Syntheses and Properties of 3-Acylimino-1-alkylimidazolium and Benzimidazolium Betaines

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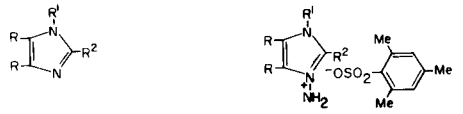
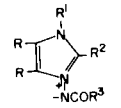
3-Amino-1-alkylimidazolium and benzimidazolium mesitylenesulfonates were readily prepared in good to high yeilds by treating the parent heterocycles with *O*-mesitylenesulfonylhydroxylamine. Treatment of the 3-amine salts with acylating agents gave crystalline 3-acylimines, which showed the characteristic ir, uv, nmr, and mass spectral properties. Deuterium exchange of the 3-acylimines occurs at the 2-position. Thermolysis of neat 3-benzoylimino-1-methylbenzimidazolium betaine afforded 2-benzamido-1-methylbenzimidazole and products derived from *N-N* bond cleavage. Irradiation of 3-benzoylimino-1-alkylbenzimidazolium betaines resulted in *N-N* bond cleavage to give 1-alkylbenzimidazoles and benzamide, while the corresponding 3-ethoxycarbonylimines underwent rearrangement to afford ethyl 1-alkyl-2-benzimidazolecarbamates.

Whereas the chemistry of the six-membered heteroaromatic *N*-imines has been explored to a considerable extent (1), the *N*-imines of the azoles have received little attention presumably because of difficult accessibility (2). Recently we have shown that various types of heteroaromatic tertiary amines can be readily aminated by *O*-mesitylenesulfonylhydroxylamine (MSH) (3, 4) to the *N*-amine salts (5), precursors of the *N*-imines, and azoles are not exceptional (6). As an initial step in the study of the chemistry of the azole *N*-imines we describe here the syntheses and properties of the 3-acylimines of 1-alkylimidazoles and 1-alkylbenzimidazoles (7).

SCHEME I



	R	R^1	R^2		R	R^1	R^2
I	H	Me	H	VII	H	Me	H
II	H	Me	Me	VIII	H	Me	Me
III	-CH=CH-CH=CH-	Me	H	IX	-CH=CH-CH=CH-	Me	H
IV	-CH=CH-CH=CH-	Et	H	X	-CH=CH-CH=CH-	Et	H
V	-CH=CH-CH=CH-	Me	Me	XI	-CH=CH-CH=CH-	Me	Me
VI	-CH=CH-CH=CH-	Et	Me	XII	-CH=CH-CH=CH-	Et	Me



	R	R^1	R^2	R^3
XIIIa	H	Me	H	Ph
XIIIb	H	Me	H	Me
XIIIc	H	Me	H	OEt
XIV	H	Me	Me	Ph
XVa	-CH=CH-CH=CH-	Me	H	Ph
XVb	-CH=CH-CH=CH-	Me	H	Me
XVc	-CH=CH-CH=CH-	Me	H	OEt
XVIa	-CH=CH-CH=CH-	Et	H	Ph
XVIb	-CH=CH-CH=CH-	Et	H	Me
XVIc	-CH=CH-CH=CH-	Et	H	OEt
XVII	-CH=CH-CH=CH-	Me	Me	Ph
XVIII	-CH=CH-CH=CH-	Et	Me	Ph

Preparation.

The 3-amine mesitylenesulfonates (VII-XII) employed in this study were prepared in good to high yields by reaction of equimolar quantities of the corresponding parent imidazoles (I-VI) and MSH in methylene chloride for 5 minutes at room temperature (Table I). Conversion of the 3-amine salts (VII-XII) into the 3-acylimines (XIII-XVIII) was effected by heating at 90° with excess acylating agents such as benzoyl chloride, acetic anhydride, or ethyl chloroformate (Table II). The 3-acylimines thus obtained are stable crystalline compounds, although some of them are hygroscopic. The structures of the 3-acylimines were confirmed by elemental analyses and ir, uv, nmr, and mass spectrometry.

