyclic structure with the *Z*-configuration (2d) was inferred. Similarly, 2-(1-phenylethyl)- (1e) and 2-fluoren-9-yl-3,5-dimethylisoxazolium perchlorate (1f), 2-benzhydryl- (1g), 2-(1-phenylethyl)- (1h), and 2-fluoren-9-yl-3-methyl-5-phenylisoxazoium perchlorate (1i) were decomposed by DBU or potassium methoxide to give the corresponding 3-amino-2-en-1-ones (2) in good yields. All these products were found to have the acyclic structure with a *Z*-configuration on the basis of their ^1H n.m.r. ,^{13}C n.m.r., and i.r. spectra, and elemental analyses, summarised in Tables 1 and 2. The fact that the R^3 methyl signals appeared around δ 2.0 in the ^1H n.m.r. spectrum also supported the *Z*-configuration, because the C-5 methyl signals of (*Z*)-4-aminopent-3-en-2-ones generally appear at δ 2.0.[9]

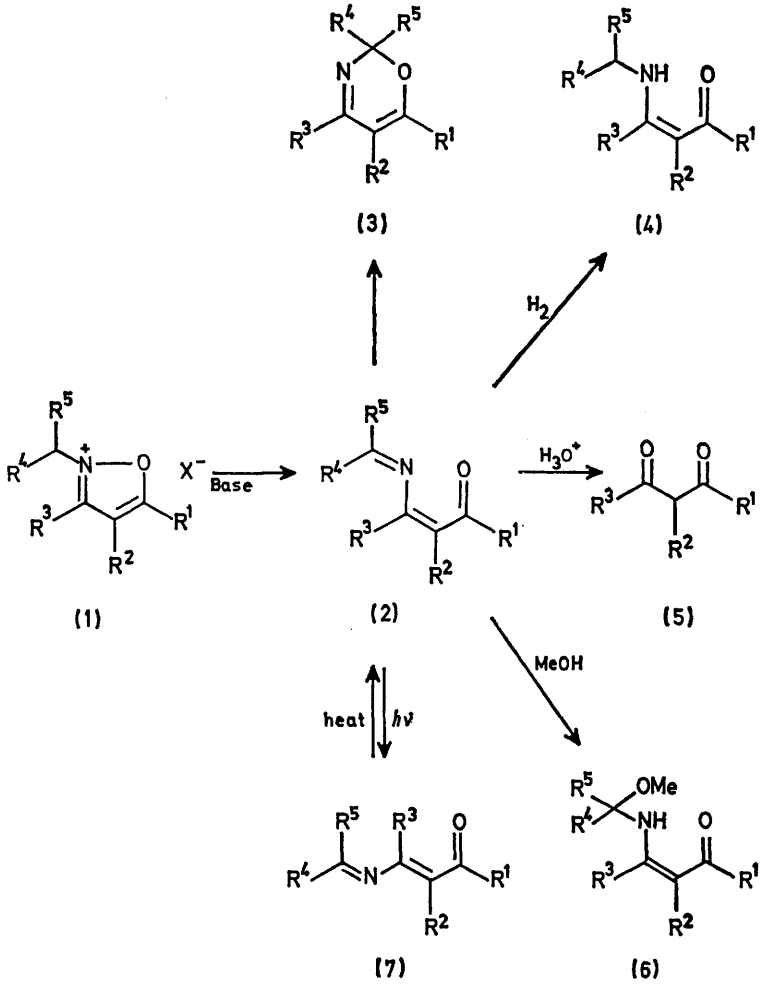
These (*Z*)-3-imino-2-en-1-ones (2) equilibrated to a

