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1, 3-DIPOLAR CYCLOADDITION OF 1-PHENYLPROPA-1, 2 -DIENE WITH PYRIDINIUM DICYANOMETHYLIDES：1-PHENYLPROPA-1, 2 -DIENE AS A SYNTHETIC EQUIVALENT OF 1-PHENYLPROPYNE

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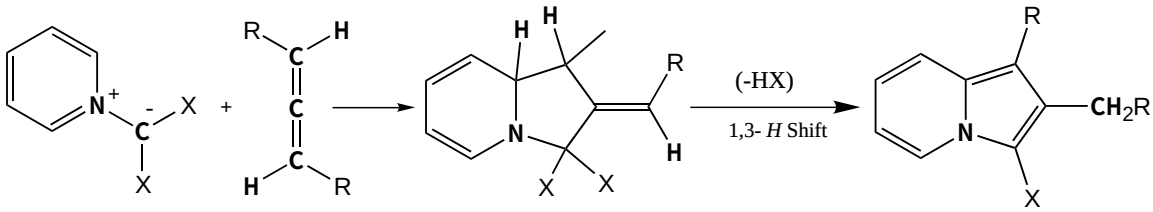
Abstract -Pyridinium dicyanomethylides (**1**) underwent 1, 3-dipolar cycloaddition with 1-phenyl-propa-1,2-diene (**2**) to give a mixture of 3-cyano-2-methyl-1-phenylindolizines (**4**) and 3-cyano-1-methyl-2-phenylindolizines (**5**), accompanied by dehydrocyanation and 1, 3-sigmatropic hydrogen shift.

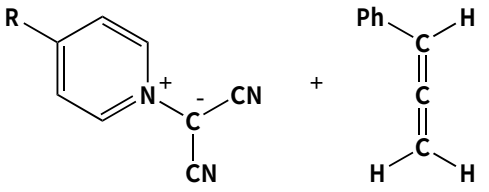
Pyridinium dicyanomethylides (**1**) and pyridinium bis(methoxycarbonyl)methylides are of synthetic utility for the preparation of novel heterocycles such as indolizines,[1]cycl[3.2.2]azines,[2] and 2-pyrones.[3] Due to their intriguing electronic properties and chemical reactivities, these stable cycloimmonium ylides have been the subject of extensive theoretical and experimental studies.[4] One of the most facile methods for construction of indolizine nucleus would be 1,3-dipolar cycloadditions of cycloimmonium ylides with activated alkynes. Indeed a variety of indolizines have been prepared by this method employing stable cycloimmonium ylides.[1,5] However, one of the drawbacks of this method using stable ylides is that the reaction is limited to only activated alkyne (and alkenes). To surmount this difficulty to some extent, we have envisaged to employ allenes as a synthetic equivalent of unactivated alkynes since an initial adduct with an allene is expected to undergo rearragement to an indolizine (Scheme 1).

Dedicated to Professor Sho Ito on the occasion of his 77th birthday.



