5

6a, R = H
b, R = D

7

8

a, R = H; R_1 = H; R_2 = Ac
b, R = H; R_1 = H; R_2 = H
c, R = H; R_1 = D; R_2 = Ac
d, R = H; R_1 = D; R_2 = H
e, R = D; R_1 = H; R_2 = Ac
f, R = D; R_1 = H; R_2 = H

9   10

a, Y = O; R = H; R_1 = H
b, tosylhydrazone of a
c, Y = O; R = H; R_1 = D
d, tosylhydrazone of c
e, Y = O; R = D; R_1 = H
f, tosylhydrazone of e

brex-4-ene-4-d (6b) gave (via 8e and 8f) the endo 4-d ketone 9e (6% d_0, 94% d_1) and then its tosylhydrazone 9f.[13]

For carbene generation by Bamford–Stevens reaction the tosylhydrazones were converted with $NaOCH_3$ to their salts, which were thoroughly dried and pyrolyzed at 170–200° to produce deuterated brex-4-ene (54–58%; >99% pure by glpc). The extent of deuterium loss (e.g., by enolization during preparation and pyrolysis of the tosylhydrazone salts) was revealed by mass spectral analysis. The deuterium at each olefinic site was determined by quantitative pmr (100 MHz with CAT integration) and subtraction of the proportion of d_0 olefin, whose presence therefore does not interfere with the deuterium distribution in the d_1 product. The ratio of D shift vs H shift from both epimers allows calculation of the primary isotope effect (k_H/k_D)[14] and determination of the inherent exo-H/endo-H migration ratio. The first two entries in Table I show that the fractional per cent D loss was low (2–11%) and that for each substrate migration of the exo group (H or D) was strongly preferred. After correction for the isotope effect $(k_H/k_D = 1.30)$ the exo/endo migration ratio was 138.

In view of the rigidity in the brexyl skeleton, we conclude that for migration to a carbene center a perpen-

(13) Authentic natural abundance samples: **8a** $C_{11}H_{16}O_2$, ir 1740, 1250 cm⁻¹; nmr δ 4.79 ($J_{cis4,5}$ = 7.2 $J_{trans4,5}$ = 4.0 Hz); **8b** $C_9H_{14}O$, ir 3605, 1068, 1012 cm⁻¹; nmr δ 3.95, ($J_{cis4,5}$ = 7.0 $J_{trans4,5}$ = 4.0 Hz); **9a**, $C_9H_{12}O$, ir 1749 cm⁻¹; **9b**, $C_{16}H_{20}O_2N_2S$, mp 214–215° dec.
(14) W. Kirmse and K. Horn, Chem. Ber., 100, 2698 (1967).

dicular orientation of the hydrogen is preferred over an antiplanar orientation. The preference is not reasonably accounted for on steric hindrance grounds because the two hydrogens have comparable steric environments and are free of serious nonbonded interactions.

Photic Bamford–Stevens reactions[15] are being used increasingly in synthetic work as putative carbene sources,[16] and it is presumed, often tacitly, that such irradiations involve diazohydrocarbons and carbenes analogous to the situation for thermal Bamford–Stevens processes.[15,16] To compare stereoselectivity, we irradiated the tosylhydrazone salt of **9c** (suspended in dry pentane in a quartz tube) at 0° for 1 hr with a 450-W medium-pressure Hg lamp and found the migration ratio reduced to 4.8 (last entry Table I). Lower stereo-

Table I. 1,2-Shifts in Thermal and Photic Bamford–Stevens Reactions

Ketone (D config)	Method	Fractional % D loss	Relative amount of shift D	Relative amount of shift H	Migration ratio exo-H/ endo-H
9c (exo-D)	Thermal	11	106	1	138[a]
9e (endo-D)	Thermal	2	1	180	
9c (exo-D)	Photic	5	4.8	1	4.8[b]

[a] Corrected for the observed isotope effect of k_H/k_D = 1.30 (170–200°). [b] Uncorrected for isotope effect because only one epimer was irradiated. Primary isotope effects of 1.16–1.36 have been reported for H shifts by carbenes from irradiation of diazohydrocarbons.[14]

selectivity in the photic Bamford–Stevens suggests a higher energy for the derived "carbene" or, perhaps, that rearrangement occurs from a noncarbene intermediate.

