Tetrahedron. Vol. 29, pp. 2359 to 2364. Pergamon Press 1973. Printed in Great Britain

PHOTOCHEMISTRY OF N-ACYLIMINO-ISOQUINOLINIUM AND -QUINOLINIUM BETAINES

Y. TAMURA,* S. MATSUGASHITA, H. ISHIBASHI and M. IKEDA

Faculty of Pharmaceutical Sciences, Osaka University, Toneyama, Toyonaka, Osaka, Japan

(*Received in Japan* 16 *February* 1973; *Received in UK for publication* 16 *April* 1973)

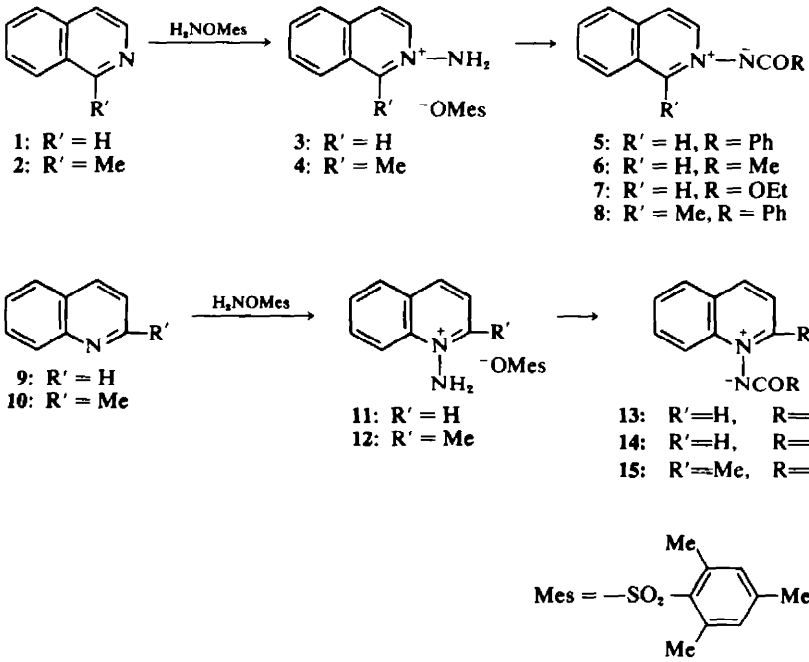
Abstract—The photochemical behavior of N-acyliminoisoquinolinium and -quinolinium betaines has been investigated. In contrast to pyridinium betaines, the principal course of reaction is the 1,2-migration of N-acylamino groups. Substituent effects as well as solvent effects are observed. The results are rationalized in terms of diaziridine intermediates.

In addition to the photochemistry of aromatic amine N-oxides,[1] the photochemical behavior of their nitrogen analogues have attracted increasing attention[2] since the first example of photoisomerization of N-acyliminopyridinium betaines to diazepines was reported.[3] To date, several types of photochemical reaction of N-substituted N-imines have been observed mainly in the pyridine series; i.e., (i) ring expansion to 1,2-diazepines,[3-5] (ii) rearrangement to 2-amino-pyridine derivatives,[5] and (iii) N-N bond fission.[4,6-8] The reactions (i) and (ii) are postulated to proceed *via* a diaziridine intermediate, analogous to an oxaziridine intermediate.[1]

We have examined the photochemical reactions of N-acyliminoisoquinolinium and -quinolinium betaines[9]* with the hope of discovering other reaction courses than those observed in the pyridine series, which might shed further light on the mechanism of product formation.

Syntheses of N-acylimino-isoquinolinium and -quinolinium betaines. N-Acylimino-isoquinolinium (**5–8**) and -quinolinium (**13–15**) betaines were prepared as outlined in Scheme 1. Isoquin-

*While our studies were in progress a brief report appeared on the photolysis of N-acyliminoquinolinium betaines. [10]Our results differ from theirs in some aspects.



1: R′ = H
2: R′ = Me

3: R′ = H
4: R′ = Me

5: R′ = H, R = Ph
6: R′ = H, R = Me
7: R′ = H, R = OEt
8: R′ = Me, R = Ph

9: R′ = H
10: R′ = Me

11: R′ = H
12: R′ = Me

13: R′=H, R=Ph
14: R′=H, R=OEt
15: R′=Me, R=Ph

SCHEME 1

olines (1 and 2) and quinolines (9 and 10) readily reacted with O-mesitylenesulfonylhydroxylamine (MSH) to give the corresponding crystalline N-amine mesitylenesulfonates in high yields.[11] N-Benzoylation of these N-amine salts was effected by a Shotten-Baumann reaction to give 5, 8, 13, and 15. The N-acetyl- and N-carbethoxyimines (6, 7 and 14) were prepared from isoquinoline N-imine dimer and quinoline N-imine dimer obtained by alkaline treatment of 3 and 11. These products were characterized by elemental analysis and IR,[12] UV,[13] and mass [14] spectral evidence, the details of which are given in the Experimental.

