Communications

See Editorial, *J. Org. Chem.*, **37**, No. 19, 4A (1972).

A Novel β-Alkylation of Pyridine and Quinoline 1-Oxides[1]

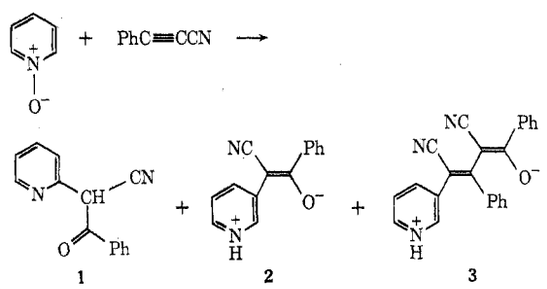
Summary: Pyridine and quinoline 1-oxide react with phenylpropiolonitrile to give a rearranged 3-alkylated derivative as the main product (whose structure has been confirmed spectroscopically, by degradation, synthesis, and, in the case of the pyridine derivative, by single-crystal X-ray analysis) together with minor amounts of the expected 2-alkylation product.

Sir: As a possible extension of the intramolecular nucleophilic substitutions leading to the direct acylamination of heteroaromatic *N*-oxides[2] we have studied the reaction of pyridine 1-oxide with phenylpropiolonitrile in boiling ethylene chloride.

The expected product (**1**) of intramolecular substitution at the α position was obtained in very low yield [mp 156–157°; ν (KBr) 2190 (C≡N), 1630 cm^{-1} (C=O); identical with an authentic sample prepared from pyridine 1-oxide, benzoylacetonitrile, and acetic anhydride]. The main product, isomeric with **1** and obtained in up to 56% yield, was a yellow solid, mp 238–239°. It exhibited bands at 2600–2340 (>NH$^+$), 2190 (C≡N), and 2120 cm^{-1} (w, br) and only a very weak broad band at 1640 cm^{-1}. Its nmr spectrum in CF_3CO_2H indicated the presence of two pyridine α protons [δ 9.44 (d, $J_{2,4}$ = 1 Hz, H_2), 8.59 (d, $J_{5,6}$ = 3 Hz, H_6)], a pyridine β proton [δ 8.07 (d d, $J_{4,5}$ = 4, $J_{5,6}$ = 3 Hz, H_5], and a γ proton [δ 8.92 (d t, H_4)] in addition to the phenyl protons and one proton which underwent H–D exchange. These data are consistent with structure **2** for this product, which was confirmed by its hydrolysis with dilute HCl to 3-pyridylacetic acid and benzoic acid, and by its synthesis from 3-pyridylacetonitrile and ethyl benzoate with NaOEt/EtOH.

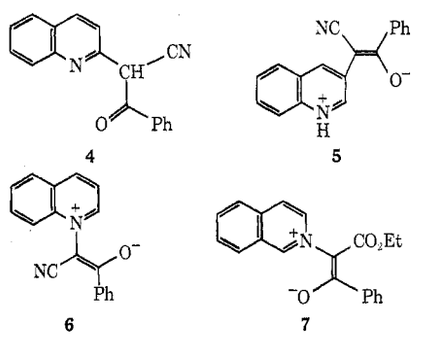
In view of the structure (**7**) of the adduct from isoquinoline 2-oxide and ethyl phenylpropiolate[3] (*vide infra*), the structure of **2** was also established by single-crystal X-ray analysis ($C_{14}H_{10}N_2O$): triclinic, $P\bar{1}$; a = 7.027 (6), b = 7.919 (6), c = 9.685 (7) Å; α = 90.75 (4), β = 95.28 (5), γ = 96.65 (5); ρ_{calcd} = 1.38 g cm^{-3} for Z = 2. Least-squares refinement gave R_1 (F) = 4.4% and R_2 (F) = 4.1% for 586 independent observed diffractometry data. The archistructure of **2** is depicted in Figure 1.

A third product, obtained in 6–17% yield, has been tentatively assigned structure **3** on the basis of its analysis, ir, and nmr spectrum (3-substituted pyridine, two Ph groups), and mass spectrum [*m/e* 349 (M$^+$), 105 (PhC≡O$^+$)].



1 2 3

Compounds **4** and **5** corresponding to **1** and **2** were obtained in 10 and 18% yields, respectively, from quinoline 1-oxide and phenylpropiolonitrile. Authentic **4** was synthesized from quinoline 1-oxide, benzoylacetonitrile, and acetic anhydride.[4] **5** had the expected nmr and mass spectra. From the complex residual reaction mixture a red solid (6.5%), mp 223–224°, was isolated by tlc and has been tentatively assigned structure **6** on the basis of its analysis and spectral properties: ν (KBr) 2170 cm^{-1} (C≡N) (no >NH$^+$); nmr ($CDCl_3$) δ 9.16 (1 H, d d, $J_{7,8}$ = 3, $J_{6,8}$ = 0.5 Hz, H_8), 8.68 (2 H, t, $J_{2,3}$ = $J_{3,4}$ = 4.5 Hz, H_2, H_4), 8.18–7.86 (4 H, m), 7.83 (2 H, t + q, $J_{2,3}$ = 4.5, $J_{7,8}$ = 3 Hz, H_3 and H_7), 7.45 (3 H, t, J = 1.5 Hz), no exchange with D_2O; mass spectrum *m/e* 272 (68) (M$^+$), 271 (86) (M$^+$ − 1), 105 (79) (PhC≡O$^+$), 77 (100) (Ph$^+$).



