Studies on Diazepines. XIII.\(^1\) Photochemical Behavior of Pyrazine, Pyrimidine, and Pyridazine N-Imides

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Photolyses of various diazine N-ethoxy-carbonylimides (3, 9, and 19), prepared from the corresponding diazines (1, 8, and 17), resulted in the formation of the pyrazole derivatives (4 and 10) from pyrazine and pyrimidine N-imides, and of the pyrrole derivatives (20) from pyridazine N-imides. These photolyses may proceed by rearrangement to diaziridinyl intermediates, followed by ring expansion to the corresponding 1,2,5-, 1,2,4-, or 1,2,3-triazepines (6, 12, or 22), which then undergo isomerization to the triaza[3.2.0]-bicycloheptadienes (7, 13, and 23), followed by elimination to give the products (4, 10, and 20, respectively).

Keywords—pyrazine N-imides; pyrimidine N-imides; pyridazine N-imides; pyrazoles; pyrroles; photolysis; rearrangement; triazepine intermediates

Since pyridine N-acylimides were shown to undergo photo-induced rearrangement to give 1,2-diazepines,\(^3\) the photochemical behavior of aromatic amine N-imides has received much attention in connection with the photochemistry of the analogous N-oxides.\(^4\) Investigations in the pyridine,\(^5\) quinoline,\(^6,7\) and isoquinoline\(^8\) series have shown that the photolysis of their N-imides involves initial rearrangement to diaziridinyl intermediates, which then undergo either ring expansion to 1,2-diazepines or N-N bond fission to 2-aminopyridine derivatives. Very recently, we reported an additional pathway; i.e., the formation of 1,3-diazepines from diaziridinyl intermediates by further rearrangement and ring expansion in the photolysis of isoquinoline and related fused pyridine N-imides.\(^8\) In view of these results, diazine N-imides were expected to undergo similar photo-induced rearrangement to give the corresponding triazepines. Of the four theoretically possible monocyclic triazepines, 1,2,4-triazepines have been reported.\(^9\) However, the fully unsaturated 1,2,3-, 1,2,5-, and 1,3,5-isomers are little known.

Therefore we examined the photochemical behavior of pyrazine,\(^10\) pyrimidine, and pyridazine N-imides as part of our studies on diazepines. The results are presented here.

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2) Location: Kanagawa-ken, Kangawa 920-11, Japan.
5) For a review, see M. Nastasi, Heterocycles, 4, 1509 (1976).
Pyrazine N-Imides

The pyrazines (1a—d) were aminated with O-mesitylenesulfonylhydroxylamine (MSH; H$_2$NOMes) according to the method of Tamura et al.\textsuperscript{11} to give the corresponding N-amino-pyrazinium mesitylenesulphonates (2) in good yields; these were treated with ethyl chloroformate in the presence of potassium carbonate to give the pyrazine N-ethoxycarbonylimides (3) in 35—75\% yields. Irradiation of the resulting N-imides (3a—d) in acetonitrile solution for 2—4 hr gave the pyrazoles (4) and the parent pyrazines (1) in the yields shown in Chart 1. Besides these products, the formation of hydrogen cyanide (from 3a), acetonitrile (from 3b and 3c), or benzonitrile (from 3d) was also observed.

![Chart 1]

Although all attempts to isolate the key intermediates (6) and (7) failed, we believe that a reasonable mechanism for the formation of the pyrazoles (4) involves initial ring expansion to the 1,2,5-triazepines (6) via the diaziridines (5), by analogy with pyridine\textsuperscript{5} and quinoline N-imides.\textsuperscript{7} The triazepines (6) may then isomerize to the bicyclic valence isomers (7) followed by extrusion of R$_3$CN to produce the pyrazoles (4). 1,2,4-Triazepines are known to undergo similar valence bond isomerization and elimination to give pyrazoles under both thermal and photochemical conditions.\textsuperscript{9,12} Such reactions are also observed in the photolysis of other heteropines such as diazepines,\textsuperscript{13} oxazepines,\textsuperscript{14} and 2,3-benzodiazepines.\textsuperscript{15} This photochemical behavior of the pyrazine N-imides is somewhat different from that of the pyrazine N-oxides, which give imidazoles by ring contraction of oxadiazipine intermediates.\textsuperscript{16} The 2,5-dimethylpyrazine 1-imide (3c) rearranges exclusively to the less hindered $\alpha$-carbon; this reaction is analogous to that observed for 2-methylpyridine N-imides.\textsuperscript{17}

