

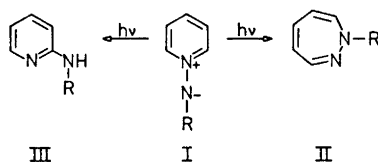
## The Photochemical Rearrangement of Isoquinolinium N-Acyl Ylides to 1-Acylaminoisoquinolines *via* the Excited Singlet State

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The light-induced rearrangement of isoquinolinium *N*-acyl ylides results in the formation of 1-acylaminoisoquinolines in high chemical yield. On the basis of flash-photolysis experiments and quantum yield measurements it is inferred that the reaction takes place *via* an excited singlet state.

It was reported, previously, that irradiation of aromatic *N*-amino ylides (I) resulted, in the formation of 1,2-diazepines (II),<sup>1-3</sup> amides (III), and the parent heterocyclic amines.



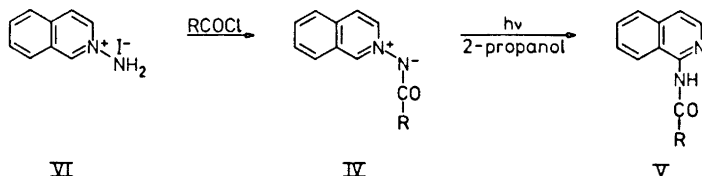
Thus it was shown that pyridinium *N*-ylides (I) gave the corresponding 1,2-diazepines (II) as the main products. In most cases small amounts of the parent amines were also isolated. Only with *N*-carbethoxyimino-3,5-dimethylpyridinium ylide as substrate was the corresponding amide, *i.e.*, 2-carbethoxyamino-3,5-dimethylpyridine<sup>3</sup> formed.

Furthermore, some preliminary results using quinoline and isoquinoline *N*-ylides as substrates were reported.<sup>4,5</sup> According to these irradiation of the quinoline *N*-ylides resulted in fragmentation to quinoline and nitrenes.<sup>4</sup> The isoquinoline *N*-ylides were, however, reported to give the 1-acylaminoisoquinolines.<sup>5</sup>

Thus, whereas the photochemistry of the various heteroaromatic amino *N*-oxides,<sup>6</sup> which are formally analogous to the *N*-ylides, shows a rather

uniform pattern, the photoreactions of the *N*-ylides appear to be much more dependent upon the type of heteroaromatic nucleus.

In this paper we report the light-induced rearrangement of a series of isoquinolinium *N*-ylides (IVa–IVg) to give high chemical yields of the isomeric 1-acylaminoisoquinolines (Va–Vg).



- |   |   |
|---|---|
| IVa, Va: R = C <sub>6</sub> H <sub>5</sub>                            | IVe, Ve: R = C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>    |
| IVb, Vb: R = <i>o</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> | IVf, Vf: R = (CH <sub>3</sub> ) <sub>3</sub> C                |
| IVc, Vc: R = <i>m</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> | IVg, Vg: R = (CH <sub>3</sub> ) <sub>3</sub> CCH <sub>2</sub> |
| IVd, Vd: R = <i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> |   |

## RESULTS

The *N*-acylaminoisoquinolinium ylides (IVa–IVg) were all prepared from 2-aminoisoquinolinium iodide (VI) by acylation (Tables 1–2). The irradiations of IVa–IVg were carried out in 2-propanol solutions, with Pyrex-filtered light from a medium pressure mercury lamp, until no more starting material could be detected by thin layer chromatography. In each case the isomeric 1-acylaminoisoquinolines (Va–Vg) were found to be the main products, with small amounts of high melting, as yet unidentified materials, also being formed. The relative quantum yields of the formation of compounds Va–Vg were found to be of the same order of magnitude, whereas the three nitro-substituted substrates *N*-(*o*-nitrobenzoyl)-, *N*-(*m*-nitrobenzoyl)-, and *N*-(*p*-nitrobenzoyl)-aminoisoquinolinium ylides \* reacted with quantum yields, one order less in magnitude.