Physical Properties

The ir spectra (in chloroform) (Table III) of the 3-acylimines show polarized carbonyl absorption bands at 1550-1560 cm^{-1} for the 3-benzoylimines (8), at 1570-1580 cm^{-1} for the 3-acetylimines, and at 1630-1640 cm^{-1} for the 3-ethoxycarbonylimines. These results closely parallel those observed for the *N*-acylimines of pyridines (1) and suggests that betaine forms B are important contributors

TABLE I

Preparation of 1-Alkyl-3-aminoimidazolium Salts

Compd.	M.P. °C	Yield (%)	Formula	Analysis Calcd. C	H	N	Found C	H	N
VII	79-82	84	$C_{13}H_{19}N_3O_3S$	52.51	6.44	14.13	hygroscopic (a)		
VIII	173-175	54	$C_{14}H_{21}N_3O_3S$	54.01	6.80	13.50	53.93	6.83	13.25
IX	219-221	96	$C_{17}H_{21}N_3O_3S$	58.78	6.09	12.10	58.62	6.05	12.15
X	170-171	90	$C_{18}H_{23}N_3O_3S$	59.82	6.42	11.62	59.67	6.48	11.67
XI	224-225 (b)	86	$C_{18}H_{23}N_3O_3S$	59.82	6.42	11.62	59.97	6.45	11.49
XII	196-197	80	$C_{19}H_{25}N_3O_3S$	60.78	6.71	11.19	60.54	6.66	11.29

(a) The picrate: m.p. 115-116° (from ethanol); *Anal.* Calcd. for $C_{10}H_{11}N_6O_7$: C, 36.70; H, 3.39; N, 25.68. Found: C, 36.93; H, 3.34; N, 25.77. (b) The melting point reported in reference (6b) should be revised to this value.

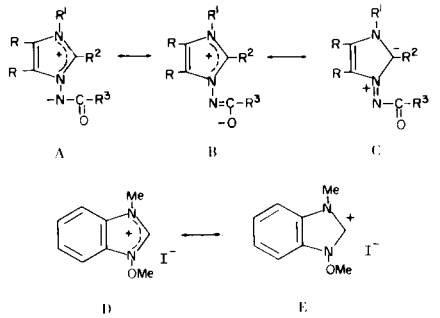
TABLE II

Preparation of 3-Acylimino Betaines

Compd.	M.P. °C	Recryst'd from	Yield (%)	Formula	Analysis Calcd. C	H	N	Found C	H	N
XIIIa	159-160	$CHCl_3$ - Et_2O	40	$C_{11}H_{11}N_3O$	65.67	5.51	20.88	65.46	5.56	20.81
XIIIb	159-160	$CHCl_3$ - pet. ether	55	$C_6H_9N_3O$	51.78	6.52	30.20	hygroscopic (a)		
XIIIc	150-151	$CHCl_3$ - pet. ether	48	$C_7H_{11}N_3O_2$	49.69	6.55	24.84	hygroscopic (b)		
XIV	173-175	Me_2CO - Et_2O	62	$C_{12}H_{13}N_3O$	66.95	6.09	19.52	66.80	6.23	19.88
XVa	180-181	Me_2CO - Et_2O	78	$C_{15}H_{13}N_3O$	71.69	5.21	16.72	71.76	5.29	16.55
XVb	127-128	$CHCl_3$ - pet. ether	63	$C_{10}H_{11}N_3O$	63.47	5.86	22.21	hygroscopic (c)		
XVc	182-183	Me_2CO - Et_2O	69	$C_{11}H_{13}N_3O_2$	60.26	5.98	19.15	60.00	5.88	19.19
XVIa	79-80	Me_2CO - Et_2O	66	$C_{16}H_{15}N_3O \cdot \frac{1}{2}H_2O$	70.05	5.88	15.32	69.64	6.10	15.17 (d)
XVIb	164-166	Me_2CO - Et_2O	60	$C_{11}H_{13}N_3O$	65.00	6.45	20.68	64.92	6.42	20.57
XVIc	140-142	Me_2CO - pet. ether	85	$C_{12}H_{15}N_3O_2$	61.78	6.48	18.02	61.61	6.47	18.04
XVII	283-284	$CHCl_3$ - Et_2O	80	$C_{16}H_{15}N_3O$	72.43	5.70	15.84	72.32	5.73	15.92
XVIII	202-203	Me_2CO - Et_2O	57	$C_{17}H_{17}N_3O$	73.09	6.13	15.04	72.95	6.16	14.80

