An Unusual Reaction of a Pyridinium Ylide with 1,1-Dicyanoethylene Derivatives

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A reaction of pyridinium perfluorophenacylide generated from pyridinium salt **1** with 1,1-dicyanoethylene derivatives **2** produced unusual products **3**, which have an ylide structure with a cyano group at the C2 and a *cis*-acrylonitrile moiety at the o-position of the perfluorophenyl group. A plausible mechanism involving intramolecular aromatic nucleophilic substitution and 1,3-migration of the cyano group is proposed for this reaction.

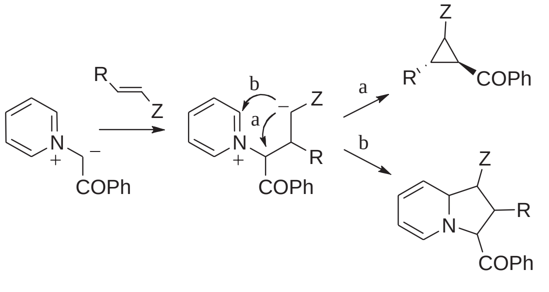
It has been reported that the reaction of a pyridinium ylide[1] with an electron-deficient olefin produces indolidine[2] or cyclopropane[3] derivatives depending on the properties of the olefin and the pyridinium nucleus. When benzylidenemalononitrile is employed as an electrophile, cyclopropane is predominantly produced,[3] whereas, the reaction with acrylonitrile gives indolidine derivatives (Scheme 1).[2]

We recently reported the first example of the enantioselective cyclopropanation of electron-deficient olefins with chiral pyridinium ylide derivatives.[4] In addition, we found that when the phenacyl group was replaced with the perfluorophenacyl group, the ylide became significantly stable and could be isolated.[5]

In this letter, we describe that the reaction of the stable pyridinium perfluorophenacylide **4** generated from **1** with 1,1-dicyanoethylene derivatives **2** provided no expected cyclopropanes, but gave unexpected products **3**.

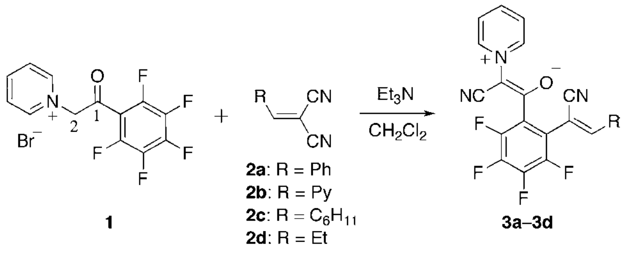
The reaction of benzylidenemalononitrile (**2a**) and pyridinium salt **1** in the presence of Et_3N afforded an unusual product **3a**[6] (Table 1). The structure of **3a** was determined by X-ray crystallographic analysis (Figure 1).[7] It is remarkable that this product has a cyano group at the C2 and an acrylonitrile moiety at the o-position of the aromatic ring with Z configuration. Both substituents could originate from the benzylidenemalononitrile (**2a**). The planar geometry of C1 and C2, and the much shorter 1.391 Å C1–C2 bond length and the much longer 1.239 Å C=O bond length than the corresponding general case[8] strongly suggest the ylide structure of **3**.

The reaction required about 24 h at rt for completion; a shorter reaction time resulted in a significantly lower yield with recovery of the ylide **4**, and no reaction proceeded at −40 °C (Entries 2 and 3). The highest yield was obtained when two equiv of the alkene was used at rt (Entry 5). The nucleophilic addition to **2b** also gave a similar result (Entry 7). For the reactions using alkyl-substituted olefins, **2c** and **2d**, similar products were obtained despite the lower yields (Entries 8 and 9). All products are obtained as a single stereoisomer about the olefinic moiety.



Scheme 1. Two general reaction modes of a pyridinium ylide with electron-deficient olefins.

Table 1. Reaction of alkene **2** with a pyridinium ylide generated from **1**



1

2a: R = Ph
2b: R = Py
2c: R = C_6H_{11}
2d: R = Et

3a–3d

Entry	Alkene (equiv)	Temp/°C	Time/h	Yield of **3**/%[a]
1	**2a**(1)	rt	24	53
2	**2a**(1)	rt	3.5	15
3	**2a**(1)	−40	24	n.r.
4	**2a**(2)	rt	16	70
5	**2a**(2)	rt	24	79
6	**2a**(3)	rt	18	67
7	**2b**(2)	rt	24	68
8	**2c**(2)	rt	24	7[b]
9	**2d**(2)	rt	24	25[b]

[a]Isolated yield. [b]The rest is a complex mixture.

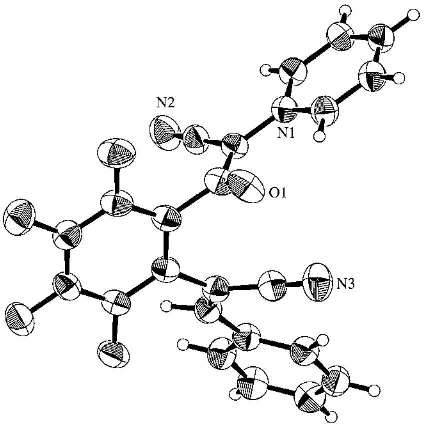


Figure 1. X-ray structure of **3a**.