(15) (a) W. G. Dauben and F. G. Willey, J. Amer. Chem. Soc., 84, 1498 (1962); (b) S. Cristol and J. K. Harrington, J. Org. Chem., 28, 1413 (1963); (c) G. L. Closs, L. E. Closs, and W. Böll, J. Amer. Chem. Soc., 85, 3796 (1963).
(16) (a) G. Büchi and J. D. White, J. Amer. Chem. Soc., 86, 2884 (1964); (b) D. M. Lemal and A. J. Fry, J. Org. Chem., 29, 1673 (1964); (c) J. R. Chapman, Tetrahedron Lett., 113 (1966); (d) S. Masamune, K. Fukumoto, Y. Yasunari, and D. Darwish, ibid., 193 (1966); (e) W. Kirmse and K.-H. Pook, Angew. Chem., Int. Ed. Engl., 5, 594 (1966); (f) S. Masamune, C. G. Chin, K. Hojo, and R. T. Seidner, J. Amer. Chem. Soc., 89, 4808 (1967); (g) R. E. Moser, J. M. Fritsch, T. L. Westman, R. M. Kliss, and C. N. Mathews, ibid., 89, 5673 (1967); (h) W. M. Jones and C. L. Ennis, ibid., 91, 6391 (1969); (i) K. Kondo and I. Ojima, J. Chem. Soc., Chem. Commun., 62, 63, 860 (1972); (j) I. Ojima and K. Kondo, Bull. Chem. Soc. Jap., 46, 1539 (1973).

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Reaction of Pyridine 1-Oxides with Benzyne.
β-Hydroxyarylation of Pyridines via $[_\sigma 2_s + _\pi 2_a + _\pi 4_s]$ Rearrangements

Sir:

In the reaction of six-membered heteroaromatic N-oxides with suitable acetylenes, β-alkylated products[1,2]

(1) R. A. Abramovitch, G. Grins, R. B. Rogers, J. L. Atwood, M. D. Williams, and S. Crider, J. Org. Chem., 37, 3383 (1972).
(2) R. A. Abramovitch and I. Shinkai, J. Chem. Soc., Chem. Commun., 569 (1973).

and N-ylides[2,3] are formed. The β-alkylation product was thought to arise from the initial 1,2-dihydropyridine adduct by a concerted symmetry allowed $[_\sigma 2_s + _\pi 2_a + _\pi 4_s]$ process rather than by 1,4- and/or 1,2-shifts in an intermediate zwitterion.[4] We suggested that ylide formation arose from an intermediate (caged?) carbene and the pyridine. An alternative mechanism proposed[5] involved a ring contraction of the initially formed 1,2-dihydro cyclo adduct to an aziridine followed by ring opening to the ylide.

Very little is known about the reaction of benzyne with heteroaromatic N-oxides. Quinoxalin-3-one 1-oxide (in which the rearrangement observed above with acetylenes is not possible) yields the 2-arylated product in good yield.[6] According to the Hamana mechanism[5] N-ylide formation should be possible from the intermediate (A) from pyridine 1-oxide and benzyne but should not be if ylide formation involves a carbene intermediate. We now report the reaction of benzyne with pyridine 1-oxides. The results support the mechanism previously proposed[2] for the reaction of acetylenes with heteroaromatic N-oxides and indicate that the benzyne reaction is a preparatively useful way of β-hydroxyarylating pyridines.

Generation of benzyne (1) (from benzenediazonium-2-carboxylate[7]) in the presence of pyridine 1-oxide (2a) gave 2-o-hydroxyphenylpyridine (3a) (5.8%)[8] and 3-o-hydroxyphenylpyridine (4a) (20.7%), mp 171–172°, identical with an authentic sample.[10,11] Several benzyne precursors were examined and the yields of 3a and 4a obtained with each are summarized in Table I.

Table I. Reaction of **2a** with **1** from Several Sources

Source of **1**	Solvent	Temp, °C	% yield 3a	% yield 4a
Benzenediazonium-2-carboxylate	THF	40–50	5.8	20.7
Diphenyliodonium-2-carboxylate[a]	o-Cl$_2$C$_6$H$_4$	179		4.0
Lithium 1-(benzotriazol-1-yl)-4-p-tolylsulfonyltetrazene[b]	THF	25	12.0	36.7
1-Aminobenzotriazole + 1-chlorobenzotriazole[c]	C$_6$H$_6$ CH$_2$Cl$_2$	0 0	4.7 6.1	37.2 52.8

[a] L. F. Fieser and M. J. Haddadin, *Org. Syn.*, **46**, 107 (1966). [b] M. Keating, M. E. Peek, C. W. Rees, and C. R. Storr, *J. Chem. Soc., Perkin Trans. 1*, 1315 (1972). [c] Reference 12.