A variety of solvents were tested by performing flash and steady state photolysis experiments. From these results it was found that 2-propanol was by far the best solvent for amide formation.

The quantum yield for the disappearance of compound IVa, as well as the one for the formation of Va in 2-propanol solution was determined under various conditions. It was found that the quantum yields were independent of the concentration of oxygen during irradiation. Although the influence of oxygen on an excited state should be analysed with caution,<sup>7</sup> these results are nevertheless in agreement with a mechanism according to which the rearrangement takes place from an excited singlet state. The formation of the triplet state of IVa was examined by flash photolysis. The flash photolysis experiments showed the existence of a transient, the spectrum of which is shown in Fig. 1. The  $\tau_{\frac{1}{2}}$  of this species in deaerated 2-propanol solutions, at room temperature was found to be 1200  $\mu$ sec, whereas the  $\tau_{\frac{1}{2}}$  of this species

\* Becher and Lohse, unpublished results.

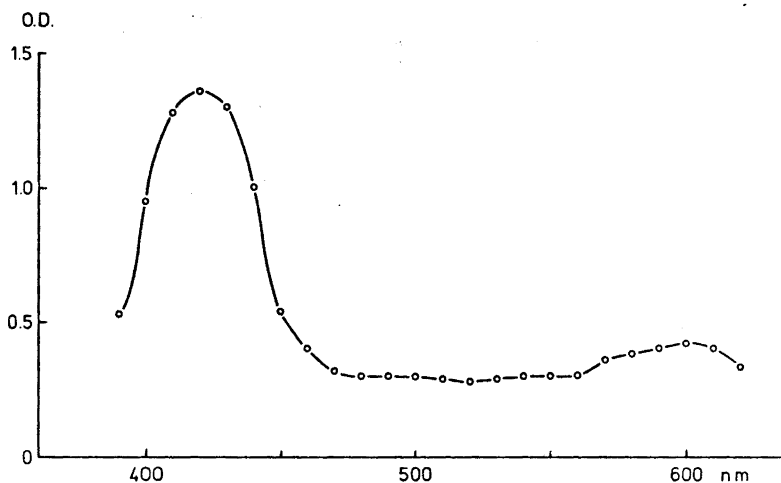


Fig. 1. The spectrum of the transient from the photolysis of IVa in 2-propanol solution 50  $\mu$ s delay.

in aerated 2-propanol solution was reduced to only 0.28  $\mu$ sec. Accordingly we believe this transient to be a triplet state, which seems to revert to the substrate, thus further confirming our proposed mechanism.

#### IDENTIFICATION OF PRODUCTS

When a sample of the assumed 1-benzoylaminoisoquinoline (Va) was hydrolysed in hydrochloric acid, two products were obtained, namely benzoic acid and 1-aminoisoquinoline (VII). 1-Aminoisoquinoline (VII) was identified by melting point determination,<sup>8</sup> elemental analyses and by diazotation and conversion to 1-hydroxyisoquinoline which was found to be identical with an authentic sample<sup>9</sup> (mixed m.p. and IR spectra).

The IR spectra of compounds Vf and Vg (Table 4) showed absorption in the 3350  $\text{cm}^{-1}$  region, due to the NH-group<sup>10</sup> and signals due to the NH-group were found in the NMR spectra of Vf and Vg.

Contrary to this, compounds Va, Vc and Vd displayed IR-absorption indicative of the presence of OH-groups, but not NH-groups. Similar indications were found in the NMR spectra. These results clearly indicate that compounds Vf and Vg have the amide structure (VIII), whereas compounds Va, Vc and Vd have the tautomeric structure (IX).

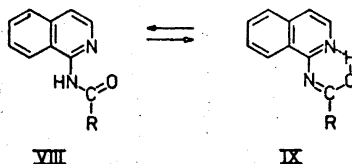


Table 1. *N*-Acyliminoisoquinolinium ylides.