(a) The picrate: m.p. 145-147° (from ethanol); *Anal.* Calcd. for $C_{12}H_{12}N_6O_8$: C, 39.13; H, 3.28; N, 22.82. Found: C, 39.23; H, 3.35; N, 22.95. (b) The picrate: m.p. 136-137° (from ethanol); *Anal.* Calcd. for $C_{13}H_{14}N_6O_9$: C, 39.20; H, 3.54; N, 21.10. Found: C, 39.32; H, 3.60; N, 21.47. (c) The picrate: m.p. 197-199° (from ethanol); *Anal.* Calcd. for $C_{16}H_{14}N_6O_8$: C, 45.94; H, 3.37; N, 20.09. Found: C, 45.91; H, 3.31; N, 19.79. (d) The picrate: m.p. 207-209° (from ethanol); *Anal.* Calcd. for $C_{22}H_{18}N_6O_8$: C, 53.44; H, 3.67; N, 17.00. Found: C, 53.52; H, 3.66; N, 17.13.

SCHEME 2



to the total structures of the 3-acylimines. Evidently, in the 3-ethoxycarbonylimines the electron-donating ability of the ethoxyl group increases the carbonyl frequency and thus decreases the contribution from form B.

In the nmr spectra (Table IV) in deuteriochloroform, the signals of H-2 (9) of the 3-acylimines are shifted to lower filed than those of the parent imidazoles, reflecting the decreased electron density due to the proximity at a quaternary nitrogen atom (*i.e.*, a contribution from forms A and/or B). However, the magnitude of the shift is highly dependent on the nature of the acyl group and is smaller than those reported for 3-methoxy-1-methylbenzimidazolium iodide (XIX), in which significant resonance is limited to canonical forms of D↔E. This is mainly attributed to the electron-donating properties of the 3-acylimino group to the imidazole ring (*i.e.*, the contribution of resonance forms C). In this respect the acylimino groups resemble the *N*-oxide group (*e.g.*, XX), although the back-donating ability of the former is weaker than the latter. It is not surprising that the low-field shift of H-2 for the 3-ethoxy-

TABLE III

Spectral Data of 3-Acylimino Betaines

Compd.	IR ν max ($CHCl_3$)cm^{-1}	UV λ max ($CHCl_3$) nm (log ϵ)	Mass m/e (rel. intensity %)
XIIIa	1595 (vs), 1550 (vs), 1350 (vs)	278 285 (4.02) (4.02)	201 (2), 200 (1), 124 (10) (b) 105 (4), 82 (20)
XIIIb	1580 (vs), 1555 (s), 1380 (m)	262 (a)	139 (100), 124 (87), 82 (64)
XIIIc	1640 (s), 1620 (s), 1295 (vs)	265 (a)	169 (57), 124 (88), 97 (80) 82 (100)
XIV	1595 (vs), 1560 (vs), 1350 (vs)	251 (3.81)	215 (100), 200 (33), 138 (73) 96 (48)
XVa	1595 (vs), 1560 (vs), 1360 (vs)	264 278sh 318 (3.65) (3.56) (3.87)	251 (100), 250 (59), 174 (73) 132 (70)
XVb	1570 (vs), 1560 (vs), 1375 (s)	274, 281, 305 (a)	189 (53), 174 (100), 132 (98)
XVc	1630 (s), 1620 (s), 1610 (s) 1300 (vs)	274 282 314 (3.54) (3.56) (3.71)	219 (6), 174 (12), 147 (24) 132 (100)
XVIa	1595 (vs), 1560 (vs), 1355 (vs)	264 278sh 317 (3.69) (3.51) (3.79)	265 (42), 264 (14), 188 (32) (c) 160 (28), 146 (38)
XVIb	1570 (vs), 1560 (vs), 1380 (s)	275 282 308 (3.62) (3.66) (3.71)	203 (58), 188 (79), 160 (100) 146 (66)
XVIc	1630 (s), 1615 (s), 1605 (s) 1295 (vs)	274 282 313 (3.37) (3.36) (3.53)	233 (14), 188 (13), 161 (27) 160 (15), 146 (100)
XVII	1595 (s), 1560 (s), 1350 (vs)	267sh 274 282 (4.06) (4.09) (4.06)	265 (78), 250 (44), 188 (55) 146 (100)
XVIII	1595 (s), 1555 (s), 1350 (vs)	266sh 274 280 (4.13) (4.13) (4.13)	279 (27), 264 (14), 202 (21) (d) 160 (38)