RESULTS AND DISCUSSION

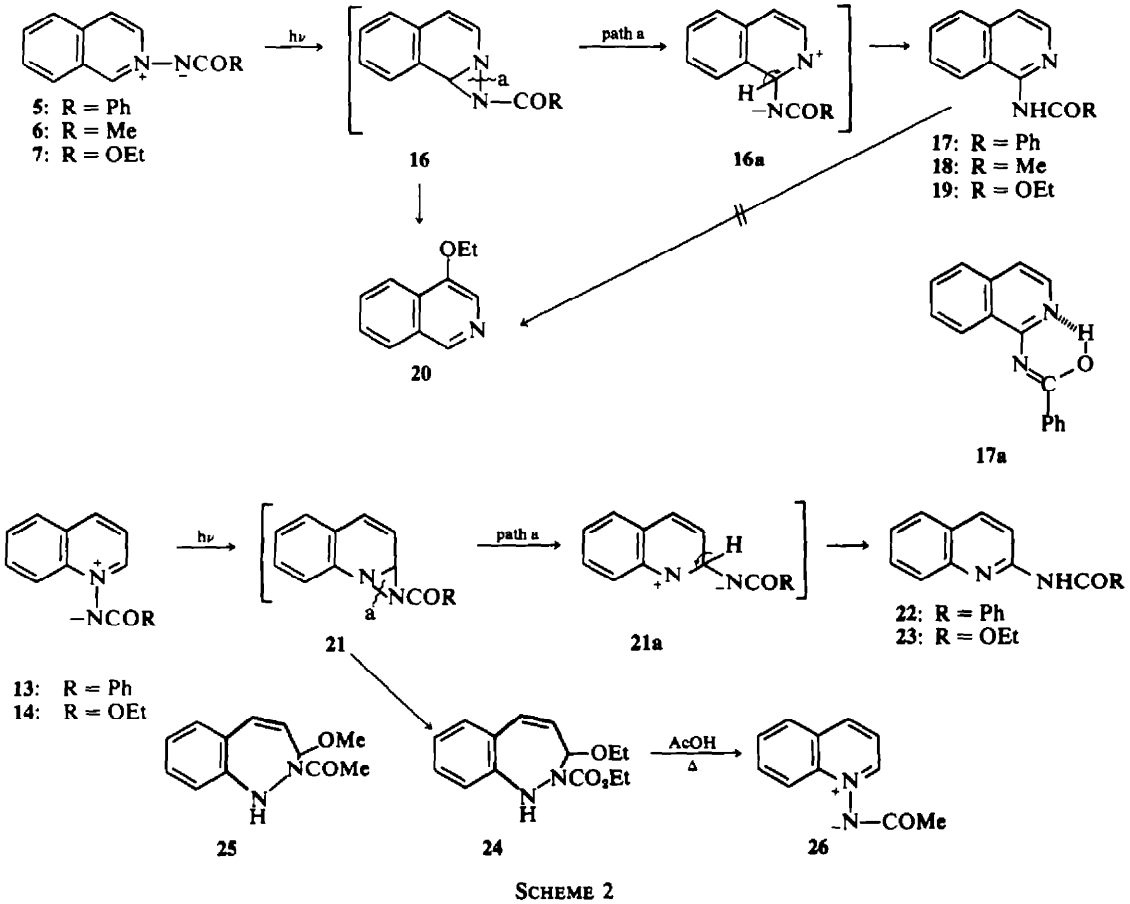
The results of the irradiation experiments are summarized in Table 1.*

*Dilute solutions of the betaines were irradiated with a 300-w high-pressure mercury lamp in a Pyrex vessel until all of the starting material had disappeared, as determined by TLC. Separation of the various components of the photolysate was achieved by means of preparative TLC on alumina.

Table 1. Photolysis products from N-acylimino-isoquinolinium and quinolinium betaines

Starting material	Solvent	Products (yield,[a] %)
5	MeOH	17 (61%)
	CH_2Cl_2	17 (61%)
	Me_2CO	17 (39%)[b]
	C_6H_6	17 (25%)[b]
6	EtOH	18 (41%) + 20 (7%)
	CH_2Cl_2	18 (42%)[b]
	Me_2CO	18 (21%)[b]
7	EtOH	19 (55%) + 20 (16%)
	CH_2Cl_2	19 (28%)
	CH_2Cl_2 + EtOH[c]	19 (61%)
	Me_2CO	19 (16%)[b]
	C_6H_6	19 (9%)[b]
13	MeOH	22 (76%)
	CH_2Cl_2	22 (18%)[b]
14	EtOH	23 (12%) + 24 (59%)

[a]Isolated yield.
[b]Accompanied by many unidentified side-products.
[c]Containing 0·5% of ethanol.