Compound	Yield %	M.p. °C	Formula	Calculated	Analyses	Found
<i>N</i> -Benzoyl iminoisoquinolinium ylide, IVa	34	185–187 <sup>a</sup>	C <sub>16</sub> H <sub>12</sub> N <sub>2</sub> O	C 77.40, H 4.87, N 11.28	C 77.20, H 4.96, N 11.17	
<i>N</i> -( <i>o</i> -Methoxybenzoyl)-iminoisoquinolinium ylide, IVb	24	179–181 <sup>a</sup>	C <sub>17</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	C 73.36, H 5.07, N 10.07	C 73.70, H 5.19, N 10.03	
<i>N</i> -( <i>m</i> -Methoxybenzoyl)-iminoisoquinolinium ylide, IVc	28	178–179 <sup>a</sup>	•	•	C 73.30, H 5.17, N 9.96	
<i>N</i> -( <i>p</i> -Methoxybenzoyl)-iminoisoquinolinium ylide, IVd	30	178–181 <sup>b</sup>	•	•	C 73.35, H 5.24, N 10.00	
<i>N</i> -Phenylacetyl-iminoisoquinolinium ylide, IVe	36	139–142 <sup>c</sup>	C <sub>17</sub> H <sub>14</sub> N <sub>2</sub> O	C 77.84, H 5.38, N 10.68	C 78.05, H 5.55, N 10.69	
<i>N</i> -Trimethylacetyl-iminoisoquinolinium ylide, IVf	39	212–214 <sup>a</sup>	C <sub>14</sub> H <sub>10</sub> N <sub>2</sub> O	C 73.65, H 7.06, N 12.27	C 73.85, H 7.13, N 12.25	
<i>N</i> - <i>t</i> -Butylacetyl-iminoisoquinolinium ylide, IVg	22	145–147 <sup>c</sup>	C <sub>15</sub> H <sub>10</sub> N <sub>2</sub> O	C 74.35; H 7.49, N 11.56	C 74.55, H 7.58, N 11.48	

Recrystallized from: <sup>a</sup> benzene, <sup>b</sup> benzene, <sup>c</sup> benzene and <sup>c</sup> benzene; dioxane and cyclohexane.

Table 2. Spectra of *N*-acyliminoisoquinolinium ylides.

Compound	UV absorption spectra $\lambda_{\max}$ nm (log $\epsilon$ ) in 2-propanol	IR absorption spectra in KBr selected bands, $\text{cm}^{-1}$	NMR spectral assignments chemical shifts $\tau$ in ppm, $J$ in cps, recorded in DMSO- $d_6$ , internal ref. TMS
IVa	336 (3.97) 278 (4.00)	1640, 1590, 1550	$\tau$ 2.50–2.63 (m, aryl H, 3 H), $\tau$ 1.35–2.15 (m, aryl H, 8 H), $\tau$ -0.03 (S, H <sub>1</sub> , 1 H)
IV	328 (3.94) 277 (3.92)	1640, 1610, 1590, 1565	$\tau$ 6.24 (S, CH <sub>3</sub> , 3 H), $\tau$ 1.45–3.25 (m, aryl H, 10 H), $\tau$ 0.10 (S, H <sub>1</sub> , 1 H)
IVc	331 (3.97) 277 (4.04)	1640, 1610, 1599, 1560	$\tau$ 6.23 (S, CH <sub>3</sub> , 3 H), $\tau$ 1.50–3.24 (m, aryl H, 10 H), $\tau$ 0.19 (S, H <sub>1</sub> , 1 H)
IVd	352 Sh (3.97) 333 (4.04) 272 Sh (4.18)	1610, 1599, 1550	$\tau$ 6.23 (S, CH <sub>3</sub> , 3H), $\tau$ 3.14 (d, $J=9$ , aryl H, 2 H), $\tau$ 1.50–2.30 (m, aryl H, 8 H), $\tau$ 0.15 (S, H <sub>1</sub> , 1 H)
IVe	323 (3.88) 273 (3.89)	1640, 1600, 1560	$\tau$ 6.47 (S, CH <sub>3</sub> , 2 H), $\tau$ 1.58–2.86 (m, aryl H, 11 H) $\tau$ 0.28 (S, H <sub>1</sub> , 1 H)
IVf	323 (3.85) 274 (3.85)	1640, 1610, 1560, 1540	$\tau$ 8.78 (S, CH <sub>3</sub> , 9 H), $\tau$ 1.60–2.25 (m, H <sub>3-7</sub> , 6 H) $\tau$ 0.36 (S, H <sub>1</sub> , 1 H)
IVg	327 (3.88) 275 (3.89)	1640, 1610, 1570	$\tau$ 8.90 (S, CH <sub>3</sub> , 9 H), $\tau$ 7.93 (S, CH <sub>3</sub> , 2H), $\tau$ 1.60–2.29 (m, H <sub>3-7</sub> , 6 H), $\tau$ 0.34 (S, H <sub>1</sub> , 1 H)

