# THERMAL BASE-INDUCED REARRANGEMENT OF A PYRIDINIUM SALT TO AN AZEPINE*

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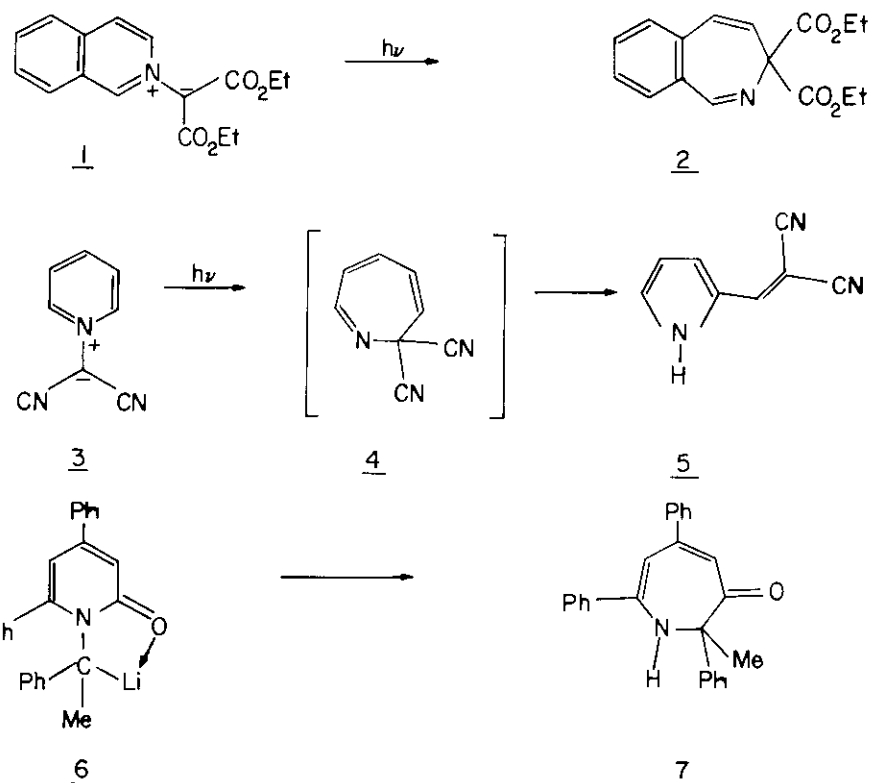
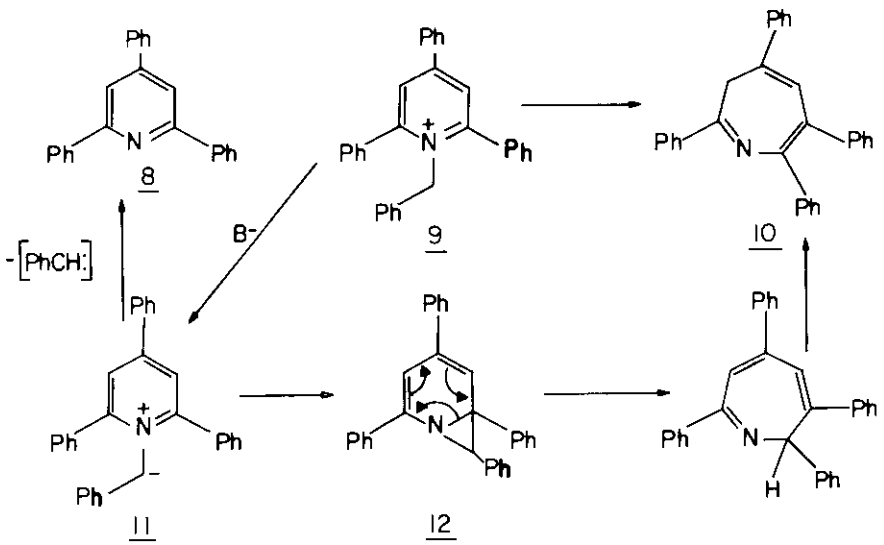
Abstract- Heating 1-benzyl-2,4,6-triphenylpyridinium tetrafluoroborate in the presence of strong base results in formation of 3H-2,4,6,7-tetraphenylazepine. The spectral data and crystal structure are discussed.