Pyrimine N-Imides

Several pyrimidine derivatives were aminated with MSH to give the corresponding N-aminopyrimidinium salts, which readily decomposed upon treatment with acylating reagents. However, treatment of 5-methylpyrimidine (8) with ethyl azidoformate gave the desired N-imide (9) in 18% yield, though the unsubstituted-, 2-methyl-, and 4-methyl- pyrimidines did not give their N-imides. Irradiation of the imide (9) gave 1-ethoxycarbonyl-4-methylpyrazole (10) and the parent amine (8) in 42% and 13% yields, respectively.

![Diagram of pyrimidine N-Imides]

This conversion of the imide (9) to the pyrazole (10) may also involve initial formation of the 1,2,4-triazepine (12) via the diaziridine intermediate (11), followed by isomerization to the bicyclic compound (13), from which HCN would then be eliminated to give the product (10). Although there is another possible route via the different intermediates (14), (15), and (16), this route seems less likely in view of the results of photolysis of 5-methylpyrimidine N-oxides, in which a preference for intermediate oxaziridine formation at C-2 rather than at C-6 is observed. However, no conclusion regarding this regioselectivity can be drawn at this time because the photolysis of 2- and 4-methylpyrimidine N-imides could not be examined, as stated above.

Pyridazine N-Imides

As in the case of pyrazines (3), the pyridazine N-ethoxycarbonylimides (19a—c) were prepared from the corresponding pyridazines (17) by N-amination followed by ethoxycarbonylation. The orientaion of the N-imide group of 19c is analogous to the orientation in the case of 3-methoxypyridazine N-oxide. Irradiation of the imides (19) resulted in the formation of the pyrrole derivatives (20) and the parent pyridazines (17) in the yields shown in Chart 3.

This photolysis may also involve the initial formation of the 1,2,3-triazepines (22), which then undergo either isomerization to 23 or ring opening to 24, followed by loss of nitrogen.

to give the pyrroles (20). Direct formation of 20 from the triazepines (22) by loss of nitrogen is also possible. This photochemical behavior of the pyridazine N-imides is analogous to that observed for pyridazine N-oxides, which give furans and/or pyrazoles via 1,2,3-oxadiazepine and diazoketone intermediates.\(^{20,21}\)

**Experimental**

Melting points were measured on a Yamato MP-2 apparatus and are uncorrected. Infrared (IR) spectra were determined with a JASCO IRA-2 spectrometer and mass (MS) spectra were recorded on a JEOL-D100 instrument. Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL JNM-MH100 spectrometer in CDCl₃ using tetramethylsilane as internal standard unless otherwise stated, and spectral assignments were confirmed by spin-decoupling experiments. Microanalyses were performed in the Microanalytical Laboratory of this School by Mrs R. Igarashi. Photolyases were carried out in an immersion apparatus equipped with a 400 W high-pressure Hg lamp and a Pyrex filter, which was cooled internally with running water.

**Materials**——2,6-Diphenylpyrazine (1d),\(^{22}\) 3,6-dimethylpyridazine (18b),\(^{23}\) and 3-methoxypyridazine (18c)\(^{24}\) were prepared by the reported procedures. The other amines are commercially available.