Indications of increased conjugation in Va, Vc, and Vd, over Vf and Vg were also found in the UV spectra of these compounds. Thus compounds Va, Vc, and Vd showed strong absorption at 373–374 nm, whereas for compounds Vf and Vg the first absorption band was observed at 361 nm. Furthermore the band at 361 nm had a lower extinction than that of the corresponding bands in compounds Va, Vc, and Vd (Table 4).

### EXPERIMENTAL

Microanalyses were carried out in the microanalytical department of the University of Copenhagen by Mr. Preben Hansen. Melting points (uncorrected) were determined on a Büchi melting point apparatus. Infrared spectra were recorded on a Perkin Elmer Infracord 137. Ultraviolet spectra were recorded on a Beckman ACTA III ultraviolet spectrophotometer by Mrs. Bodil Kroneder. Proton magnetic resonance spectra were recorded on a Jeol C-60HL NMR spectrometer, or on a Varian A60 NMR spectrometer.

*2-Aminoisoquinolinium iodide (VI)*. VI was prepared according to the method given by Gösl and Meuwesen.<sup>11</sup> Thus isoquinoline (0.2 mol) gave 15.7 g (29 %) of I as brown crystals. Two recrystallizations from 96 % ethanol gave yellow crystals, m.p. 180–183°C. (Found: C 39.95; H 3.39; N 10.45; I 46.52. Calc. for C<sub>8</sub>H<sub>8</sub>IN<sub>2</sub>: C 39.72; H 3.33; N 10.30; I 46.64.) UV spectra in 2-propanol:  $\lambda_{sh}$  242 (log  $\epsilon$  4.30),  $\lambda_{max}$  295 (log  $\epsilon$  3.74),  $\lambda_{sh}$  317 (log  $\epsilon$  3.52),  $\lambda_{max}$  331 (log  $\epsilon$  3.40) nm.

*N-Acyliminoisoquinolinium ylides IVa–IVg* (Table 1 and Table 2) were all prepared according to the general method given below.

*N-Benzoyliminoisoquinolinium ylide (IVa)*. IVa was prepared by modification of the method given by Balasubramanian, McIntosh and Snieckus.<sup>3</sup> To a solution of 2-amino-

Table 3. Irradiation of *N*-acyliminoisoquinolinium ylides in 2-propanol.

Compound	Yield %	m.p. °C	Analyses found <sup>e</sup>
1-(Benzoylamino)-isoquinoline, Va	96	102–104 <sup>a,b</sup>	C 77.50, H 4.98, N 11.23
1-( <i>o</i> -Methoxybenzoylamino)-isoquinoline, Vb	60	128–131 <sup>d</sup>	C 73.30, H 5.19, N 9.93
1-( <i>m</i> -Methoxybenzoylamino)-isoquinoline, Vc	69	103–105 <sup>d</sup>	C 73.10, H 5.03, N 9.95
1-( <i>p</i> -Methoxybenzoylamino)-isoquinoline, Vd	97	96–99 <sup>c</sup>	C 73.20, H 5.17, N 10.02
1-(Phenylacetyl-amino)-isoquinoline, Ve	61	152–154 <sup>d</sup>	C 77.60, H 5.51, N 10.60
1-(Trimethylacetyl-amino)-isoquinoline, Vf	60	150–152 <sup>d</sup>	C 73.70, H 7.14, N 12.22
1-( <i>t</i> -Bytylacetyl-amino)-isoquinoline, Vg	73	131–133 <sup>c</sup>	C 74.45, H 7.52, N 11.51