(a) Precise extinctions were not determined since the compound was hygroscopic. (b) The base peak is m/e 42. (c) The base peak is m/e 77. (d) The base peak is m/e 105.

TABLE IV

Comparison of Chemical Shifts (τ_2) between 3-Acylimino Betaines and Parent Imidazoles

Compd.	τ_2 (a)	Δ(b)	Compd.	τ_2 (a)	Δ(b)
XIIIa	0.19	2.44	XX	1.26 (c)	0.81
XIIIb	0.38	2.25	III	2.07	
XIIIc	0.95	1.68			
I	2.63		XVIa	-0.68	2.78
			XVIb	-0.35	2.45
XIV	7.55	0.10	XVIc	0.02	2.08
II	7.65		IV	2.10	
XVa	-0.55	2.62	XVII	7.28	0.22
XVb	-0.12	2.19	V	7.50	
XVc	0.05	2.02			
XIX	-1.0 (c)	3.07	XVIII	7.30	0.15
			VI	7.45	

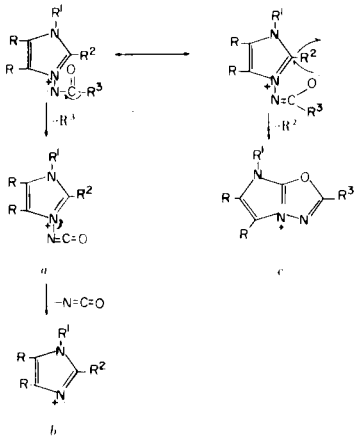
(a) In deuteriochloroform. (b) Δ = (τ_2 of parent imidazoles) - (τ_2 of 3-acylimino betaines). (c) S. Takahashi and H. Kano, *Chem. Pharm. Bull. (Tokyo)*, 14, 375 (1966) and a private communication from Dr. Takahashi.

carbonylimines is smaller in magnitude than for the 3-benzoylimines or 3-acetylimines. In contrast, the effect of the acyl group on the signal of the methyl group at the 2-position of XIV, XVII, and XVIII is rather small and the methyl signal appears at positions close to the values of the parent imidazoles.

The uv spectra (Table III) in chloroform reveal that the 3-acylimines of 1-alkylimidazoles (XIIIa-c) show the longest absorption maxima at 262-285 nm. The maxima are shifted to longer wavelength in the benzo series (XVa-c, XVIa-c), which have maxima at 305-318 nm. Variation of the acyl group has relatively little effect on the position of the maxima. This absorption band disappeared by addition of one drop of 1 *N* hydrochloric acid to the chloroform solution and reappeared by further addition of one drop of 1 *N* sodium hydroxide. It is interesting to note that XIV, XVII, and XVIII show no such characteristic absorption band.