**N-Aminopyrazinium Mesitylenesulphonates** (2a–d)——General Procedure: The salts were prepared according to the procedure of Tamura \textit{et al.}\(^{21}\) A solution of O-mesitylenesulfonylhydroxylamine (MSH) (1.1 mol equiv.) in CH₂Cl₂ (100–150 ml) was added dropwise to a solution of the pyrazine (1: 0.65–0.1 mol) in CH₂Cl₂ (50–80 ml) with constant stirring in an ice bath. The reaction mixture was stirred at room temperature for an additional 20 min and then ether (300–400 ml) was added to the mixture. The resulting crystalline precipitates were collected by filtration and recrystallized from ethanol or ethanol–ethyl acetate to give the salts (2).

2a: 85% yield, mp 147.5—149°, colorless prisms. *Anal.* Calcd for C_{18}H_{17}N_{2}O_{5}S: C, 52.87; H, 5.80; N, 14.23. Found: C, 52.59; H, 5.86; N, 14.44.

2b: 92% yield, mp 165—165.5°, colorless prisms. *Anal.* Calcd for C_{18}H_{17}N_{2}O_{5}S: C, 55.71; H, 6.55; N, 12.99. Found: C, 55.50; H, 6.56; N, 13.01.

2c: 89% yield, mp 122—123.5°, colorless prisms. *Anal.* Calcd for C_{18}H_{17}N_{2}O_{5}S: C, 55.71; H, 6.55; N, 12.99. Found: C, 55.61; H, 6.63; N, 12.78.


**Pyrazine N-Ethoxycarbonylimides (3a—d)**—General Procedure: Solid potassium carbonate (1.5 mol equiv.) and ethyl chloroformate (1.1 mol equiv.) were added to a solution of the salt (2: 0.02—0.03 mol) in ethanol (100 ml) with stirring. The mixture was stirred at room temperature for a further 15—20 hr and the resulting inorganic precipitate was filtered off. The filtrate was concentrated in vacuo and the residue was extracted with CH_{2}Cl_{2}. The extract was dried over MgSO_{4} and evaporated to dryness in vacuo. The resulting residue was chromatographed on silica gel, using CH_{2}Cl_{2}-methanol (50: 1) as an eluent, to give the imides (3).

3a: 65% yield, mp 105—106°, colorless plates (from benzene-isopropyl ether). MS *m/z: 167 (M^+). IR v_{max} cm^{-1}: 1650 (C=O). NMR δ: 8.71 (2H, m, 3- and 5-H), 9.20 (2H, m, 2- and 6-H), 1.32 and 4.18 (3H, t, and 2H, q, CO_{2}Et). *Anal.* Calcd for C_{18}H_{17}N_{2}O_{5}: C, 50.29; H, 5.43; N, 25.14. Found: C, 50.12; H, 5.43; N, 24.87.

3b: 35% yield, mp 93°, colorless needles (from isopropyl ether). MS *m/z: 195 (M^+). IR v_{max} cm^{-1}: 1640 (C=O). NMR δ: 2.68 (6H, s, br, 3- and 5-Me), 8.83 (2H, s, br, 2- and 6-H), 1.31 and 4.16 (3H, t, and 2H, q, CO_{2}Et). *Anal.* Calcd for C_{18}H_{17}N_{2}O_{5}: C, 55.37; H, 6.71; N, 21.53. Found: C, 55.27; H, 6.82; N, 21.41.

3c: 30% yield, mp 78—79°, colorless needles (from isopropyl ether). MS *m/z: 195 (M^+). IR v_{max} cm^{-1}: 1630 (C=O). NMR δ: 2.58 (6H, s, br, 2- and 5-Me), 8.60 (1H, s, br, 3-H), 9.42 (1H, s, br, 6-H), 1.32 and 4.16 (3H, t, and 2H, q, CO_{2}Et). *Anal.* Calcd for C_{16}H_{15}N_{2}O_{5}: C, 55.37; H, 6.71; N, 21.53. Found: C, 55.17; H, 6.66; N, 21.36.