In no case was any N-ylide observed. The highest yields of **4a** were obtained using 1-chlorobenzotriazole as an oxidizing agent for 1-aminobenzotriazole.[12] A

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

(4) T. Sasaki, K. Kanematsu, and A. Kakehi, *J. Org. Chem.*, **36**, 2978 (1971); T. Sasaki, K. Kanematsu, A. Kakehi, and G. Ito, *Bull. Chem. Soc. Jap.*, **45**, 2050 (1972).

(5) M. Hamana, *J. Heterocycl. Chem.*, **9**, S-51 (1972).

(6) J. C. Mason and G. Tennant, *J. Chem. Soc., Chem. Commun.*, 218 (1972).

(7) F. M. Logullo, A. H. Seitz, and L. Friedman, *Org. Syn.*, **48**, 12 (1968).

(8) The picrate had mp 154–155° dec (lit.[9] mp 176–178°). An authentic sample of the base was prepared from 2-o-nitrophenylpyridine.

(9) T. A. Geissman, M. J. Schlatter, I. D. Webb, and J. D. Roberts, *J. Org. Chem.*, **11**, 741 (1946).
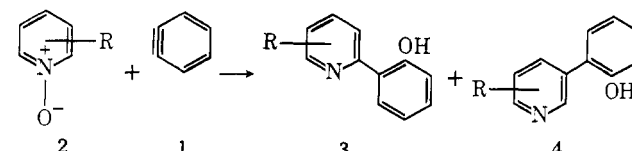
(10) An authentic sample was prepared from 3-o-nitrophenylpyridine.

(11) All new compounds were fully characterized by microanalysis, by ir, nmr, and mass spectra, and by comparison with authentic samples wherever possible.

(12) C. W. Rees and R. C. Storr, *Chem. Commun.*, 1305 (1968).

number of substituted pyridine 1-oxides were also examined,[13] and the results are summarized in Table II.

Table II. Reactions of Substituted Pyridine 1-Oxides with Benzyne in THF

R in **2**	Products[11]	Mp, °C	Yield (%)[a]
2-CN (**2b**)	**4b**	139–140	35.5
4-CN (**2c**)	**4c**	132–133	18.3
2-Me (**2d**)	**4d**[b]	147–149	30.5
3-Me (**2e**)	**4e**	182–183	4.1
	3e	97	1.7
3,5-Me$_2$ (**2f**)	**3f**	114–115	53.5

[a] Isolated yields. [b] A trace of 2-benzylpyridine 1-oxide was also obtained.

Only in the case where the 3- and 5-positions were blocked (**2f**) was a good yield of the 2-o-hydroxyphenylpyridine (**3f**) obtained.

To get more information about the mechanism of this unusual rearrangement the reaction of benzyne with 3,5-lutidine 1-oxide (**2f**) was examined in greater detail. In THF at temperatures below 45° two isomeric 1:1 dihydropyridine adducts (C$_{13}$H$_{13}$NO) were formed, together with **3f** (24.4%), and resolved by preparative tlc.[14] Thus were obtained **5** (24.8%), mp 95–96° dec (nmr δ 7.72 (d, 1, $J_{4,6}$ = 1.20 Hz, H$_6$), 6.57–7.20 (m, 4, aromatic), 5.42 (m, 1, H$_4$), 4.70 (d, 1, $J_{2,4}$ = 1.88 Hz, H$_2$), 1.91 (d, 3, J_{4,Me^3} = 1.58 Hz, 3-Me), and 1.61[15] (s, 3, 5-Me)), and **6** (23.1%), pale yellow oil, bp 63–65° (1 μ) (nmr δ 7.70 (dd, 1, $J_{2,6}$ = 2.63 Hz, $J_{4,6}$ = 1.88 Hz, H$_6$), 6.60–7.50 (m, 4, aromatic), 5.82 (dq, 1, $J_{4,6}$ = 1.88 Hz, J_{4,Me^5} = 1.80 Hz, H$_4$), 5.08 (d, 1, $J_{2,6}$ = 2.63 Hz, H$_2$), 1.82 (d, 3, J_{4,Me^5} = 1.80 Hz, 5-Me), and 1.44[15] (s, 3, 3-Me)). Spin decoupling experiments confirmed the above assignments.[16] Both **5** and **6** rearranged thermally (100°, 30–45 min, neat) to **3f** (64 and 97% yields, respectively). Reduction of **5** and **6** with NaBH$_4$ in EtOH at 0–5° gave the tetrahydropyridines **7** (51.6%), mp 135–136° dec, and **8** (34.7%), mp 34–35°, respectively. The ir and nmr spectra of these tetrahydropyridines confirmed their structures and, therefore, those assigned to the dihydropyridine precursors.[17]

(13) No attempt was made to optimize yields in these reactions.