The mass fragmentation patterns of the 3-acylimines are similar to those previously reported for the pyridine counterparts (11). Thus, one of the most important features in all the spectra examined is loss of phenyl, methyl, and ethoxyl radicals from the molecular ion of the 3-benzoylimines, 3-acetylimines, and 3-ethoxycarbonylimines, respectively, to lead to the same species *a*. This ion further decomposes by elimination of NCO to give an ion *b*. A diagnostically useful feature of the mass spectra of the 3-benzoylimines is the appearence of an intense (M-1) or (M-15) peak which arises by loss of hydrogen or methyl radical from the 2-position of the molecular ions. In analogy to the pyridine case (11), the resulting ion can be represented by a cyclized ion *c*. The 3-ethoxycarbonylimines and 3-acetylimines do not show the M-1 peaks.

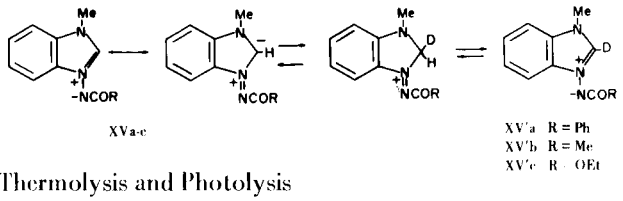
SCHEME 3



Deuterium Exchange Studies

Chemical evidence for the contribution from the resonance form C was obtained from deuterium exchange studies. Thus, when 3-acetylimine XVb and 3-ethoxycarbonylimine XVc were treated with deuteriochloroform-deuterium oxide in an nmr tube at 35°, rapid (within 5 minutes) and complete exchange of H-2 occurred to give XV'b and XV'c, respectively. Similarly, H-2 of 3-benzoylimine XVa was also exchanged but at a much slower rate (after 24 hours). It should be noted that in the case of *N*-benzoyliminopyridinium betaine, H-2 has been reported to be exchanged with deuterium only in the presence of base (12).

SCHEME 4



XVa-c

XV'a R = Ph
XV'b R = Me
XV'c R = OEt

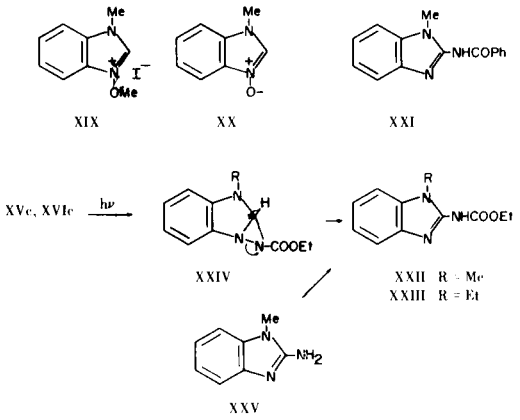
Thermolysis and Photolysis

For further comparison with the pyridine or quinoline cases, the thermal and photochemical behavior of 3-acylimino-1-alkylbenzimidazolium betaines was examined.

Thermolysis of 3-benzoylimine XVa without solvent at 200-210° (20-30° above its melting point) for 15 minutes gave 2-benzamido-1-methylbenzimidazole (XXI) in addition to III, unreacted XVa, and an unidentified compound. The formation of XXI under the pyrolytic conditions is especially interesting because in the pyridine (11) or quinoline cases (13) only the *N-N* bond cleavage had been known to take place. The formation of XXI could be explained by a mechanism similar to that proposed for the photolysis of XVc, as described later. Similar treatment of 3-ethoxycarbonylimine XVc, however, gave an intractable mixture.

