BENZYLIDENE(CYANO)BENZYLAMINE AS A 1,3-DIPOLE

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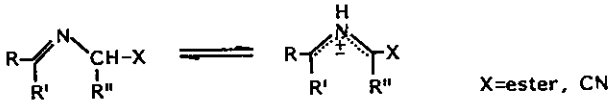
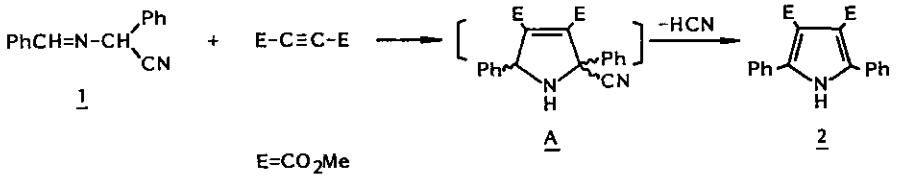
Abstract —— Benzylidene(cyano)benzylamine reacted as an azomethine ylide with DMAD and olefinic dipolarophiles. In most cases, however, the products derived from the initially formed [3 + 2] cycloadducts with the elimination of hydrogen cyanide were obtained.

Recently, imines of α-amino acid esters have been found to undergo 1,3-dipolar cycloadditions via their 1,3-dipolar tautomers, azomethine ylides[1-7]. An imine bearing electron-withdrawing cyano group in place of an ester group might be also expected to behave as a 1,3-dipole via tautomerism.



In the present communication we wish to report 1,3-dipolar cycloaddition reactions of benzylidene-(cyano)benzylamine 1.

A solution of equimolar amounts of the imine 1[8] and dimethyl acetylenedicarboxylate (DMAD) in toluene was refluxed for 3 h. The reaction mixture was then concentrated in vacuo to leave a residue, which was purified by chromatography on silica gel using chloroform as an eluent to give a 52% yield of the pyrrole 2, mp 131-133°C, as colorless prisms: IR (KBr) 3300, 1720, 1700 cm^{-1}; NMR ($CDCl_3$) δ 3.75 (6H, s), 7.30-7.65 (10H, m), 8.85 (1H, broad, NH); MS m/e 305 (M^+).

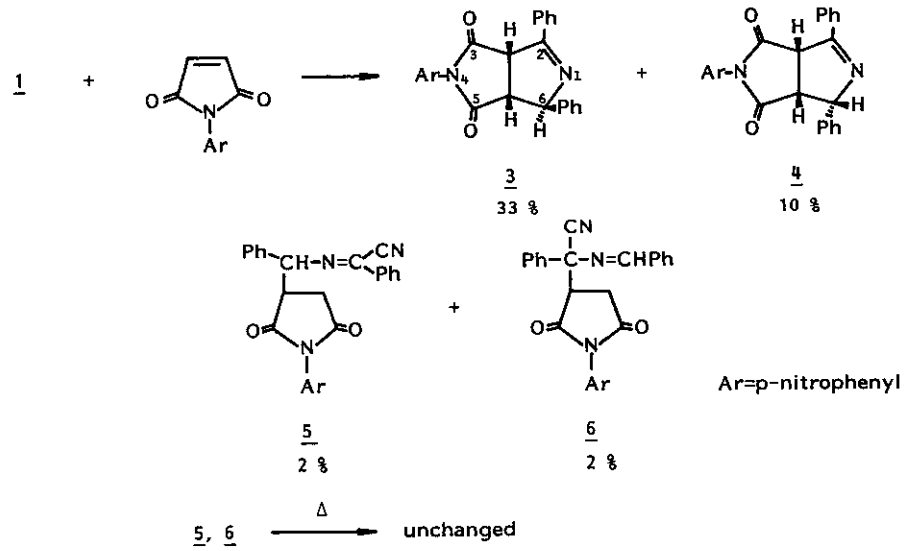


Scheme 1

The pathway for the formation of 2 is outlined in Scheme 1. In a similar manner as imines of α-amino acid esters, the imine 1 undergoes a 1,3-dipolar cycloaddition reaction with DMAD via its

tautomer to yield initial [3 + 2] cycloadduct(s) A. Subsequent elimination of hydrogen cyanide of A, followed by aromatization, gives final product 2.