(14) The nmr spectrum of the crude reaction product in CCl$_4$ showed the presence of only small amounts of **3f** (5:6:3f = 13:13:1). During the separation procedure, **5** and **6** rearrange to **3f**, as confirmed by treatment of pure **5** or **6** with catalytic amounts of silica gel in CCl$_4$–ether solvent.

(15) The singlet at δ 1.61 for **5** and 1.44 for **6** supports the presence of a methyl group attached to a fully substituted (bridgehead in this case) carbon. A. Crabtree, L. M. Jackman, and A. W. Johnson, *J. Chem. Soc.* 4417 (1962).

(16) Coupling (*i.e.*, $J_{4,6}$ = 1.20 Hz in **5**) between protons separated by three carbon atoms, two of which are sp^2 hybridized has been observed in a number of molecules of well-defined stereochemistry [S. Sternhell, *Rev. Pure Appl. Sci.*, **14**, 15 (1964)]. In **6**, allylic coupling ($J_{2,6}$ = 2.63 Hz) across the C=N bond was observed, while in **5** $J_{2,6}$ = 0 Hz. This can be explained on the basis of the allylic angle θ. The σ–π overlap would be at a maximum with θ = 90° (**6**, H$_2$ axial) and at a minimum with θ = 0° (**5**, H$_2$ equatorial).

(17) **7** and **8** both exhibited NH bands in the ir: **7** nmr δ 6.55–7.10 (m, 4, aromatic), 5.38 (m, 1, H$_4$), 3.66 (m, 1, H$_2$), 3.52 (d, 1, J_{ae} = 13.0 Hz, H$_6$ (axial)[18]), 2.80 (d, 1, J_{ae} = 13.0 Hz, H$_6$ (equat)[18]), 2.06 (s, 1, D$_2$O exch, NH), 1.88 (d, 3, J_{4,Me^3} = 1.8 Hz, 3-Me), and 1.42 (s, 3, 5-Me);

A probable mechanism for these rearrangements is as follows

A

B
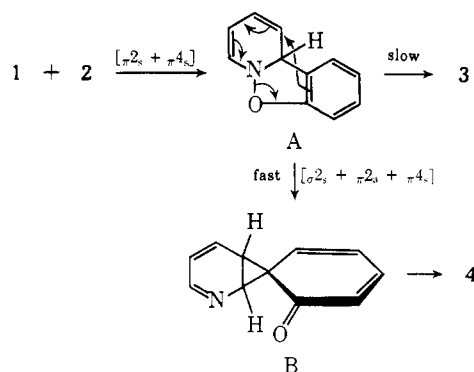
When the 3- and 5-positions are blocked, aromatization leading to 4 is not possible and the intermediate A' can undergo further sigmatropic shifts to give 5 and 6.[19]
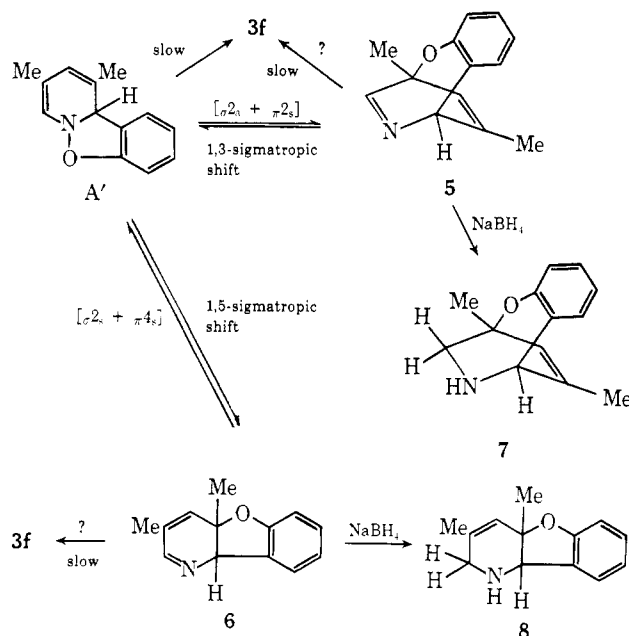
The alternative mode of ring opening of spirodienone (B) to give 3 is unlikely and, indeed, has been shown not to occur in the corresponding adduct formed from benzoylcyanocarbene and pyridine.[2]

To test the hypothesis of the above 1,5-sigmatropic shift (A' → 6) the reaction of benzyne with 3,5-dichloropyridine 1-oxide at 0° was studied. As expected, 3-chloropyrido[3,2-b]benzofuran (9) (66.5%), mp 136–137°

9
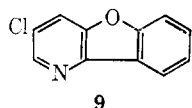
dec, was obtained by the facile elimination of HCl from the dichloro derivative corresponding to 6. This appears to be a convenient one-step route to this heterocyclic ring system.