<sup>a</sup> Ref. 5 gives the m.p. 105–106°. Recrystallized from: <sup>b</sup> cyclohexane, <sup>c</sup> cyclohexane-carbon tetrachloride and <sup>d</sup> ethanol-water. <sup>e</sup> Calculated values, see Table 1.

Table 4. Spectra of 1-acylaminoisoquinolines.

Compound	UV absorption spectra $\lambda_{\max}$ m $\mu$ (log $\epsilon$ ) in abs. ethanol	IR absorption spectra in KBr selected bands, cm <sup>-1</sup>	NMR spectral assignments chemical shifts $\tau$ in ppm $J$ in cps, recorded in CDCl <sub>3</sub> , internal ref. TMS.
Va	373 (3.90) 357 (3.94) 320 (3.73) 279 (4.05)	1590 broad 3440 OH	$\tau$ 2.28–3.09 (m, aryl H, 9 H), $\tau$ 1.55–1.62 (m, aryl H, 2 H), $\tau$ 1.15 (broad S, OH, 1 H)
Vb	367 (2.22) 318 (3.85) 282 (3.95)	1680, 1640, 1599, 1590 3380 NH 3450 OH	$\tau$ 6.00 (s, CH <sub>3</sub> , 3 H), $\tau$ 1.70–3.14 (m, aryl H, 10 H), $\tau$ -0.06–1.70 (broad S, OH, NH, 1 H)
Vc	373 (3.88) 358 (3.92) 318 (3.75) 280 (4.06)	1640, 1610 3440 OH	$\tau$ 6.16 (s, CH <sub>3</sub> , 3 H), $\tau$ 2.04–3.14 (m, aryl H, 10 H), $\tau$ 1.40 (center of m, OH, 1 H)
Vd	374 (4.00) 358 (4.05) 321 (3.89) 271 (4.25)	1670, 1640, 1590 3440 OH	$\tau$ 6.16 (s, CH <sub>3</sub> , 3 H), $\tau$ 1.10–3.20 (m, aryl H, OH, 11 H)
Ve	360 (2.67) 318 (3.71) 272 (3.84)	1680, 1640, 1595 3230 NH 3440 OH	$\tau$ 6.07 (s, CH <sub>3</sub> , 2 H), $\tau$ 1.94–2.85 (m, aryl H, 11 H), $\tau$ 0.00–1.50 (broad S, OH, NH, 1 H)
Vf	362 (2.88) 318 (3.59) 271 (3.75)	1680, 1630, 1590 3330 NH	$\tau$ 8.58 (s, CH <sub>3</sub> , 9 H), $\tau$ 1.80–2.80 (m, aryl H, 6 H), $\tau$ 0.50–1.42 (broad S, NH, 1 H)
Vg	360 (2.27) 318 (3.64) 272 (3.74)	1675, 1640, 1595 3280 NH	$\tau$ 8.83 (s, CH <sub>3</sub> , 9 H), $\tau$ 7.99 (s, CH <sub>2</sub> , 2 H) $\tau$ 1.81–2.66 (m, aryl H, 6 H), $\tau$ ca. 0.20 (broad S, NH, 1 H)

isoquinolinium iodide (VI) (10.0 g, crude product) in 96 % ethanol (350 ml) was added at 35°C benzoylchloride (8.9 ml) dissolved in dioxane (40 ml). pH was fixed at 8 with an automatic titrator (Radiometer 28), by addition of 1 N ethanolic potassium hydroxide. After the addition (15 min) stirring was continued for 1 h at 30°C.