The photolysis of stabilized pyridinium ylides is known to give azepines: thus, the isoquinolinium ylide (1) yields the benzazepine (2)[1] and the azepine (4) was suggested as an intermediate in the formation of pyrrole (5) by photolysis of the pyridinium ylide (3)[2]. The 2-pyridone carbanion (6) is rearranged to the azepinone (7) by attack on the carbonyl group followed by Cope rearrangement and protonation.[3]




* In honor of the 65th birthday of Gilbert Stork.

However, monocyclic azepines have not previously been formed from unactivated pyridinium ylides. During investigations in a related area[4], we reacted 1-benzyl-2,4,6-triphenylpyridinium tetrafluoroborate (9) with the ethyl 2-methylacetoacetate carbanion in refluxing toluene and obtained 3H-2,4,6,7-tetraphenylazepine (10) as a yellow crystalline solid (Scheme I). Compound (10) was independently prepared (30%) from the pyridinium salt and excess sodium hydride; some 2,4,6-triphenylpyridine (8) was also obtained (Scheme I).




Scheme I

In the presence of strong base, (9) forms the pyridinium ylide (11); the anionic carbon attacks the α-position of the pyridinium ring to give the bicyclic structure (12) which undergoes Cope rearrangement followed by tautomerization to afford the observed product (10). Ylide (11) can alternatively decompose to form phenylcarbene and the other observed product (8). Carbene formation has been previously observed in the photolysis of some pyridinium ylides.[1]

Structure elucidation. The infrared spectrum of (10) shows the absence of bands at 1620-1610 $cm^{-1}$ (typical of pyridinium salts) and at 1050 $cm^{-1}$ (tetrafluoroborate anion).

In the $^{1}H$-nmr spectrum, aromatic absorptions are found between 8.0 and 7.2 ppm; the olefinic proton resonates at 6.7 ppm as a singlet, and the geminal methylene

protons appear as two broad doublets at 5.0 and 2.1 ppm with a coupling constant of ca 11 Hz. The $^{13}$C-nmr spectrum, which shows one aliphatic carbon at 36.9 ppm that in the off-resonance spectrum resonates as a triplet, is consistent with the structure.

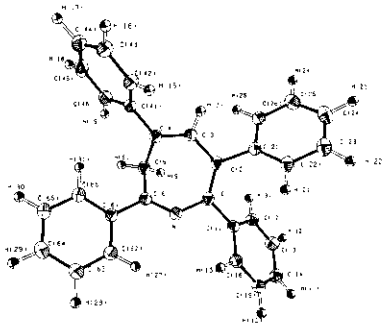


Figure 1. An ORTEP drawing of 3H-2,4,6,7-tetraphenylazepine illustrating the thermal ellipsoids for the non-hydrogen atoms and the atomic numbering. The hydrogen atoms were given a small isotropic thermal parameter for illustrative purposes.

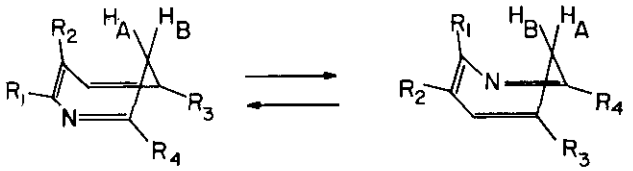
The ultraviolet spectrum displays absorptions at 262 and 348 nm; the latter band extends into the visible region and is responsible for the light yellow color of this compound.[5] The mass spectrum shows an intense molecular ion peak at m/z 397; the base peak at m/z 294 is originated by loss of benzonitrile from the molecular ion.

These data, while clearly pointing to an azepine structure, did not allow the distinction between the 3H-azepine (10) and the corresponding 4H-isomer. The 3H-azepine structure of (10) was confirmed by an X-ray structure determination.[6] The molecule is illustrated in Figure 1. The distance of 1.354(3) Å between C(3) and C(4) and 1.283(3) Å between N(1) and C(6) clearly establishes the 3H-structure. Furthermore, two H atoms were located on C(5) where the C(5)-C(6) and C(5)-C(4) distances of 1.509(3) and 1.497(3) Å are close to the expected values. The C-C distances in the phenyl rings are the usual values. Tables of positional parameters, distances and angles are available from the the authors and will be deposited in the Cambridge Structural Database.