TABLE 1

^{1}H N.m.r., i.r. and u.v. spectral data

Compound	δ R^2	R^1	R^3	R^4	R^5	$\nu_{max.}$ (cm^{-1})	$\lambda_{max.}$/nm (log ε)
(3a)	6.8—7.7			5.58		1 625, 1 570	239 (4.20), 338 (3.79)
(3b)	6.63	7.2—7.95		5.66		1 625, 1 570	253 (4.03), 328 (3.54)
(2c)	5.30	2.04	1.88	7.1—7.4		1 665, 1 635, 1 575	207 (4.30), 279 (4.03)
(2d)	5.21	2.02	1.79	7.13, 7.32	2.38	1 660, 1 640, 1 580	273 (4.17)
(2e)	5.18	1.91	1.86	7.1—7.7	1.95	1 660, 1 640, 1 575	213 (4.58), 247 (4.57), 316 (4.62)
(2f)	5.47	2.20	2.05	7.0—7.85		1 660, 1 640, 1 595	206 (4.45), 247 (4.70), 255 (4.80), 270 (4.35), 291 (4.17), 300 (4.20)
(2g)	5.97	2.08	7.15—7.7, 7.7—8.0			1 650, 1 620, 1 585	209 (4.34), 323 (3.92)
(2h)	5.85	2.15	7.1—7.6, 7.6—8.0		1.97	1 665, 1 645, 1 590	206 (4.16), 223 (3.98), 326 (4.01)
(2i)	6.25	2.33	7.1—7.6, 7.6—8.0			1 670, 1 630, 1 595	
(7c)	5.39	1.97	2.23	7.1—7.7			
(7f)	5.86	2.15	2.54	6.9—7.8		1 660, 1 645, 1 600	
(7g)	6.10	7.23	2.37		7.23		

mixture of the isomers (2) and (7) by irradiation in benzene or methanol solution, as summarised in Table 3. Though we did not succeed in separating the isomeric mixture of (2) and (7), the spectral data of the photo-isomers (7) are listed in Tables 1 and 2. The R^3 methyl signals of (7) appear at *ca.* δ 2.4 in the ^{1}H n.m.r. spectra, while the C-5 methyl signals of (*E*)-4-aminopent-3-en-2-ones generally appear at δ 2.4.[9] In addition, no signals



a; R^1 = R^2 = R^3 = Ph, R^4 = R^5 = H. X = $FeCl_4$
b; R^1 = R^3 = Ph, R^2 = R^4 = R^5 = H, X = ClO_4
c; R^1 = R^3 = Me, R^2 = H, R^4 = R^5 = Ph, X = ClO_4
d; R^1 = R^3 = Me, R^2 = H, R^4 = R^5 = C_6H_4Me-*p*, X = ClO_4
e; R^1 = R^3 = R^5 = Me, R^2 = H, R^4 = Ph, X = ClO_4
f; R^1 = R^3 = Me, R^2 = H, R^4,R^5 = Fluoren-9-yl, X = ClO_4
g; R^1 = R^4 = R^5 = Ph, R^2 = H, R^3 = Me, X = ClO_4
h; R^1 = R^4 = Ph, R^2 = H, R^3 = R^5 = Me, X = ClO_4
i; R^1 = Ph, R^2 = H, R^3 = Me, R^4, R^5 = Fluoren-9-yl, X = ClO_4

due to a cyclic isomer could be observed in the ^{13}C n.m.r. spectrum of (7). When the mixture of (2) and (7) was heated above 50 °C, the ratio of the mixture was changed without any other decomposition (Table 3). An attempt to confirm the structures (7) as (*E*)-3-imino-2-en-1-ones by analysis of the europium-shifted ^1H n.m.r. spectra was unsuccessful.

TABLE 3

Photochemical and thermal isomerisation of (2)

Compound	Irradiation	Temperature (°C)	Solvent	Time/h	Product ratio (2) : (7)
(2c)	>300nm	25	CD_3OD	45	70 : 30
	>300nm	25	C_6D_6	36	28 : 72
	Dark	60	C_6D_6	45	67 : 33
(2f)	>300nm	25	C_6D_6	40	19 : 81
	Dark	80	C_6D_6	150	42 : 58
(2g)	>300nm	25	CD_3OD	45	55 : 45
	>300nm	25	C_6D_6	45	33 : 67
	Dark	60	C_6D_6	90	75 : 25

In summary, 2-aralkylisoxazolium perchlorates give 3-imino-2-en-1-one compounds in good yield, while 2-methylisoxazolium salts are decomposed to afford 2*H*-1,3-oxazine derivatives. Furthermore, the thermally stable structure of these 3-imino-2-en-1-ones is unexpectedly the *Z*-configuration and these *Z*-isomers are isomerised to the *E*-isomer by irradiation.

The mechanism of the formation of *Z*-3-imino-2-en-1-ones (2) and 2*H*-1,3-oxazines (3) is assumed to be as follows. The first step is the deprotonation of the substituent group on the nitrogen atom of (1). The resulting ylide is then converted intramolecularly into (2). Finally, (2) is cyclised to (3) in the case of (1a) and (1b). Since diphenyldiazomethane generates diphenylcarbene at high temperatures, 3,5-dimethylisoxazole was treated with diphenyldiazomethane at 80 °C. The product was identical with (2c), and therefore, the formation of an ylide as the intermediate was proved.