SCHEME 2

Irradiation of N-benzoyl, N-acetyl-, and N-carbethoxyiminoisoquinolinium betaines (**5**, **6**, and **7**) resulted in the formation of 1-benzamido-(**17**),* 1-acetamido-(**18**), and 1-carbethoxyamino-(**19**)-isoquinolines, respectively. The structures of these photoproducts were proved by direct comparisons with corresponding authentic samples prepared from 1-aminoisoquinoline. The irradiation of **6** and **7** in ethanol yielded 4-ethoxyisoquinoline (**20**) as a minor product.

As seen from Table 1, product distribution is dependent on the solvent used. In particular, alcoholic solvents favour the formation of rearranged products. This became more apparent by the following experiments; irradiation of **7** in methylene chloride produced only 28% yield of **19** accompanied by many side-products, while, on irradiation in methylene chloride containing a small amount of ethanol, the yield of **19** increased to 61%.

Irradiation of N-benzoyliminoquinolinium betaine (**13**) in methanol afforded 2-benzamidoquinoline (**22**),† identified by direct comparison with an authentic sample. In contrast, when N-carbethoxyiminoquinolinium betaine (**14**) was irradiated in ethanol, only 12% yield of a rearranged product, 2-carbethoxyaminoquinoline (**23**), was obtained and, instead, a ring expanded product (**24**) became the major product. The structure of the former was confirmed by comparison with an authentic sample. The major compound (**24**) was shown to contain two OEt groups by the appearance of NMR signals at τ 8·68 (t, 6H), τ 5·89 (q, 2H), and 6·29 (q, 2H). The rest of the NMR spectrum contains a broad doublet (J = 7 Hz) at τ 3·46 (1H), a broad doublet at τ4·0–4·1 (2H), and a multiplet at τ 2·8–3·2 (4H), corresponding to C_5, C_4, C_3 protons and four aromatic protons. In its IR spectrum, it showed an N-H absorption at 3380 cm^{-1}, a CO absorption at 1710 cm^{-1}, and a double bond absorption at 1640 cm^{-1}. The UV absorption maxima of **24** appeared at 225, 259 and 308 nm, which closely resemble those of *o*-aminostyrene.[15] The final proof for the assigned structure was obtained by conversion of **24** to the known N-acetyliminoquinolinium betaine (**26**). The structure of **24** is structurally related to the product **25** isolated by Shiba *et al.*[10]

A mechanistic rationalization of these results is based on the assumption that the initial photoexcitation of the betaines induces the formation of diaziridine intermediates (**16** and **21**).‡ A similar intermediate has already been proposed to account for the isomerization of pyridinium betaines to diazepines.[2–5] This step would be then followed by an N—N bond cleavage (path *a*) of the diaziridine ring and subsequent rearomatization to produce the rearranged products **17–19**, **22** and **23**. As stated earlier, this rearrangement process showed the marked dependency upon the solvents employed and the nature of substituents on the imino nitrogen; the use of an alcoholic solvent and the presence of a benzoyl substituent on the imino nitrogen favor the formation of the rearranged products. The solvent effects are analogous to what has been observed in the photolysis of quinoline N-oxide and isoquinoline N-oxide.[1] If a similar mechanism proposed for the N-oxides which involves a zwitterionic intermediate,§ is assumed, both the solvent effects and the substituent effects are readily explained. Thus a developing negative charge (see **16a** and **21a**) on the imino N atom in the transition state for path *a* is expected to be dispersed by solvation of an alcoholic solvent or by delocalization over a CO group (a benzoyl group is the most effective in stabilizing the negative charge[16]), so that the activation energy for the rearrangement process is lowered.

