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. 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 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 (CDCl₃) δ 3.75 (6H, s), 7.30-7.65 (10H, m), 8.85 (1H, broad, NH); MS m/e 305 (M⁺).

![Scheme 1](image-url)

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 respectively.

\[
\begin{align*}
\text{I} & \quad \text{+} \\
\text{Ar-N=C=NCN} & \quad \text{+} \\
\text{O} & \quad \text{O} \\
\text{N=CH-CN} & \quad \text{N=CH-CN} \\
\text{Ar} & \quad \text{Ar} \\
\text{Ar} & \quad \text{Ar} \\
\text{5} & \quad \text{5} \\
\text{6} & \quad \text{6} \\
\text{2%} & \quad \text{2%} \\
\end{align*}
\]

\[
\begin{align*}
5, 6 & \quad \Delta \\
& \quad \text{unchanged}
\end{align*}
\]

Scheme 2

spectively, 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\(_3\)) \& 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\(_3\)) \& 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\(_3\)CN) \& 3.06, 3.62 (each 3H, s), 3.56 (1H, broad, NH, ex-
The stereochemistry of $1$ (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 $1$, and of 5-phenyl and 3-methoxycarbonyl in $8$ are provided by the unusually low $\delta$-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 $\alpha$-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. 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. 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(cyano)benzylamines is in progress.
REFERENCES AND NOTES

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 (CDCl₃) 6 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⁺).
5: mp 195-196°C; IR (KBr) 2240, 1710 cm⁻¹; NMR (CDCl₃) 6 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 (CDCl₃) 6 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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