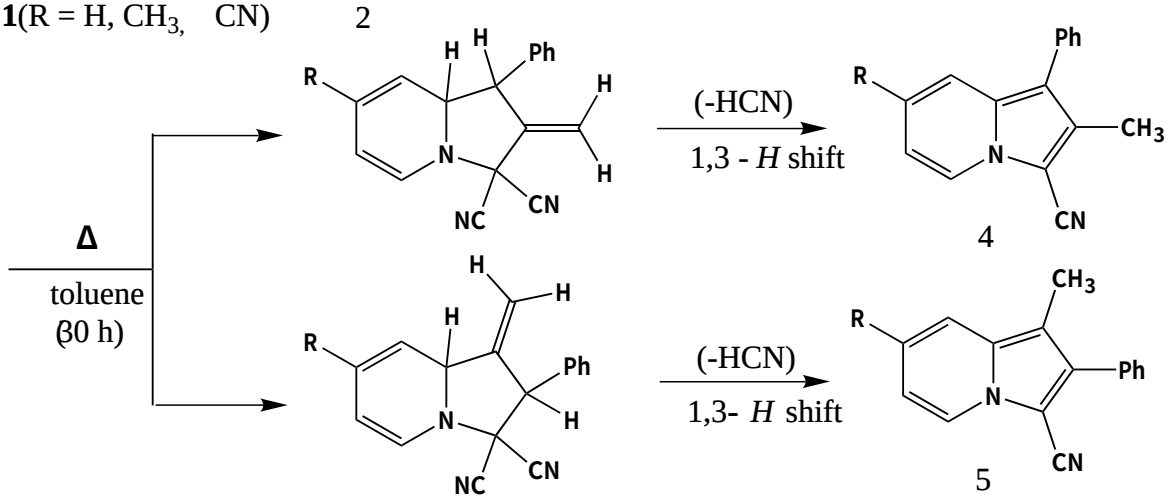
Scheme 1

As a model study, we chose phenylallene (**2**) that could serve as an equivalent of 1-phenylpropyne (methylphenylacetylene) (**3**) because **2** is readily prepared from commercially available propargyl alcohol.[6] First, as a controlled experiment, reaction of 1-phenylpropyne (**3**) with pyridinium dicyanomethylide (**1a)** was performed in refluxing toluene for 30 h, where no reaction was observed. Next, heating of pyridinium dicyanomethylide (**1a**) with **2** in refluxing toluene afforded, to our delight but albeit in low yield, a mixture of 3-cyano-2-methyl-1-phenylindolizine (**4**) and 3-cyano-1-methyl-2-phenylindolizine (**5**) after separation by medium pressure liquid chromatography (Merck: Lobar-size B, LiChroprep Si60; eluent: hexane/ethyl acetate=19/1).[7] Analogous reactions of 4-methyl- (**1b**) and 4-cyanopyridinium dicyanomethylide (**1c**) with **2** gave the corresponding indolizines (**4**) and (**5**) (Scheme 2). The regiochemical assignments were established by X-Ray analyses of the 7-methyl analogs (**4b**) and (**5b**).[8] On the basis of inspection of NMR data, it has turned out that ^{1}H and ^{13}C resonances of 1-CH_3 group (e.g.. **5**) always



1(R = H, CH_3, CN) 2

Products	Yields (%) **4**	**5**
a: R = H	18	11
b: R = CH_3	32	13
c: R = CN	7	13



4

5

Scheme 2

appear at higher field than those of 2-methyl group (e.g.. **4**) probably due to paramagnetic shielding effect of phenyl group, thus enabling us to assign regiochemical structure in this system. The considerably low yields of the products (**4** and **5**) might be filled to some extent because of the ready availability of **2**.

The formation of **4** and **5** is explained by an initial 1, 3-dipolar cycloaddition of **1** to 1, 2-bond of **2** to give the corresponding adducts, followed by dehydrocyanation and 1, 3-H shift. The initial 1, 3-dipolar reactions are apparently controlled by dipole (LUMO)-allene (HOMO) since the values of the energy difference between dicyanomethylide (LUMO)-allene (HOMO) are smaller than those of dicyanomethylide (HOMO)-allene (LUMO).[9]

Further studies on generality of this reaction using a variety of ylides as well as on cycloadditions of ylides with other kind of allenes are in progress.