When the photolysis of **6**, **7** and **14** was carried out in ethanol, path *a* competes with alternative ring-opening processes (Scheme 3). This involves nucleophilic attack of ethanol either at the C-5 position of **16** or at the C-3 position of **21** to give 4-ethoxyisoquinoline (**20**) and the ring expanded product (**24**), respectively. One possible explanation for the different behavior observed between the isoquinoline and quinoline series is provided by an examination of Dreiding models of each diaziridine intermediate. Thus the C-1 position of the diaziridine (**16**) is shown to be hindered to approach of ethanol by the H atom at C-9. Consequently it would be understood that **16** undergoes an Sn2′-type displacement reaction at the C-5 position as shown in Scheme 3 followed by elimination of acetamide or ethyl carbamate to give 4-ethoxyisoquinoline (**20**).‖ This type of reaction has a precedent in the photolysis of 1-trifluoromethylisoquinoline N-oxide in methanol.[17] In contrast, the diaziridine intermediate (**21**, R=OEt) could undergo ring-opening by attack of ethanol at the unhindered C-3 position to lead to the formation of the ring-expanded product (**24**). Attack of ethanol at the C-5 position may revert to the starting material. However, an alternative mechanism involving valence

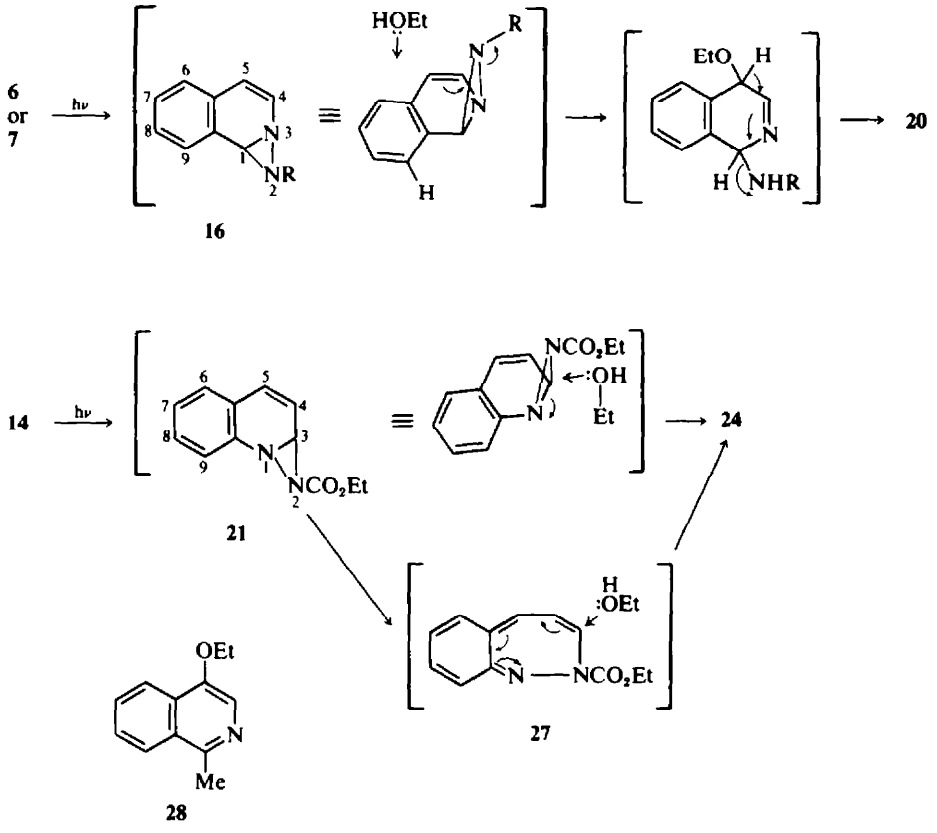
*In the IR spectrum of **17**, no CO absorption band was observed in the expected region. However, its methiodide showed a strong band at 1680 cm^{-1}. These data suggest that **17** exists in an enolic form **17a**.

†In contrast to this result, Shiba *et al.*[10] reported that in the photolysis of **13** the fragmentation to quinoline and 'nitrene derivative' was the main reaction path and no isomeric product could be isolated. We were unable to detect even trace quantities of quinoline.

‡Thermolysis of neat **5** (or **13**) at 190–200° results in the N—N bond fission to give isoquinoline (or quinoline), benzanilide, diphenylurea (trace), and benzamide (trace).[9]

§Zwitterionic intermediates for quinoline N-oxide and isoquinoline N-oxide have now received experimental verification.[1]

‖The fact that **19** was recovered unchanged upon irradiation in ethanol implicates that **19** is not an intermediate in the production of **20**.



SCHEME 3

tautomerization (**21** → **27** → **24**) suggested by Shiba *et al*[10] cannot be excluded with certainty.