Scheme 2 outlines a plausible pathway for the formation of product **3**. The nucleophilic addition of the ylide **4** to the alkene **2a** produces the intermediary betaine **A**. While a betaine with a

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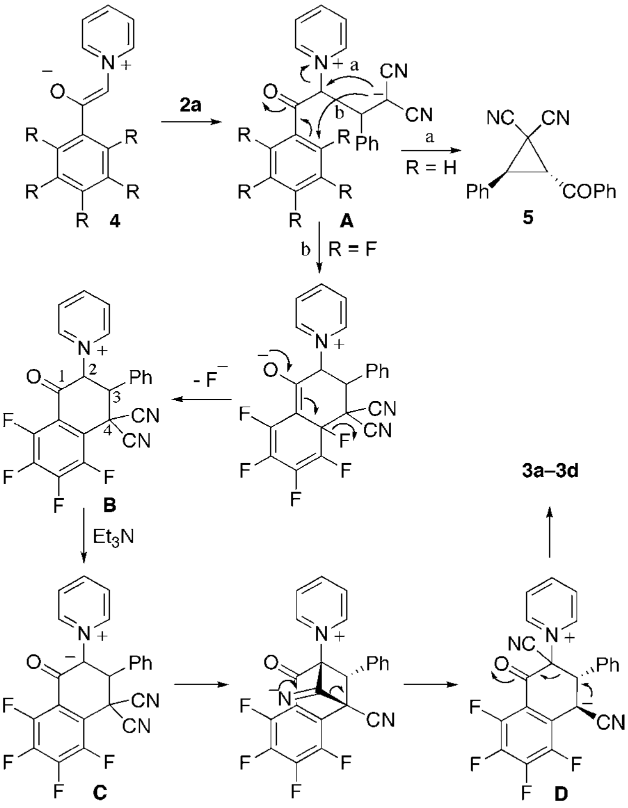
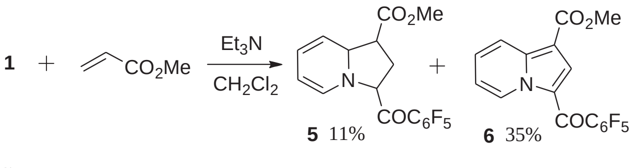


Scheme 2. Plausible reaction pathway for the formation of **3**.

phenyl group (R = H) preferentially attacks the C2 to produce cyclopropane **5** as reported in the literature,[3] betaine **A** possessing a perfluorophenyl group (R = F) undergoes an intramolecular aromatic nucleophilic substitution to give the intermediary bicyclic product **B**. The deprotonation of the C2-proton would produce the second ylide **C**. The anion-mediated cyano group migration through a four-membered intermediate affords betaine **D**. The Grob-type fragmentation[9] of **D** results in the product ylide **3a**, the Z configuration of which would be a result of the fragmentation controlled by the overlap between the σ^* orbital of the C2–C3 bond and the sp^3 orbital of the carbanion. The driving force of this rearrangement would be the formation of ylide **3a** stabilized with a cyano group at C2.[10] A similar 1,3-cyano migration has been reported for the radical-mediated reactions via the four-membered iminyl radical intermediate.[11]

When methyl acrylate was used as an electrophile, the 1,3-dipolar addition proceeded to give the tetrahydroindolidine and indolidine derivatives in 11 and 35% yields, respectively (Scheme 3). The structure of the indolidine **6** was confirmed by X-ray structural analysis.[12] It should be noted that no product related to **3** was obtained in this reaction.

In summary, we found a new type of reaction with pyridinium ylide. The reaction of pyridinium perfluorophenacylide with 1,1-dicyanoethylene derivatives gave unusual adducts **3** via intramolecular aromatic nucleophilic substitution and 1,3-migration of a cyano group.



Scheme 3. Reaction of **1** with methyl acrylate in the presence of Et_3N.

This work was partly supported by a Grant-in-Aid for Scientific Research (B) (no. 17350046) from the Japan Society for the Promotion of Science.

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6 **3a**: yellow crystal; mp 175.8–176.5 °C; IR (KBr) 3094, 2213, 2187, 1572, 1467, 1389 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.29 (d, $J = 5.86$ Hz, 2H), 8.03 (t, $J = 7.81$ Hz, 1H), 7.87 (m, 2H), 7.79 (t, $J = 7.32$ Hz, 2H), 7.45 (m, 4H); MS m/z 421 (M$^+$, 0.4%), 369 (89), 338 (100), 242 (24), 195 (41), 94 (32), 57 (26). ^{13}C NMR (100 MHz, $CDCl_3$) δ 92.8, 99.4, 116.4, 117.8, 119.2, 124.4, 126.7, 128.7, 129.3, 131.1, 132.6, 139.0, 139.2, 140.0, 142.4, 143.3, 145.8. 150.9, 168.9.

7 Crystallographic data for **3a**: $C_{23}H_{11}F_4N_3O$, $M_r = 421.35$, monoclinic, $P2_1/a$, $a = 14.3211(3)$, $b = 7.08750(10)$, $c = 18.2058(4)$ Å, $\beta = 94.6735(10)°$, $V = 1841.76(6)$ Å^3, $T = 298$ K, $Z = 4$, $D_{calcd} = 1.519$ g cm^{-1}, A total of 27699 reflections were collected and 3356 are unique ($R_{int} = 0.057$). R_1 and wR_2 are 0.0630 [$I > 2\sigma(I)$] and 0.2225 (all data), respectively. CCDC 682165.

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12 Crystallographic data for **6**: $C_{17}H_8F_5NO_3$, $M_r = 369.25$, monoclinic, $P2_1/c$, $a = 7.0294(5)$, $b = 23.8012(17)$, $c = 18.4727(13)$ Å, $\beta = 94.405(3)°$, $V = 3081.5(4)$ Å^3, $T = 298$ K, $Z = 8$, $D_{calcd} = 1.592$ g cm^{-1}, A total of 45501 reflections were collected and 5399 are unique ($R_{int} = 0.107$). R_1 and wR_2 are 0.0736 [$I > 2\sigma(I)$] and 0.2311 (all data), respectively. CCDC 682166.