The reaction mixture was evaporated *in vacuo*, 1 M sodium carbonate added (200 ml) and the mixture extracted with dichloromethane (2 × 200 ml), dried over sodium sulfate and concentrated *in vacuo*. This yielded a semicrystalline oil (16.8 g). Recrystallization from benzene gave yellow crystals of IIa 3.07 g (34 %), m.p. 185–187°C.

*Irradiation of N-acylisoquinolinium ylides in solution.* The irradiations (Table 3 and Table 4) were carried out according to the general method given below.

*I-(m-Methoxybenzoyl)amino isoquinoline (Vb).* A solution of IIIa (2.5 g) in distilled 2-propanol (8.96 mmol/l) was irradiated for 10 h at 18°C, through a pyrex filter using a medium pressure mercury lamp (Philips No. 134–10007). The photolysis was followed by thin layer chromatography, and the reaction mixture was concentrated *in vacuo* when all of the starting material was consumed.

The crystals hereby obtained were treated with activated carbon and recrystallized from ethanol-water to give analytically pure Vb as pale yellow needles, 1.71 g (69 %), m.p. 103–105°C.

*Flash photolyses.* The triplet-triplet absorption spectrum was obtained by a conventional flash spectrographic equipment.<sup>12</sup> The flash energy was 3000 Joule and the delay times were varied between 4 μsec and 50 msec and were reproducible to 10 % or better. The concentration of the samples was between 10<sup>-4</sup> and 10<sup>-6</sup> mol/l. The decay rate in the degassed solution was obtained with conventional flash photoelectric equipment.<sup>12</sup> The decay rate in the aerated solution was obtained with laser flash kinetic equipment.<sup>13</sup>

*Hydrolyses of 1-benzoylaminoisoquinoline (Va).* Va was refluxed in 4 N hydrochloric acid for 4 h. Extraction with chloroform gave benzoic acid. After this, the reaction mixture was made alkaline and extracted with chloroform to give 1-aminoisoquinoline (VII); a sample recrystallized from water had m.p. 119–121°C. (Ref. 8 gives the m.p. 122–123°C for VII.) 1-Aminoisoquinoline was then diazotized in 25 % sulfuric acid to give pale yellow crystals identified as 1-hydroxyisoquinoline (identical IR and no depression of the mixed m.p. with that of an authentic sample).<sup>9</sup>

## REFERENCES

1. Streith, J., Luttringer, J. P. and Nastasi, M. *J. Org. Chem.* **36** (1971) 2962, and references cited therein.
2. Sasaki, T., Kanematsu, K., Kakehi, A., Ichikawa, I. and Hayakawa, K. *J. Org. Chem.* **35** (1970) 426, and references cited therein.
3. Balasubramanian, A., McIntosh, J. M. and Snieckus, V. *J. Org. Chem.* **35** (1970) 433.
4. Shiba, T., Yamane, K. and Kato, H. *Chem. Commun.* **1970** 1592.
5. Tamura, Y., Ishibashi, H., Tsujimoto, N. and Ikeda, M. *Chem. Pharm. Bull. (Tokyo)* **19** (1971) 1285.
6. Spence, G. G., Taylor, E. C. and Buchardt, O. *Chem. Rev.* **70** (1970) 231.
7. Calvert, J. G. and Pitts, J. N. *Photochemistry*, Wiley, New York 1967.
8. Bergstrom, F. W. *Ann.* **515** (1935) 34.
9. Robinson, M. M. and Robinson, B. I. *J. Org. Chem.* **21** (1957) 1337.
10. Bellamy, L. J. *The Infrared Spectra of Complex Molecules*, Methuen, London 1964.
11. Gösl, R. and Meuwssen, A. *Chem. Ber.* **92** (1959) 2521.
12. Porter, G. In Weissberger, A., Ed., *Technique of Organic Chemistry*, Interscience, New York 1963, Vol. 8, Part II, p. 1055.
13. Porter, G. and Topp, M. R. *Proc. Roy. Soc. Ser. A* **315** (1970) 163.

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