Finally, it was of obvious interest to examine the photochemical behavior of 1-methylisoquinoline and 2-methylquinoline derivatives, where rearrangements are blocked by the presence of the Me group. Indeed, irradiation of N-benzoylimino-1-methyl-isoquinolinium betaine (**8**) in ethanol resulted in the formation of benzamide (in 83% yield) and 4-ethoxy-1-methylisoquinoline (**28**) (20%) accompanied by several minor products. The formation of **28** can be readily explained by the similar mechanism proposed for that of 4-ethoxyisoquinoline (**20**) from **6** and **7** (Scheme 3). This process also accounts for the formation of benzamide in part. However, lower yield of **28** compared with that of benzamide suggests that other routes to benzamide may exist. Since 1-methylisoquinoline was not detected in the products, a direct N—N bond cleavage of **8** may be not important. In contrast to the case of **8**, irradiation of N-benzoylimino-2-methylquinolinium betaine (**15**) in ethanol led to the formation of a complex mixture accompanied by polymeric substance, from which only benzamide (28%) was characterized.

EXPERIMENTAL

All m.ps are uncorrected. Analytical TLC was performed using Alumina GF_{254} (E. Merck) and for preparative TLC alumina PF_{254} was used. UV spectra were determined with a Hitachi 124 spectrophotometer, NMR spectra (TMS as internal standard) with a Hitachi R-20A instrument, and mass spectra with a Hitachi RMU-6D spectrometer at 70 eV. Irradiations were carried out using an Eikosha 300w high-pressure mercury lamp in a Pyrex vessel.

N-Aminoisoquinolinium mesitylenesulfonate (**3**). To a soln of **1** (5 g) in CH_2Cl_2 (10 ml) was added a soln of MSH (8·34 g) in CH_2Cl_2 (10 ml) at room temp over 5 min. Ether (30 ml) was then added yielding a yellow ppt of **3** (10·0 g; 71%). Recrystallization from isopropanol afforded colorless needles of **3**, m.p. 134–135°. (Found: C, 62·69; H, 5·72; N, 7·99. $C_{18}H_{20}N_2O_3S$ requires: C, 62·78; H, 5·85; N, 8·14%).

N-Benzoyliminoisoquinolinium betaine (**5**). An aqueous soln of **3** (670 mg) was made alkaline with 20% NaOH. To the resulting suspension was added benzoyl chloride (544 mg) with stirring at 0° and the mixture was stirred overnight at room temp. Yellow crystals were filtered off and recrystallized from benzene to give white needles of **5** (310 mg; 64%), m.p. 186–187° (lit.[13] 185–186°).

N-Acetyliminoisoquinolinium betaine (**6**). An aqueous soln of **3** (5·7 g) was made alkaline with 20% NaOH. A yellow ppt which formed was filtered off and washed with

EtOH to give quantitatively isoquinoline N-imine dimer.[13] The dimer (3·35 g) was dissolved in Ac_2O (70 ml) and the mixture was allowed to stand overnight at room temp. The excess Ac_2O was evaporated under reduced pressure and a 20% NaOH aq was added under ice cooling. Insoluble material was filtered off and the filtrate was extracted with chloroform. The extract was dried over $MgSO_4$ and concentrated to give brown hygroscopic crystals of **6** (1·2 g; 44%); $\nu_{max}^{CHCl_3}$ 1570 cm^{-1}; λ_{max}^{EtOH} 235, 273, and 323 nm. This compound was characterized by the picrate, m.p. 234–235°. (Found: C, 49·09; H, 3·28; N, 16·92. $C_{17}H_{13}N_5O_8$ requires: C, 49·16; H, 3·16; N, 16·86%.)

N-*Carbethoxyiminoisoquinolinium betaine* (**7**). A suspension of isoquinoline N-imine dimer (2·5 g) in a large excess of ethyl chloroformate was heated under reflux for 3 hr. After cooling, the mixture was washed with benzene several times and the residual solid was recrystallized from EtOH to give a yellow powder. The powder was dissolved in water and the soln was made alkaline with 10% Na_2CO_3 aq. The mixture was extracted with chloroform and the extract was dried over $MgSO_4$. Evaporation of the solvent gave white needles of **7** (0·765 g; 31%), which were recrystallized from benzene, m.p. 129–130°; ν_{max}^{KCl} 1610 and 1310 cm^{-1}; λ_{max}^{EtOH} 225 (log ϵ 4·51) and 335 nm (4·00); *m/e* (rel. int.) 216 (M^+, 16), 171 (27), 144 (15), 129 (100), and 102 (16). (Found: C, 66·74; H, 5·59; N, 12·60. $C_{12}H_{12}N_2O_2$ requires: C, 66·65; H, 5·59; N, 12·96%).

N-*Aminoquinolinium mesitylenesulfonate* (**11**). Using the procedure described for **3**, **11** was obtained from **9** (5·0 g) and MSH (8·34 g). Recrystallization from isopropanol afforded colorless needles of **11** (9·5 g; 67%), m.p. 132–133°. (Found: C, 62·58; H, 5·70; N, 8·14. $C_{18}H_{20}N_2O_3S$ requires: C, 62·78; H, 5·85, N, 8·14%).