In addition, compound (2c) was treated with methanol in the presence of potassium methoxide to afford the methanol adduct, 4-{[diphenyl(methoxy)methyl]-amino}pent-3-en-2-one (6c). This fact supports the previous assumption [3] of 2-(3,5-dimethylisoxazolium)-methylide and 4-methylideneaminopent-3-en-2-one as the intermediates in the reaction of 2,3,5-trimethylisoxazolium salts with sodium methoxide.

TABLE 2

^{13}C N.m.r. spectral data of (2) and (3)

Compound	δ C-1	C-2	C-3	C-4	R^1	R^3	Ar
(3a)	166.7	115.7	159.4	79.6			138.0, 135.3, 133.0, 131.5, 129.3, 128.8, 128.5, 128.4, 128.0, 127.8, 127.5, 126.9
(3b)	163.5	95.7	162.7	80.9			136.9, 132.1, 130.9, 130.5, 128.6, 128.5, 126.6, 126.0
(2c)	*	106.8	160.4	139.2	27.3	23.5	129.2, 128.4, 128.2, 128.1, 127.9, 127.8
(2d)	197.6	109.6	160.5	141.3	31.9	23.5	140.4, 139.7, 136.9, 134.3, 130.1, 128.8, 128.2, 126.4, 21.4
(2f)	196.5	109.3	160.0	142.4	30.5	22.9	134.0, 132.4, 128.4, 124.8, 120.2
(2g)	*	99.7	162.3	141.7		24.3	130.9, 128.3, 128.2, 128.0, 127.9, 127.1, 126.3

* Undetectable.

EXPERIMENTAL

Materials.—2-Methyl-3,5-diphenylisoxazolium perchlorate (1b) was prepared from the corresponding isoxazole by Adachi's procedure.[10] 2-Benzhydryl- (1c), 2-(bis-*p*-tolylmethyl)- (1d), 2-(1-phenylethyl)- (1e), and 2-fluoren-9-yl-3,5-dimethylisoxazolium perchlorates (1f), and 2-benzhydryl- (1g), 2-(1-phenylethyl)- (1h), and 2-fluoren-9-yl-3-methyl-5-phenylisoxazolium perchlorates (1i) were prepared from the corresponding isoxazoles according to Woodman's procedure.[11]

2-Methyl-3,5-diphenylisoxazolium perchlorate (1b), yield 69%, m.p. 235—236 °C (decomp.); $\nu_{max.}$ (KBr) 1 605, 1 545, and 1 460 cm^{-1}; δ([$^2H_6$]DMSO) 4.49 (s, 3 H), 7.7—8.2 (m, 10 H), and 8.31 (s, 1 H) (Found: C, 57.2; H, 4.1; N, 4.3. $C_{16}H_{14}ClNO_5$ requires C, 57.23; H, 4.20; N, 4.17%).

2-(Bis-p-tolylmethyl)isoxazolium perchlorate (1d), yield 63%, m.p. 137—138 °C (decomp.); $\nu_{max.}$ (KBr) 1 600 and 1 480 cm^{-1}; δ([$^2H_6$]DMSO) 2.17 (s, 3 H), 2.25 (s, 6 H), 2.33 (s, 3 H), 5.61 (s, 1 H), 6.04 (s, 1 H), and 6.9—7.4 (AB q, 8 H) (Found: C, 61.4; H, 5.6; N, 3.75. $C_{20}H_{22}ClNO_5$ requires C, 61.30; H, 5.66; N, 3.58%).

2-Fluoren-9-yl-3,5-dimethylisoxazolium perchlorate (1f), yield 30%, m.p. 250—252 °C (decomp.); $\nu_{max.}$ (KBr) 1 590, 1 445, and 1 080 cm^{-1} (Found: C, 59.45; H, 4.4; N, 3.95. $C_{18}H_{16}ClNO_5$ requires C, 59.75; H, 4.45; N, 3.87%).

2-Benzhydryl-3-methyl-5-phenylisoxazolium perchlorate (1g), yield 74%, m.p. 137—138 °C (decomp.); $\nu_{max.}$ (KBr) 1 610, 1 570, and 1 470 cm^{-1}; δ([$^2H_6$]DMSO) 2.29 (s, 3 H), 5.63 (s, 1 H), 6.80 (s, 1 H), and 6.9—7.9 (m, 15 H) (Found: C, 64.7; H, 4.75; N, 3.4. $C_{23}H_{20}ClNO_5$ requires C, 64.87; H, 4.73; N, 3.29%).