4 5 6 7

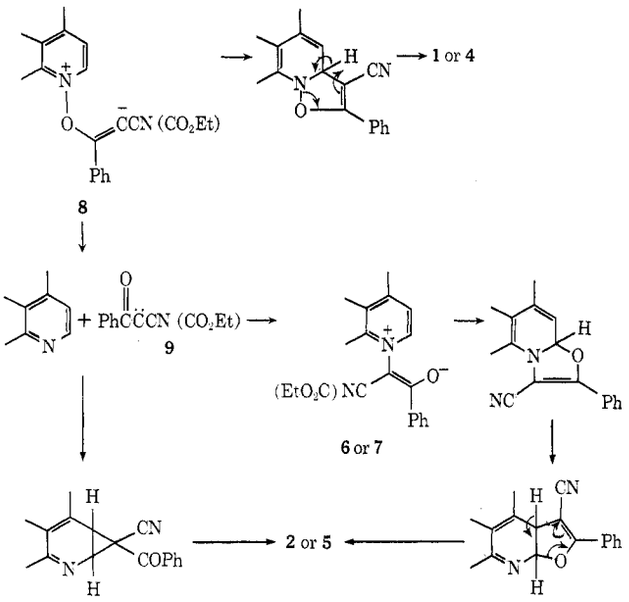
Huisgen, Seidl, and Wulff[3] reported the formation of the ylide **7** from isoquinoline 2-oxide and ethyl phenylpropiolate but no product of C-alkylation was found nor was a mechanism proposed for the formation of **7**. Our results and Huisgen's can be explained if the first step in the reaction is assumed to be the addition of the *N*-oxide to the triple bond to give **8**. This can either undergo intramolecular cyclization and ring opening to give **1** and **4** (alternatively these could arise by 1,3-dipolar addition) or heterolysis to give the pyridine and the highly electrophilic benzoylcyano- (or

(1) Detailed experimental procedures and X-ray crystallographic data will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to code number JOC-37-3383. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

(2) R. A. Abramovitch and G. M. Singer, *J. Amer. Chem. Soc.*, **91**, 5672 (1969); R. A. Abramovitch and R. B. Rogers, *Tetrahedron Lett.*, 1951 (1971).

(3) R. Huisgen, H. Seidl, and J. Wulff, *Chem. Ber.*, **102**, 915 (1969).

(4) M. Hamana and M. Yamazaki, *Chem. Pharm. Bull. (Tokyo)*, **11**, 415 (1963).



carbethoxy-) carbene (**9**) which, on recombination, would give **6** or **7**. Two routes can then be envisioned to **2** and **5**: (i) cyclization of the ylide followed by a 1,5-sigmatropic shift,[2] or (ii) addition of the carbene to C_2–C_3 of the pyridine ring followed by ring opening, in an analogous fashion to the formation of 3-benzenesulfonylaminopyridines from benzenesulfonylnitrene.[5] The mechanism of the reaction is now under investigation. A similar pathway may be followed in the formation of the products of the reaction of 1-alkoxycarbonyliminopyridinium ylides with dimethyl acetylenedicarboxylate.[6]

(5) R. A. Abramovitch and T. Takaya, *J. Org. Chem.*, **37**, 2022 (1972).

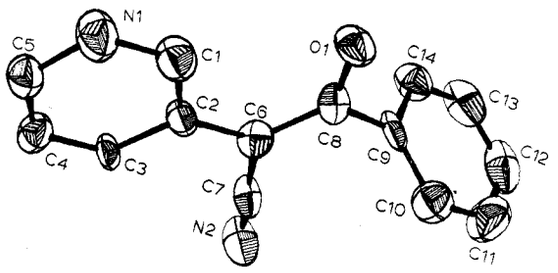


Figure 1.—Molecular structure of **2** with the thermal motions of the atoms represented by their 50% probability ellipsoids. Relevant bond distances follow: C6–C8, 1.424 (6); C6–C5, 1,450 (6); C6–C7, 1.426 (6); C8–C9, 1.485 (7); C8–O1, 1.265 (5); C7–N2, 1.161 (6) Å. The closest intermolecular approach is 2.609 (5) Å between N1 (H) and O1′. C2, C6, C7, C8, C9, and O1 are coplanar to within 0.03 Å; the plane thus constituted makes a dihedral angle of 81° with the plane of the phenyl group (C9, C10, C11, C12, C13, C14).

Acknowledgments.—This work was carried out with the support of an NIH grant (GM 16626) for which we are grateful.

(6) T. Sasaki, K. Kanematsu, and A. Kakehi, *J. Org. Chem.*, **36**, 2979 (1971).

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