N-*Benzoyliminoquinolinium betaine* (**13**). N-Amine salt **11** (5·0 g) was benzoylated with benzoyl chloride (4·1 g) as described for **5** to afford colorless plates of **13** (1·08 g; 30%), m.p. 193–194° (from benzene); ν_{max}^{KCl} 1600, 1550, and 1330 cm^{-1}; λ_{max}^{EtOH} 234 (log ϵ 4·51) and 320 nm (3·90); *m/e* (rel. int.) 248 (M^+, 47), 247 (100), 161 (43), 129 (72), and 102 (19). (Found: C, 77·56; H, 5·14; N, 11·08. $C_{16}H_{12}N_2O$ requires: C, 77·40; H, 4·87; N, 11·28%).

N-*Carbethoxyiminoquinolinium betaine* (**14**). An aqueous soln of **11** (3·4 g) was made alkaline with 10% NaOH. A ppt which formed was filtered off and washed with EtOH to give a yellow powder of quinoline N-imine dimer in quantitative yield. The dimer (2·33 g) was suspended in a large excess of ethyl chloroformate and the mixture was heated under reflux for 3 hr. Working-up as described for **7** gave yellow plates of **14** (0·33 g; 14%), m.p. 112–113·5° (from benzene); ν_{max}^{KCl} 1610 and 1280 cm^{-1}; λ_{max}^{EtOH} 240 (log ϵ 4·49) and 325 nm (3·70); *m/e* (rel. int.) 216 (11), 171 (32), 144 (20), 129 (100), and 102 (12). (Found: C, 66·66; H, 5·42; N, 12·90. $C_{12}H_{12}N_2O_2$ requires: C, 66·65; H, 5·59; N, 12·96%).

N-*Amino*-1-*methylisoquinolinium mesitylenesulfonate* (**4**). Using the procedure described for **3**, compound **4** was obtained from **2** (1·0 g) and MSH (1·5 g). Recrystallization from EtOAc-MeOH afforded plates of **4** (1·6 g; 64%), m.p. 175–176°. (Found: C, 63·50; H, 6·22; N, 7·89. $C_{19}H_{22}N_2O_3S$ requires: C, 63·67; H, 6·19; N, 7·82%).

N-*Benzoylimino*-1-*methylisoquinolinium betaine* (**8**). N-Amine salt **4** (1·13 g) was benzoylated with benzoyl chloride (0·89 g) as described for **5**. Recrystallization from benzene afforded needles of **8** (0·26 g; 33%), m.p. 246–247°; ν_{max}^{KCl} 1600, 1560, and 1340 cm^{-1}; λ_{max}^{EtOH} 231 (log ϵ 4·59) and 320 nm (3·89); *m/e* (rel. int.) 262 (M^+, 4), 247 (54), 143 (100), 129 (11), 115 (38), and 103 (66).

N-*Amino*-1-*methylquinolinium mesitylenesulfon* (**12**). Using the procedure described for **3**, compound was obtained from **10** (286 mg) and MSH (430 m Recrystallization from EtOH-i-PrOH (1 : 1) afforded c orless needles of **12** (580 mg, 81%), m.p. 201–20 (Found; C, 63·41; H, 5·93; N, 7·79. $C_{19}H_{22}N_2O_3S$ requir C, 63·67; H, 6·19; N, 7·82%.)

N-*Benzoylimino*-1-*methylquinolinium betaine* (**15**). Amine salt **12** (1·01 g) was benzoylated with benz chloride (0·32 g) as described for **5**. Recrystallization fr benzene afforded needles of **15** (0·18 g; 22%), m.p. 23 239°; ν_{max}^{KCl} 1600, 1540, and 1340 cm^{-1}; λ_{max}^{EtOH} 238 (lo 4·65) and 321 nm (4·22); *m/e* (rel. int.) 262 (M^+, 4), 2 (55), 143 (100), 129 (11), 115 (38), and 103 (66). (Four C, 77·62; H, 5·47; N, 10·51. $C_{17}H_{14}N_2O$ requires: C, 77· H, 5·38; N, 10·68%.)

Irradiation of **5**. A soln of **5** (150 mg) in MeOH (20 r was irradiated until the starting material disappear (8 hr) (checked by TLC). Evaporation of MeOH afford a crude oil which crystallized on standing. The cryst were purified by preparative TLC using chloroform solvent to give colorless needles of **17** (91·5 mg; 61% m.p. 105·5–106·5 (from petroleum benzin) which w identical in all respects with an authentic sample; ν_n^k 1610, 1590, and 1360 cm^{-1}; $\nu_{max}^{CCl_4}$ 1580 and 1340 cm (Found: C, 77·19; H, 4·85; N, 11·18. $C_{16}H_{12}N_2O$ require C, 77·40; H, 4·87; N, 11·28%.)