3-Methyl-5-phenyl-2-(1-phenylethyl)isoxazolium perchlorate (1h), yield 79%, m.p. 132—134 °C (decomp.); $\nu_{max.}$ (KBr) 3 032, 1 610, 1 578, and 1 479 cm^{-1}; δ([$^2H_6$]DMSO) 2.05 (d, 3 H), 2.35 (s, 3 H), 6.41 (q, 1 H), and 7.3—8.1 (m, 11 H) (Found: C, 59.5; H, 5.0; N, 3.85. $C_{18}H_{18}ClNO_5$ requires C, 59.43; H, 4.99; N, 3.85%).

2-Fluoren-9-yl-3-methyl-5-phenylisoxacolium perchlorate (1i), yield 50%, m.p. 156—157 °C (decomp.); $\nu_{max.}$ (KBr) 1 605, 1 570, 1 470, and 1 460 cm^{-1} (Found: C, 65.25; H, 4.25; N, 3.35. $C_{23}H_{18}ClNO_5$ requires C, 65.17; H, 4.28; N, 3.30%).

General Decomposition of (1).—DBU (1 mmol) was added

dropwise to a solution of (1) (1 mmol) in anhydrous ether or dioxan (15 ml). After stirring overnight at room temperature, water was added, the product was extracted with dichloromethane, and the organic layer was dried over anhydrous magnesium sulphate and concentrated. The residue was chromatographed on silica gel eluting with benzene–ethyl acetate. The yellow fraction was recrystallised from hexane. When potassium methoxide was used as the base, the decomposition reaction was carried out in methanol. The elemental analyses and spectral data are summarised in Tables 1, 2, and 4.

Hydrolysis of (2c).—A solution of (2c) (1 mmol) in methanol (10 ml) was treated with dilute hydrochloric acid at room temperature for 12 h. The mixture was extracted with dichloromethane and the organic layer was dried over anhydrous magnesium sulphate. The residue was identical with authentic pentane-2,4-dione (5) by chromatographic and ^{1}H n.m.r. spectral comparison.

Hydrogenation of (2).—An ethanolic solution (15 ml) of (2) (1 mmol) was hydrogenated in the presence of platinum oxide. After absorption of hydrogen was complete, the catalyst was filtered off, and the residue recrystallised from hexane.

4-*Benzhydrylaminopent*-3-*en*-2-*one* (4c), yield 95%, m.p. 135—137 °C; δ($CDCl_3$) 1.88 (s, 3 H), 2.03 (s, 3 H), 5.02 (s, 1 H), 5.70 (d, 1 H), 7.26 (s, 10 H), and 11.7 (br s, 1 H) (Found: C, 81.35; H, 7.25; N, 5.2. $C_{18}H_{19}NO$ requires C, 81.47; H, 7.22; N, 5.28%).

4-(1-*Phenylethylamino*)*pent*-3-*en*-2-*one* (4e), yield 32%, m.p. 70—71 °C; $\nu_{max.}$ (KBr) 3 025, 1 605, 1 490, and 1 430 cm^{-1}; δ($CDCl_3$) 1.40 (d, 3 H), 1.65 (s, 3 H), 1.91 (s, 3 H), 4.42—4.88 (m, 1 H), 4.96 (s, 1 H), 7.26 (s, 5 H), and 11.2 (br s, 1 H) (Found: C, 76.8; H, 8.4; N, 6.8. $C_{13}H_{15}NO$ requires C, 76.81; H, 8.43; N, 6.80%).

Addition of Methanol to (2c).—A methanol (20 ml) solution of (2c) (0.5 mmol) was treated with potassium methoxide (1.5 mmol) for several hours under reflux. After extraction with dichloromethane, the crude product was purified by flash chromatography [12] on silica gel, eluting with hexane–ethyl acetate to give 4-{[methoxy(diphenyl)-methyl]amino}pent-3-en-2-one (6c), yield 98%, b.p. 80—83 °C at 10^{-3} mmHg; $\nu_{max.}$ (liquid) 1 600, 1 490, 1 430, 740, and 700 cm^{-1}; δ($CDCl_3$) 1.12 (s, 3 H), 2.08 (s, 3 H), 3.14 (s, 3 H), 5.13 (s, 1 H), and 7.0—7.7 (m, 10 H) (Found: C, 77.0; H, 6.9; N, 4.7. $C_{19}H_{21}NO_2$ requires C, 77.25; H, 7.16; N 4.74%).