Next, the reaction of 1 with olefinic dipolarophiles was investigated under similar conditions. The imine 1 reacted with n-(p-nitrophenyl)maleimide in refluxing toluene for 3 h to give a mixture of four products, 3, 4, 5, and 6, together with recovery of the maleimide. On the basis of spectral data, the major products 3 and 4 were assigned as stereoisomeric 1-pyrrolines arising from initially formed [3 + 2] cycloadduct(s) with the elimination of hydrogen cyanide. On the other hand, the minor products 5 and 6 were deduced to be an ene-reaction product and Michael adduct re-



Scheme 2

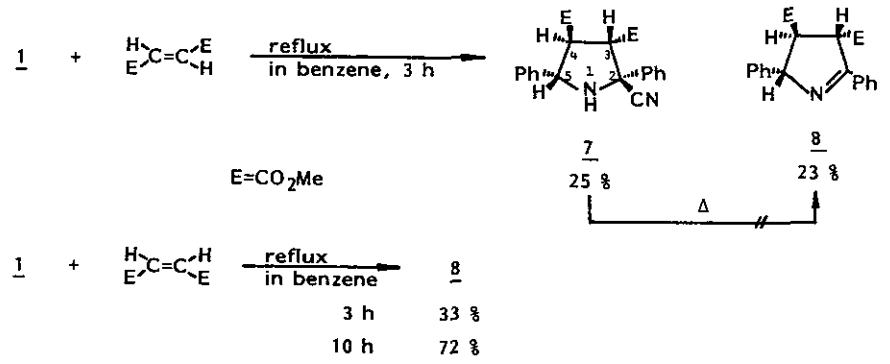
spectively[9], which were unchanged even when heated in refluxing toluene for a long time (Scheme 2).

3: mp 265-266°C; colorless needles; IR (KBr) 1720 cm^{-1}; NMR ($CDCl_3$) δ 4.20 (1H, dd, 5a-H, J=9.0, 9.0 Hz), 4.90 (1H, d, 2a-H, J=9.0 Hz), 6.15 (1H, d, 6-H, J=9.0 Hz), 6.90-8.40 (14H, m); MS m/e 411 (M^+). 4: mp 239-241°C; colorless prisms; IR (KBr) 1720 cm^{-1}; NMR ($CDCl_3$) δ 3.85 (1H, dd, 5a-H, J=3.0, 9.0 Hz), 4.95 (1H, dd, 2a-H, J=3.0, 9.0 Hz), 5.90 (1H, dd, 6-H, J=3.0, 3.0 Hz), 7.30-8.45 (14H, m); MS m/e 411 (M^+).

The stereochemistry of 3 (2a-H, 5a-H—cis—5a-H, 6-H—trans) and 4 (2a-H, 5a-H, 6-H—all cis) was deduced on the basis of NMR data; the long-range coupling between 2a-H and 6-H was observed in 4, but not in 3.

The imine 1 reacted with dimethyl fumarate in refluxing benzene to give a mixture of the pyrrolidine 7, mp 131-133°C, and 1-pyrroline 8, mp 106-107°C, whereas the reaction of 1 with dimethyl maleate under similar conditions afforded 8 as the sole product (Scheme 3).

7: IR (KBr) 3350, 2230, 1740 cm^{-1}; NMR (CD_3CN) δ 3.06, 3.62 (each 3H, s), 3.56 (1H, broad, NH, ex-



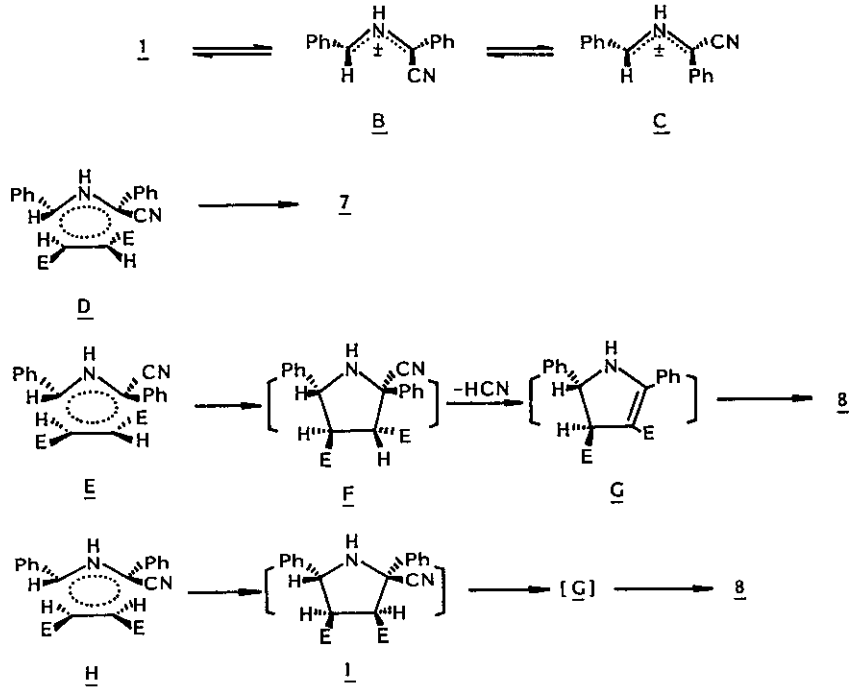
Scheme 3

changed with D_2O), 3.80-4.05 (2H, m, 3-H, 4-H), 5.00 (1H, m, 5-H, changed to dd (J=6.0, 3.0 Hz) when treated with D_2O), 7.30-8.10 (10H, m); MS m/e 337 (M^+ - HCN). 8: IR (KBr) 1750 cm^{-1}; NMR ($CDCl_3$) δ 3.14, 3.70 (each 3H, s), 4.00 (1H, dd, 4-H, J=9.0, 5.0 Hz), 4.92 (1H, dd, 3-H, J=5.0, 2.0 Hz), 5.95 (1H, dd, 5-H, J=9.0, 2.0 Hz), 7.20-8.20 (10H, m); MS m/e 337 (M^+).