An analysis of the torsion angles in terms of theoretical predictions for a seven-membered ring[7] indicates a boat conformation with C(5) the prow. The torsion angles are virtually identical to those calculated for other reported uncomplexed azepines.[8-10] A recently reported 3H-azepine[11] has errors in the data and was not included in the comparisons.

Ring inversion. The possible two stable boat forms are interconvertible by azepine ring inversion (Scheme II). The barrier to ring inversion can be relatively high for highly substituted azepines, for example, 13.7 kcal.mol$^{-1}$ for 3H-azepine (13).[12]

The $^1$H-nmr pattern of two doublets for the geminal methylene protons of (10) indicates no fast ring inversion at room temperature. Increasing the temperature broadens these signals, and coalescence is observed at 80°C. From this value, the $\Delta G^{\neq}$ for ring inversion is calculated[13] to be 16.3 kcal.mol$^{-1}$.




(10) $R_1 = R_2 = R_3 = R_4 = Ph$

(13) $R_1 = R_4 = Me$; $R_2 = R_3 = CO_2Me$

Scheme II

EXPERIMENTAL

Preparation of (10). 1-Benzyl-2,4,6-triphenylpyridinium tetrafluoroborate[14] (2.2 g; 4.58 mmol) was added to a stirred suspension of 97% sodium hydride (0.17 g; 6.87 mmol) in dry toluene (15 ml). The mixture was refluxed for 45 h. After cooling, ethanol was added slowly to destroy excess sodium hydride. Water was then added, the layers separated, the aqueous layer extracted with dichloromethane, the organic layer washed with water and dried ($MgSO_4$). Evaporation of the solvents left a solid that, after recrystallization from toluene afforded 0.54 g of (10), yellow microcrystals, mp 214-215°C (Found: C, 90.68; H, 6.11; N, 3.28%. $C_{30}H_{23}N$ requires C, 90.68; H, 5.78; N, 3.52%); $\nu_{max}$($CHBr_3$) 1590 (m), 1565 (m), 1490 (m), 1445 (m); $\delta_H$ ($CDCl_3$) 8.0 (2H, m), 7.8-7.2 (18H, m), 6.7 (1H, s), 5.0 (1H, br d, J = ca. 11 Hz), 2.1 (1H, br d, J = ca. 11 Hz); $\delta_C$ ($CDCl_3$) 149.1, 142.7, 141.4, 149.5, 139.3, 136.8, 131.5, 129.7, 128.8, 128.7, 128.4, 128.1, 127.8, 127.7, 127.0, 126.3, 125.9, 36.9; $\lambda_{max}$ ($\varepsilon$) ($CH_3CN$) 348 (16,666), 262 (35,416); m/z (%) 397 (97.11, $M^+$), 396 (38.96), 295 (31.90), 294 (100), 217 (19.12), 216 (17.23), 215 (46.32), 202 (19.05), 91 (39.45). The residue after evaporation of the mother liquors was triturated with ether, filtered, and the solvent evaporated to afford 2,4,6-triphenylpyridine (8), mp 128-130°C (lit.[15] mp 135-136°C), identical in spectroscopic (ir and $^1$H-nmr) properties to an authentic sample.

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6. Crystal Data, $C_{30}H_{23}N$, M = 397.52, monoclinic, space group $P2_1/c$, a = 17.7537(33), b = 5.5683(8), c = 22.9233(45) Å, β = 105.40(1)°, Vol = 2184.8(7) $Å^3$, $D_c$ = 1.209 $g.cm^{-3}$, Z = 4. A total of 3224 measurements with Cu-Ni filtered radiation gave a set of 2272 reflections with $I > 2\sigma(I)$ which was used in the analysis. Hydrogen atoms were determined from a difference Fourier synthesis and refined. The final R and $R_w$ values are 0.041 and 0.047, respectively.
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