Irradiations of **5** in CH_2Cl_2, acetone and benzene we performed as described. The results are listed in Table 1

1-*Benzamidoisoquinoline* (**17**). A mixture of 1-amin isoquinoline (21·6 mg) and phenyl benzoate (29·7 mg) tetralin (0·1 ml) was heated at 180–200° for 2 hr. Aft removal of tetralin *in vacuo*, the residual solid was r crystallized from ligroin to give white crystals (8 mg), m. 105·5–106·5°.

Irradiation of **6**. A soln of **6** (150 mg) in EtOH (20 r was irradiated as described for a period of 10 hr. Tv major compounds were isolated by preparative TL using chloroform as solvent.

Compound **18** (62 mg; 41%), m.p. 148° (from petroleu benzin), was identical in all respects with an authent sample.[18]

Compound **20** was isolated as a colorless oil (10 m 7%); ν_{max}^{EtOH} 212, 284, and 325 nm; NMR ($CDCl_3$) τ 8·· (t, 3H), 5·80 (q, 2H), 1·8–2·85 (m, 6H). The picrate, m. 169–171° (lit.[19] 170°). (Found: C, 50·40; H, 3·52; N, 13·5 $C_{17}H_{14}N_4O_8$ requires: C, 50·75; H, 3·51; N, 13·93%.)

Irradiations of **6** in other solvents were performed the similar manner. The results are listed in Table 1.

Irradiation of **7**. A soln of **7** (150 mg) in EtOH (20 r was irradiated for a period of 7·2 hr. The mixture consis ed of two components (on TLC), which were isolated b preparative TLC using benzene as solvent.

Compound **19** (82·5 mg; 55%), m.p. 134–136°, was ide tical in all respects with an authentic sample prepared b Tanida.[20]

Compound **20** was isolated in 16% yield. The resul of irradiation in other solvents are listed in Table 1.

Irradiation of **13**. A soln of **13** (150 mg) in MeOH (2 ml) was irradiated in a period of 8·5 hr. The product wa isolated by preparative TLC using chloroform as solve to give colorless needles of **22** (114 mg; 76%), m.p. 122 123°, identical in all respects with an authentic sample.[21]

Irradiation of **13** in CH_2Cl_2 afforded a complex mixtur from which **22** was isolated in 18% yield.

Irradiation of **14**. A soln of **14** (150 mg) in EtOH (20 m

was irradiated in a period of 8·5 hr. The mixture, consisting of two major components, was separated by preparative TLC using benzene-EtOAC (10:1) as solvent.

Compound **23**, m.p. 90–91°, isolated in 12% yield, was identical in all respects with an authentic sample.

Compound **24**, m.p. 86–87° (from petroleum benzin), was isolated in 59% yield; ν_{max}^{KCl} 3380 (NH), 1710 (C=O), and 1640 (C=C) cm^{-1}; λ_{max}^{EtOH} 225 (log ε 4·59), 259 (3·90), and 308 nm (3·27); NMR (100 MHz, $CDCl_3$) τ 8·68 (t, 6H), 6·29 (q, 2H), 5·89 (q, 2H), 4·0–4·1 (bd, 2H), 3·46 (bd, J = 7 Hz, 1H), and 2·8–3·2 (m, 4H); *m/e* (rel. int.) 262 (M^+, 24), 171 (47), 144 (40), 129 (100), 118 (40), and 102 (19). (Found: C, 63·89, H, 6·95; N, 10·83. $C_{14}H_{18}N_2O_3$ requires: C, 64·10; H, 6·92; N, 10·68%.)

Transformation of **24** *to* **26**. A soln of **24** (30 mg) in AcOH (1 ml) was refluxed for 1 hr. After evaporation to dryness, the residue was subjected to preparative TLC using benzene-EtOAc (10:1) as solvent to give **26** (6·9 mg; 32%), m.p. 162–163° (lit.[10] 166–167°), which gave a picrate, m.p. 200° (lit.[22] 198°). The identity was also established by spectroscopic means.

2-*Carbethoxyaminoquinoline* (**23**). A soln of 2-aminoquinoline (58 mg) in pyridine (5 ml) and ethyl chloroformate (5 ml) was allowed to stand overnight at room temp. The mixture was poured into ice water and extracted with ether. The extract was dried over $MgSO_4$ and concentrated to give colorless needles of **23** (52 mg; 59%). An analytical sample was purified by sublimation at 90° (0·08 mmHg), m.p. 90–91°; $\nu_{max}^{CHCl_3}$ 3400 (NH) and 1735 (C=O) cm^{-1}. (Found: C, 67·06; H, 5·40; N, 12·67. $C_{12}H_{12}N_2O_2$ requires: C, 66·65; H, 5·59; N, 12·96%.)