The stereochemistry of 7 (2-phenyl, 3-H—trans—3-H, 4-H—trans—4-H, 5-H—trans) and 8 (3-H, 4-H—trans—4-H, 5-H—trans) was based on the NMR data. In both 7 and 8 the long-range coupling between 3-H and 5-H was observed, indicating that 3-H and 5-H are cis. An argument for the cis-relations of 2-, 5-phenyl and 3-methoxycarbonyl in 7, and of 5-phenyl and 3-methoxycarbonyl in 8 are provided by the unusually low δ-values for the 3-methoxycarbonyls compared with those at the 4-position, respectively.

The pyrrolidine 7 was unchanged even on heating in benzene under reflux for a long time; this implies that 8 was derived from the elimination of hydrogen cyanide of other initial cycloadduct(s) than 7. We now wish to postulate the pathways for the formation of 7 and 8 as shown in Scheme 4. In analogy with the cycloadditions of imines of α-amino acid esters, it is reasonable to assume that the reaction proceeds via a concerted 1,3-dipolar cycloaddition of an azomethine ylide B or C, generated from a prototropy of 1, to the fumarate or maleate.

Among four transition states leading to cycloadducts between 1 and the fumarate, D or E has more preferable geometry than others[10]. The compound 7 evidently forms from D. As mentioned above, 7 did not undergo dehydrocyanation; this suggests that in pyrrolidine derivatives dehydrocyanation does not occur between neighboring NH and cyano groups. It can thus be presumed that 8 forms via an anti-elimination of hydrogen cyanide from initial cycloadduct F, which derived through E, to yield 2-pyrroline G, followed by a hydrogen shift. On the other hand, H has the most favorable geometry among the transition states leading to cycloadducts between 1 and the maleate[11]. A cycloadduct I derived from H undergoes anti-elimination of hydrogen cyanide to yield G, which gives 8. Study on intramolecular cycloaddition reactions of benzylidene(cyanao)benzylamines is in progress.



Scheme 4

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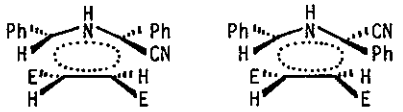
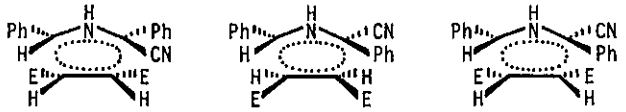
7. O. Tsuge, K. Ueno, and I. Ueda, Heterocycles, 1981, 16, 1503.
8. The imine 1 was prepared from the reaction of benzaldehyde with cyanobenzylamine: mp 51.5-52°C; IR (KBr) 2210, 1625 cm^{-1}; NMR ($CDCl_3$) δ 5.80 (1H, d, J=2.0 Hz), 7.10-8.20 (10H, m), 8.65 (1H, d, J=2.0 Hz); MS m/e 220 (M^+).
   All new compounds in this paper gave satisfactory elemental analyses.
9. An analogous formation of an ene-reaction product and Michael adduct has been reported in the reaction of benzylidenebenzylamine with diethyl azodicarboxylate (M. M. Shemyakin, L. A. Neiman, S. V. Zhukova, Y. S. Nekrasov, T. J. Pehk, and E. T. Lippmaa, Tetrahedron, 1971, 27, 2811). 5: mp 195-196°C; IR (KBr) 2240, 1710 cm^{-1}; NMR ($CDCl_3$) δ 2.91 (1H, dd, J=9.0, 18.0 Hz), 3.10 (1H, dd, J=6.0, 18.0 Hz), 3.63 (1H, ddd, J=6.0, 7.0, 9.0 Hz), 5.53 (1H, d, J=7.0 Hz), 7.22-8.32 (14H, m); MS m/e 438 (M^+). 6: mp 250-252°C; IR (KBr) 2250, 1720 cm^{-1}; NMR ($CDCl_3$) δ 2.90 (2H, m), 4.35 (1H, m), 7.30-8.30 (14H, m), 8.80 (1H, s); MS m/e 438 (M^+).
10. Other transition states than D and E are as follows.



11. Other transition states than H are as follows.



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