Reaction of Diphenyldiazomethane with 3,5-*Dimethylisoxazole*.—A mixture of 3,5-dimethylisoxazole (5.6 mmol), diphenyldiazomethane (4.7 mmol), and cuprous iodide (33 mg) in dry benzene (25 ml) was refluxed for 12 h, and the mixture was poured into aqueous sodium hydroxide and extracted with benzene and dichloromethane. The combined organic layers were washed with water, dried over anhydrous magnesium sulphate, solvent evaporated off, and the residue chromatographed on silica gel eluting with benzene–ethyl acetate. The product was *identical with* (2c) by ^{1}H n.m.r. spectral and chromatographic comparison, yield 9%.

Europium-induced Shift Configurational Analysis of (2d).—The ^{1}H n.m.r. spectrum of a $CDCl_3$ solution of (2d) (35.64 mg) was measured in the presence of Eu(dpm)$_3$, and the molar induced shift values are summarised in Table 5.

TABLE 4

Elemental analytical and physical data

Compound	Base	Yield (%)	M.p. (°C) [B.p. (°C)/mmHg]	Analysis (%) Found C	Found H	Found N	Calc. C	Calc. H	Calc. N
(3b)	DBU	63	68—69.5	81.65	5.45	5.95	81.67	5.56	5.95
(2c)	DBU	87	97.5—99.5	82.25	6.6	5.3	82.10	6.51	5.32
	KOMe	87							
(2d)	KOMe	89	[178—183/5]	82.1	7.15	4.35	82.43	7.26	4.80
(2e)	KOMe	83	[111—115/3]	77.45	7.60	6.95	77.57	7.60	6.95
(2f)	DBU	75	87—88	83.1	5.8	5.4	82.73	5.78	5.36
(2g)	KOMe	41	85—85.5	84.8	5.95	4.3	84.89	5.88	4.31
(2h)	KOMe	73	80.5—81.5	82.75	6.5	5.35	82.10	6.51	5.32
(2i)	DBU	46	131—132.5	85.6	5.35	4.3	85.42	5.29	4.33

Photochemical and Thermal Isomerisation of (2).—A [$^2H_6$]benzene or [$^2H_4$]methanol solution of (2) (50 mg in 0.3 ml) was irradiated in a Pyrex n.m.r. tube by a high-pressure mercury lamp, and the isomer ratio was measured directly from the ^{1}H n.m.r. spectrum of the mixture. The mixture after photolysis was then heated in the dark, monitoring by ^{1}H n.m.r. spectroscopy. The results are summarised in Table 4.

TABLE 5

Europium-induced molar shift values for (2d)

	R^1	R^2	R^3	*o*-H	*m*-H	*p*-Me
δ	2.02	5.21	1.79	7.32	7.13	2.38
Δδ	6.51	7.06	1.80	1.85	0.40	0.15

[9/1074 *Received*, 10*th July*, 1979]

REFERENCES

[1] C. Kashima, Y. Yamamoto, and Y. Tsuda, *Heterocycles*, 1977, **6**, 805.
[2] C. Kashima, K. Arai, S. Imada, and Y. Tsuda, *Bull. Chem. Soc. Japan*, 1978, **51**, 1844.
[3] C. Kashima, N. Mukai, Y. Yamamoto, Y. Tsuda, and Y. Omote, *Heterocycles*, 1977, **7**, 241.
[4] J. Barluenga, S. Fustero, V. Rubio, and V. Gotor, *Synthesis*, 1977, 780.
[5] C. Kashima, S. Imada, and T. Nishio, *Chem. Letters*, 1978, 1391.
[6] S. Auricchio, O. Vajna de Papa, and E. Vera, *Synthesis*, 1979, 116.
[7] E. P. Kohler and A. H. Blatt, *J. Amer. Chem. Soc.*, 1928, **50**, 1217.
[8] J. F. King and T. Durst, *Canad. J. Chem.*, 1962, **40**, 882.
[9] C. Kashima and Y. Yamamoto, *Bull. Chem. Soc. Japan*, 1979, **52**, 1735.
[10] I. Adachi, K. Harada, M. Miyazaki, and H. Kano, *Chem. Pharm. Bull. (Japan)*, 1974, **22**, 61.
[11] D. J. Woodman, *J. Org. Chem.*, 1968, **33**, 2397.
[12] W. C. Still, M. Kahn, and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.