Irradiation of **8**. A soln of **8** (150 mg) in EtOH (20 ml) was irradiated as described for **5** The mixture, consisting two major components, was separated by preparative TLC using chloroform-benzene (1:1). Benzamide and **28** were isolated in 83 and 21% yields, respectively. The structure of **28** was evident from a comparison of its spectral data with those of **20**. The IR, UV [λ_{max}^{EtOH} 209, 288, and 326 nm], and NMR [(CCl_4) τ 8·48 (t, 3H), 7·15 (s, 3H), 5·75 (q, 2H), 1·6–2·45 (m, 5H)] were very similar to those of **20**. The picrate, m.p. 203–204° (from EtOH). (Found: C, 52·07; H, 4·04; N, 13·68. $C_{18}H_{18}N_4O_8$ requires: C, 51·92; H, 3·87; N, 13·46%.) No further characterization of the other minor products was made.

REFERENCES

[1]For recent reviews: [a]G. G. Spence, E. C. Taylor, and O. Buchardt, *Chem. Rev.* **70**, 231 (1970); [b]C. Kaneko, *J. Synth. Org. Chem. Japan* **26**, 758 (1968)

[2]For a recent review see H. J. Timpe, *Z. Chem.* **12**, 250 (1972).

[3a]J. Streith and J. M. Cassal, *Angew. Chem.* **80**, 117 (1968); [b]*Tetrahedron letters* 4541 (1968); [c]*Bull. Soc. Chim. Fr.* 2175 (1969); [d]J. Streith, A Blind, J. M. Cassal, and O. Sigwalt, *Bull. Soc. Chim. Fr.*, 948 (1969); [e]J. Streith, J. P. Luttringer, and M. Nastasi, *J. Org. Chem.* **36**, 2962 (1971).

[4a]T. Sasaki, K. Kanematsu, and A. Kakehi, *Chem. Commun.* 432 (1969); [b]T. Sasaki, K. Kanematsu, A. Kakehi, I. Ichikawa, and K. Hayakawa, *J. Org. Chem.* **35**, 426 (1970).

[5a]V. Snieckus, *Chem. Commun.* 831 (1969); [b]A. Balasubramanian, J. M. McIntosh, and V. Snieckus, *J. Org. Chem.* **35**, 433 (1970).

[6]V. Snieckus and G. Ken, *Chem. Commun.* 172 (1970)

[7]K. T. Potts and R. Dugas, *Ibid.* 732 (1970)

[8]S. F. Gait, C. W. Rees, and R. C. Stoor, *Ibid.* 1545 (1971).

[9]A preliminary report has been published: Y. Tamura, H. Ishibashi, N. Tsujimoto, and M. Ikeda, *Chem. Pharm. Bull.* **19**, 1285 (1971).

[10]T. Shiba, Y. Yamane, and H. Kato, *Chem. Commun.* 1952 (1970)

[11]Y. Tamura, J. Minamikawa, Y. Miki, S. Matsugashita, and M. Ikeda, *Tetrahedron Letters* 4133 (1972)

[12]Y. Tamura, Y. Miki, T. Honda, and M. Ikeda, *J. Heterocyclic Chem.* **9**, 865 (1972)

[13]Y. Tamura, N. Tsujimoto, and M. Uchimura, *J. Pharm. Soc. Japan* **91**, 72 (1971)

[14]M. Ikeda, N. Tsujimoto, and Y. Tamura, *Org. Mass Spectrom.* **5**, 61 (1971)

[15]M. J. S. Dewar and R. Dietz, *J. Org. Chem.* **26**, 3253 (1961)

[16]E. S. Gould, *Mechanism and Structure in Organic Chemistry* p. 365, Holt, (1960)

[17]C. Kaneko, *Kagaku no Ryoiki*, Special Edition, No. **92**, 149 (1970)

[18]J. J. Craig and W. E. Cass, *J. Am. Chem. Soc.* **64**, 783 (1942)

[19]M. Pesson and D. Richer, *C. R. Acad. Sci. Ser. C.* **262**, 1719 (1966)

[20]H. Tanida, *J. Pharm. Soc. Japan* **79**, 1063 (1959)

[21]K. Takatori and M. Ueda, *Ibid.* **71**, 1373 (1951)

[22]T. Okamoto, M. Hirobe, and T. Yamazaki, *Chem. Pharm. Bull. Tokyo* **14**, 512 (1966)