8, nmr δ 6.58–7.40 (m, 4, aromatic), 5.52 (m, 1, H_4), 4.03 (s, 1, H_2), 2.95 (m, 2, H_6), 1.65 (d, 3, J_{4,Me^5} = 0.75 Hz, 5-Me), 1.70 (s, 1, D_2O exch, NH), and 1.36 (s, 3, 3-Me). Decoupling experiments confirmed the assignments.

(18) The rigid structure of 7 is supported by the presence of two distinct C_6 methylene proton peaks. See, for example, F. Böhlmann, D. Schumann, and C. Arndt, *Tetrahedron Lett.*, 2705 (1965).

(19) Other modes of aromatization of 5 and 6 to 3f are also conceivable.

We are currently extending the synthetic scope of this new β-hydroxyarylation reaction and investigating further aspects of the mechanisms of the rearrangements observed.

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Phosphorane Formation from the Reaction of Trivalent Phosphorus Compounds with Tetramethyl-1,2-dioxetane

Sir:

The reaction of tetramethyl-1,2-dioxetane (TMD) with triphenylphosphine has been shown[1] to form a stable phosphorane, 1, in 94% yield. We now report the formation of phosphoranes 2, 3, and 4 from the
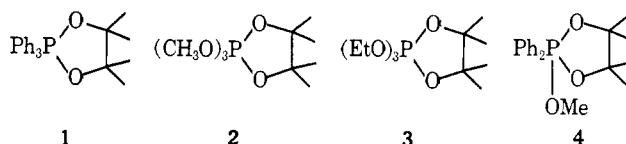
reaction of TMD with trimethyl phosphite, triethyl phosphite, and methyl diphenylphosphinite. The kinetics of phosphorane formation was also investigated.

Trimethyl phosphite (2.0 mg, 0.016 mmol) was added[2] to 1.8 mg TMD (0.016 mmol) in dry benzene at room temperature (~22°). Phosphorane 2 was formed rapidly in 69% yield.[3] Pinacolone and trimethyl phosphate accounted for the remaining products (31%). Triethyl phosphite (3.0 mg, 0.018 mmol) was added to 1.8 mg of TMD (0.016 mmol) in dry benzene at 22° yielding phosphorane 3[4] in 70% yield as well as 30% pinacolone and triethyl phosphate. Methyl diphenylphosphinite (3.3 mg, 0.015 mmol) was added to TMD (1.6 mg, 0.014 mmol) in benzene to yield phosphorane 4 in 84% yield. Pinacolone and methyl diphenylphosphinate accounted for 16% of the reaction products. The ^1H and ^{31}P nmr data for phosphoranes 1–4 are shown in Table I.

Unlike phosphorane 1,[1] phosphoranes 2–4 were found to be thermally stable in benzene at 70° for 120 min. Phosphorane 2 (purified sample)[5] was heated in benzene (sealed tube) at 90° for 12 hr with only slight decomposition. These observations were in accord with the prediction that replacement of an apical alkyl or aryl group by an alkoxy group should stabilize the phosphorane.[6]

Phosphoranes 1–4 were found to cleave with rearrangement to pinacolone and the corresponding phosphoryl compound when treated with concentrated sul-

(1) P. D. Bartlett, A. L. Baumstark, and M. E. Landis, *J. Amer. Chem. Soc.*, **95**, 6486 (1973).

(2) Order of addition had no effect on product yields.

(3) Yields determined by nmr integrations.

(4) D. B. Denney and D. H. Jones, *J. Amer. Chem. Soc.*, **91**, 5821 (1969), report the synthesis of phosphorane 3 from the reaction of tetramethylethylene ethyl phosphite with diethyl peroxide.

(5) Pinacolone and most of the trimethyl phosphate were removed at high vacuum.

(6) (a) D. Gorenstein, *J. Amer. Chem. Soc.*, **92**, 644 (1970); (b) D. Gorenstein and F. H. Westheimer, *ibid.*, **92**, 634 (1970).