3d: 35% yield, mp 156—158°, colorless needles (from benzene). MS *m/z: 319 (M^+). IR v_{max} cm^{-1}: 1640 (C=O). NMR δ: 7.3—8.1 (10H, m, Ph-H), 9.30 (2H, s, 2- and 6-H), 1.37 and 4.16 (3H, t, and 2H, q, CO_{2}Et). *Anal.* Calcd for C_{18}H_{17}N_{2}O_{5}: C, 71.45; H, 5.37; N, 13.16. Found: C, 71.35; H, 5.51; N, 13.03.

**Photolysis of the Pyrazine N-Imides (3)**—General Procedure: A solution of the imide (3: 0.3—0.5 g) in acetone or benzene (200—300 ml) was irradiated for 2—4 hr. After removal of the solvent in vacuo, the residue was chromatographed on silica gel using n-hexane-CH_{2}Cl_{2} as an eluent to give the pyrazoles (4) and the parent pyrazines (1) successively, in the yields shown in Chart 1. The N-ethoxycarbonylpyrazoles (4a—c) were identical with authentic samples prepared from the corresponding N-unsubstituted pyrazoles by treatment with ethyl chloroformate according to the reported method. The compound (4d) was characterized by spectral comparison with 4a—c and reported analogs.

**5-Methylpyrimidine 1-Ethoxycarbonylimide (9)**—A mixture of 5-methylpyrimidine (10 g) and ethyl azidoformate (6 g) was heated at 90° for 60 hr with stirring and then evaporated to dryness in vacuo. The resulting solid was recrystallized from benzene to give the imide (9): 3.48 g, 18% yield, mp 143—145°, colorless needles. MS *m/z: 216 (M^+). IR v_{max} cm^{-1}: 1760 (C=O). NMR δ: 7.1—7.5 (5H, m, Ph-H), 7.95 (1H, s, br, 3-H), 8.29 (1H, s, br, 5-H), 1.42 and 4.43 (3H, t, and 2H, q, CO_{2}Et). *Anal.* Calcd for C_{14}H_{12}N_{2}O_{5}: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.57; H, 5.60; N, 12.78.

**Photolysis of the Imide (9)**—A solution of 9 (0.5 g) in benzene (300 ml) was irradiated for 3 hr and then the solvent was removed in vacuo. The residue was chromatographed on silica gel using n-hexane-CH_{2}Cl_{2} (1: 1) as an eluent to give 1-ethoxycarbonyl-4-methylpyrazole (10—4b: 260 mg, 42% yield) and the parent pyrimidine (8: 60 mg, 13% yield).

**N-Aminopyridazinium Mesitylenesulfonates (18a—c)**—General Procedure: The pyridazines (17:}


10—15 g) were treated with MSH and worked up as described for 1 to give the salts (18), which were purified by recrystallization from ethanol—isopropyl ether.

18a: 76% yield, mp 156—157° (lit.37 mp 154—155°).

Pyrazidine N-Ethoxycarbonylimides (19a—c)—Method A: The salt (18: 10—20 g) was treated with ethyl chloroformate and worked up as described for 2 to give the imide (19). Method B: A mixture of the salt (18: 10—20 g) and ethyl chloroformate (150 ml) was heated at 105° with stirring for 5 hr. After removal of the excess reagent in vacuo, the resulting residue was dissolved in CH₂Cl₂ (300—500 ml), dried over MgSO₄, and then concentrated in vacuo. The residue was chromatographed on silica gel using CH₂Cl₂—methanol as an eluent to give the imide (19).