Photolysis of XVa in ethanol in a quartz vessel for 38 hours resulted in the *N-N* bond cleavage to give III, benzamide and unreacted XVa. Similarly, XVII gave V, benzamide, and unreacted XVII. When the irradiation was carried out in a Pyrex vessel, no reaction occurred. In contrast, irradiation of 3-ethoxycarbonylimines XVc or XVIc in ethanol in a Pyrex vessel for 46 hours gave 2-ethoxycarbonylamino-1-methyl and 1-ethylbenzimidazoles (XXII and XXIII) as major products. Compound XXII was identical with an authentic sample prepared from 2-amino-1-methylbenzimidazole (XXV). The formation of XXII and XXIII may be rationalized in terms of an intermediacy of a diaziridine (XXIV) which undergoes the *N-N* bond cleavage, as proposed for the similar photo-rearrangement observed in the photolyses of *N*-acyliminoquinolinium and isoquinolinium betaines (13,5b).

SCHEME 5



XIX XX XXI

XXIV

XXII R = Me
XXIII R = Et

XXV

EXPERIMENTAL

Recently an explosion has been reported for O-mesitylenesulfonylhydroxylamine [Chem. Eng. News, Dec. 17, (1973)***].***

All melting points are uncorrected. The ir spectra were recorded on Shimadzu IR-27G and Hitachi EPI-G2 spectrophotometers, uv spectra on an Hitachi 124-spectrophotometer, and nmr spectra on an Hitachi R-20A spectrometer (tetramethylsilane as internal standard). Mass spectra were obtained with an Hitachi RMU-6D instrument with a direct inlet system operating at 70 eV. Preparative tlc was carried out on Merck Alumina PF_{254}. Irradiation was carried out using an Eikosha 300 W high-pressure mercury lamp.

Materials.

1-Methylimidazole (I) and 1,2-dimethylimidazole (II) were obtained commercially. 1-Methylbenzimidazole (III), 1-ethylbenzimidazole (IV), 1,2-dimethylbenzimidazole (V), and 1-ethyl-2-methylbenzimidazole (VI) were synthesized by application of a procedure of Hodges and Grimmett (14); III, b.p. 143-145°/5 mm. [Lit. 138-140°/4 mm. (15)], IV, b.p. 165-167°/10 mm. [Lit. b.p. 148-150°/4 mm. (15)], V, m.p. 111° [Lit. m.p. 112° (16)], and VI, b.p. 158-160°/10 mm. [Lit. b.p. 166-168°/15 mm. (16)].

3-Amino-1-alkylimidazolium and Benzimidazolium Mesitylenesulfonates (VII-XII).

To an ice-cooled solution of a 1-alkylimidazole (2 mmoles) in methylene chloride (5 ml.) was added dropwise a solution of MSH (2 mmoles) in methylene chloride (10 ml.). The reaction mixture was stirred at room temperature for 5 minutes. After addition of ether, the precipitated crystals were collected and recrystallized from ether-ethanol. The results are summarized in Table I.

3-Acylimino-1-alkylimidazolium and Benzimidazolium Betaines (XIII-XVIII).

A mixture of a 3-amine salt (1 mmole) and an acylating agent (benzoyl chloride, acetic anhydride, or ethyl chloroformate) (1 ml.) was heated at 90° for 4-7 hours, until all the crystals of the starting 3-amine salt dissolved. The excess reagent was evaporated *in vacuo* and the residue was dissolved in methanol and the solution passed through a column of Amberlite IRA-410 ion-exchange resin (OH form). The methanolic eluate was concentrated to give white crystals, which were purified by recrystallization. When the product was hygroscopic, it was characterized as the picrate. The results are summarized in Tables II, III, and IV.

Deuterium Exchange Studies.

A 3-acylimine (XVa-c) (*ca.* 0.1 mmole) was dissolved in deuteriochloroform (0.4 ml.) in an nmr tube and the nmr spectrum was then recorded at 35°. Deuterium oxide (one drop) added and the mixture was shaken for a few seconds. The spectrum was immediately recorded again.

Thermolysis of XVa.

Compound XVa (100 mg.) was heated without solvent at 200-210° for 15 minutes to give a dark brown oil, from which unreacted starting material XVa (41 mg.), III (15 mg.), XXI, m.p. 158-159° [Lit. m.p. 161-162° (17)] (31 mg.), and an unidentified compound (13 mg.) were obtained by preparative tlc using chloroform as solvent.