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7. Selected physical and spectroscopic data for 3-cyano-2-methyl-1-phenylindolizine **(4a)**: mp 102-103 °C (ethanol); MS (m/z) 232(M^+), 217(M^+-CH_3); IR(KBr): 2202 cm^{-1}. ^{1}H-NMR(500 MHz, $CDCl_3$) δ 2.46(s, 3H, CH_3), 6.77(dd, *J* = 7.0 and 7.9 Hz, 1H, H-6), 6.97(dd, *J* = 7.0 and 8.6 Hz, 1H, H-7), 7.3-7.5(m, 5H, Ph-H), 7.51(d, *J* = 8.6 Hz, 1H, H-8), 8.20(d, *J* = 7.9 Hz, 1H, H-5). ^{13}C-NMR(125 MHz, $CDCl_3$) δ 11.0(CH_3), 95.4(C-3), 112.8(CN), 114.1(C-6), 115.6(C-1), 117.7(C-7), 122.3(C-8), 125.1(C-5), 126.8(PhC-4'), 128.7(PhC-2'), 129.5(PhC-3'), 132.3(C-2), 133.3(C-8a), 143.2(PhC-1'). *Anal*. Calcd for $C_{16}H_{12}N_2$: C, 82.73; H, 5.21; N, 12.06. Found: C, 82.77; H, 4.97; N, 11.94. 3-Cyano-1- methyl-2-phenylindolizine (**5a**): mp 167-169°C (ethanol); MS (m/z) 232(M+); IR(KBr): 2194 cm^{-1}. ^{1}H-NMR(500 MHz, $CDCl_3$) δ 2.36(s, 3H, CH_3), 6.80(dd, *J* = 6.7 Hz, 1H, H-6), 7.00(dd, *J* = 6.7 Hz, 1H, H-7), 7.4-7.6(m, 5H, Ph-H), 7.41(d, *J* = 6.7 Hz, 1H, H-8), 8.24(d, *J* = 6.7 Hz, 1H, H-5). ^{13}C-NMR(125 MHz, $CDCl_3$) δ 9.2(CH_3), 93.1(C-3), 109.2(C-1), 112.9(CN), 114.8(C-6), 117.8(C-7), 121.2(C-8), 125.2(C-5), 128.0(PhC-4'), 128.7(PhC-2'), 129.4(PhC-3'), 132.4(C-2), 135.0(C-8a), 136.5(PhC-1'). *Anal*. Calcd for $C_{16}H_{12}N_2$: C, 82.73; H, 5.21; N, 12.06. Found: C, 82.60; H, 5.27; N, 11.97.

8. Crystal data for **4b**: $C_{17}H_{14}N_2$, M=246.31, dimensions 0.12 x 0.28 x 0.48 mm, monoclinic, space group = $P2_1/n$, a = 10.624 (5), b = 7.458 (4), c = 34.304 (4) Å, β = 98.26 (2)°, U = 2689 (1) Å^3, Z = 8, Dc= 1.216 gcm^{-3}, μ=0.76 cm^{-1}, F(000)=1040. Data were collected on a Rigaku AFC5S difractometer using graphite-monochromated Mo-Kα radiation (λ=0.71069). Of 6929 reflections which were collected, 6422 were unique (R_{int}=0.066). The structure was solved by direct methods and all non-hydrogen atoms were refined anisotropically using full-matrix least squares to give R=0.078, and Rw =0.142 for 1995 independent observed reflections with I >1.90s(I) and 343 variables for $2\theta_{max}$= 55.0o. **5b**: $C_{17}H_{14}N_2$, M=246.31, dimensions 0.34 x 0.54 x 0.96 mm, triclinic, space group = P1 , a = 11.296 (5), b = 13.616 (3), c = 9.924 (4) Å, α = 99.85 (5)°, β = 98.26 (2)°, γ = 79.04 (3)°, U = 1355 (1) Å^3, Z = 4, Dc= 1.207 gcm^{-3}, μ=0.72 cm^{-1}, F(000)=520. Data were collected on a Rigaku AFC5S difractometer using graphite-monochromated Mo-Kα radiation (λ=0.71069). Of 6531 reflections which were collected, 6217 were unique (R_{int}=0.023). The structure was solved by direct methods and all non-hydrogen atoms were refined anisotropically using full-matrix least squares to give R=0.095, and Rw=0.149 for 2562 independent observed reflections with I >1.90σ(I) and 343 variables for $2\theta_{max}$= 55.0°.

9. The HOMO and LUMO energy levels of **1** and **2** were obtained using CAChe systems (Version 3.7, CAChe Scientific, Oxford Molecular Group; PM3 method: J. J. P. Stewart, *J. Comp. Chem.*, 1989, **10**, 209.

Ylide **(1)**	HOMO (eV)	Difference HOMO(1)-LUMO(2)	LUMO (eV)	Difference LUMO(1)-HOMO(2)
a: **H**	-8.653	8.517	-1.473	7.493
b: **Me**	-8.544	8.408	-1.456	7.510
c: **CN**	-9.001	8.865	-2.092	6.874
Phenylallene **(2)**	-8.966		-0.136	