19a: 25% yield (Method B); ca. 5% yield (Method A), yellow oil (pictate: mp 144—145.5°, yellow plates from ethanol). MS m/e: 167 (M+). IR νₑₓₑₐₜ cm⁻¹: 1640 (C=O). NMR δ: 7.63 (1H, dd, 4-H), 8.10 (1H, m, 5-H), 8.95 (1H, m, 3-H), 9.82 (1H, d, 6-H), J₈.₄ = 4, J₄.₇ = 8, J₅.₄ = 5 Hz, 1.35 and 4.26 (3H, t, and 2H, q, CO₂Et). Anal. Calcd for C₁₃H₁₁N₂O₄ (pictate): C, 39.40; H, 3.05; N, 21.21. Found: C, 39.56; H, 3.01; N, 20.97.

19b: 15% yield (Method A), mp 117—120°, yellow needles (from ethyl acetate). MS m/e: 197 (M+). IR νₑₓₑₐₜ cm⁻¹: 1640 (C=O). NMR δ: 2.65 (3H, s br, 3-Me), 2.70 (3H, s br, 6-Me), 7.51 (1H, d, 4-H), 7.89 (1H, d, 5-H), 1.32 and 4.19 (3H, t, and 2H, q, CO₂Et), J₄.₅ = 8 Hz. Anal. Calcd for C₉H₁₃N₂O₂: C, 55.37; H, 6.71; N, 21.53. Found: C, 55.09; H, 6.88; N, 21.36.

19c: 80% yield (Method A), mp 147—149°, yellow needles (from benzene). MS m/e: 207 (M+). IR νₑₓₑₐₜ cm⁻¹: 1640 (C=O). NMR δ: 4.16 (3H, s, OMe), 7.07 (1H, d, 4-H), 7.84 (1H, dd, 5-H), 9.88 (1H, d, 6-H), 1.37 and 4.25 (3H, t, and 2H, q, CO₂Et), J₄.₅ = 8, J₅.₄ = 5 Hz. Anal. Calcd for C₉H₁₃N₂O₂: C, 48.72; H, 5.62; N, 21.31. Found: C, 48.78; H, 5.66; N, 21.21.

Photolysis of the Pyrazidine N-Imides (19a—c)—A solution of the imide (19: 0.5 g) in benzene (300 ml) was irradiated and worked up as described for 3 to give the pyrrole derivatives (20) and the parent pyrazidines (17) successively, in the yields shown in Chart 3. Irradiation times were as follows: 19a: 12 hr, 19b: 22 hr, and 19c: 1.5 hr. The compound (20a) was identical with an authentic sample prepared from pyrrole by the reported procedure28 and 20b was characterized by spectral comparison with reported data.29

20a: colorless oil. MS m/e: 139 (M+). IR νₑₓₑₐₜ cm⁻¹: 1740 (C=O). NMR δ: 6.13 (2H, m, 5- and 4-H), 7.15 (2H, m, 2- and 5-H), 1.39 and 4.34 (3H, t, and 2H, q, CO₂Et).

20b: colorless oil. MS m/e: 167 (M+). IR νₑₓₑₐₜ cm⁻¹: 1740 (C=O). NMR δ: 2.13 (6H, s, 2- and 5-Me), 6.60 (2H, s, 3- and 5-H), 1.35 and 4.31 (3H, t, and 2H, q, CO₂Et). Anal. Calcd for C₁₄H₁₅NO₂: C, 64.65; H, 7.84; N, 8.38. Found: C, 64.51; H, 7.88; N, 8.27.

20c: colorless oil. MS m/e: 169 (M+). IR νₑₓₑₐₜ cm⁻¹: 1740 (C=O). NMR δ: 9.92 (3H, s, OMe), 5.36 (1H, dd, 3-H), 6.07 (1H, dd, 4-H), 6.88 (1H, dd, 5-H), J₄.₅ = 4, J₃.₆ = 2, J₅.₄ = 4 Hz, 1.40 and 4.43 (3H, t, and 2H, q, CO₂Et). Anal. Calcd for C₁₄H₁₅NO₂: C, 56.79; H, 6.55; N, 8.28. Found: C, 56.63; H, 6.51; N, 8.21.