Irradiation of XVa.

A solution XVa (75 mg.) in ethanol (20 ml.) in a quartz vessel was irradiated for 38 hours. Evaporation of ethanol afforded an iol, from which III (5.6 mg.), benzamide (11.7 mg.), m.p. 128-129°, and starting material XVa (7.5 mg.) were isolated by preparative tlc using benzene: 1-propanol (10:1) as solvent.

Irradiation of XVII.

Using a similar procedure described above, V (30 mg.), benzamide (35 mg.) and starting material XVII (5 mg.) were obtained from XVII (100 mg.).

Irradiation of XVc.

A solution of XVc (150 mg.) in ethanol (20 ml.) in a Pyrex vessel was irradiated for 46 hours. After evaporation of ethanol, the residual oil was submitted to preparative tlc using chloroform as solvent to give colorless crystals of ethyl 1-methyl-2-benzimidazolecarbamate (XXII), m.p. 131-132° (from chloroform-petroleum ether), yield, 19 mg. (20%); ir (potassium chloride): cm^{-1} 3310 (s), 1620 (vs), 1595 (vs) and 1560 (vs); uv λ max (ethanol): 237 nm (log ε 4.34), 292 (4.32) and 297 (4.38); nmr (deuteriochloroform): τ 2.81 (4H, s, aromatic H), 5.80 (2H, q, J = 7 Hz, $-CH_2CH_3$), 6.42 (3H, s, CH_3) and 8.67 (3H, t, J = 7 Hz, $-CH_2CH_3$). The mass spectrum shows the parent ion at m/e 219 (Calcd. 219).

Anal. Calcd. for $C_{11}H_{13}N_3O_2$: C, 60.26; H, 5.98; N, 19.15. Found: C, 59.98; H, 6.05; N, 18.91.

Starting material XVc (4 mg.) was recovered.

Ethyl 1-Methyl-2-benzimidazolecarbamate (XXII).

To a mixture of XXV (145 mg.) (18) in a 5% sodium bicarbonate solution (6 ml.) was added a solution of ethyl chloroformate (150 mg.) in chloroform (1 ml.) with stirring. After stirring for 20 minutes at room temperature, the reaction mixture was extracted with chloroform. The dried extract was concentrated and the residue was recrystallized from chloroform-petroleum ether, m.p. 129-130°, yield, 100 mg. (46%).

Irradiation of XVIc.

Using a similar procedure described above, XVIc (150 mg.) gave colorless crystals of XXIII, m.p. 105-106° (from methylene chloride-petroleum ether), yield, 40 mg. (32%); ir (potassium chloride): cm^{-1} 3320 (s), 1620 (vs), 1590 (vs) and 1560 (vs); uv λ max (ethanol): 238 nm (log ε 4.33) 293 (4.32) and 297 (4.37); nmr (deuteriochloroform); τ 2.81 (4H, s, aromatic H), 5.77 (2H, q, J = 7 Hz, $-CH_2CH_3$), 5.86 (2H, q, J = 7 Hz, $-CH_2CH_3$), 8.56 (3H, t, J = 7 Hz, $-CH_2CH_3$) and 8.60 (3H, t, J = 7 Hz, $-CH_2CH_3$). The mass spectrum shows the parent ion at m/e 233 (Calcd. 233).

Anal. Calcd. for $C_{12}H_{15}N_3O_2$: C, 61.78; H, 6.48; N, 18.02. Found: C, 61.67; H, 6.49; N, 17.75.

Starting material XVIc (26 mg.) was also recovered.

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(8) The ir band at 1590 cm^{-1} in the 3-benzoylimines is ascribed to that of the aromatic C=C bond.

(9) It is known that the H-2 of 1-methylimidazole is coupled to H-4 and H-5 with $J_{24(5)}$ = 0.8-1.5 Hz (10). In the corresponding 3-acylimines a similar small coupling interaction of H-2 with H-4 and H-5 was also observed.

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