Catalytic and thermal hydrocarbonation of methyleneaziridines

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Dedicated to Professor Keiichiro Fukumoto on the occasion of his 70th birthday

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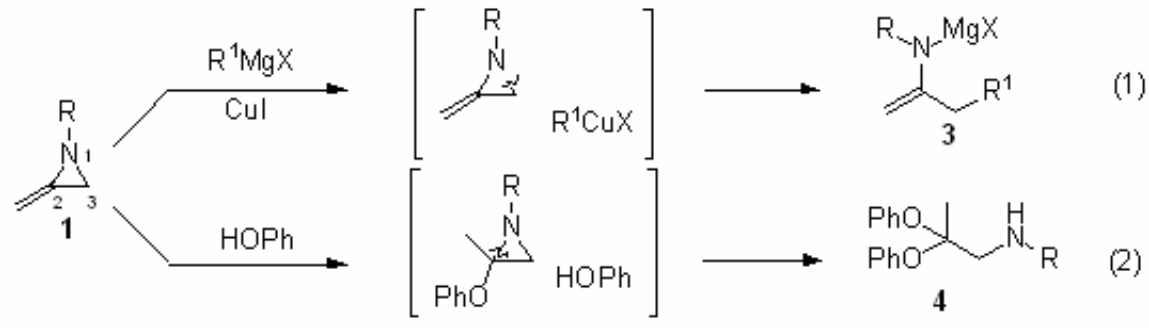
Abstract

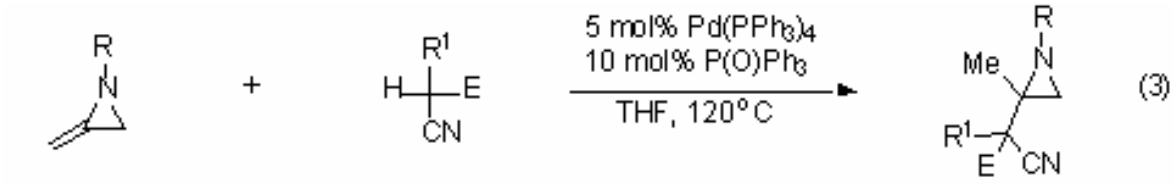
Reaction of the methyleneaziridine **1** with carbon pronucleophiles (**2**, H-CR_3) proceeds smoothly in the presence of a palladium catalyst affording the corresponding hydrocarbonation products **5** in good to high yields. In the absence of palladium catalysts, the reaction of **1a** with **2a** at 120 °C afforded the ring opened product **9** in good yield.

Keywords: Methyleneaziridine, pronucleophile, palladium, hydrocarbonation

Introduction

2-Methyleneaziridines are small-ring compounds containing a nitrogen atom, which have high ring strain. It is known that the ring opening of methyleneaziridines with Grignard reagents (or organolithium compounds),[1a-d] acid chlorides,[1e-f] and HCl[1g] occurs through N-C3 bond cleavage (eq 1), while ring opening with HOPh proceeds through N-C2 bond cleavage[1h] (eq 2). Accordingly, the normal reaction of 2-methyleneaziridines with nucleophiles produces ring-opened derivatives. Recently we reported that the reaction of the methyleneaziridines **1** with carbon pronucleophiles **2** proceeds smoothly in the presence of a palladium catalyst to give, in good- to high yields, the ring products **5** (eq 3).[2] Formally, this is a hydrocarbonation reaction of the double bond of **1** with carbon pronucleophiles. In this paper, we report the detailed study of the palladium-catalyzed hydrocarbonation of methyleneaziridines together with an attempt at asymmetric hydrocarbonation using chiral phosphine ligands.





1a ; R = Bn
1b ; R = Hex
1c ; R = Bu
1d ; R = $CH_2CH_2CH_2OMe$
1e ; R = $CH_2CH(OMe)_2$
1f ; R = CH_2-*p*-C_6H_4Cl

2a ; R^1 = Me, E = CN
2b ; R^1 = Me, E = CO_2Et
2c ; R^1 = *i*-Pr, E = CN
2d ; R^1 = Bn, E = CN

5a ; R = Bn, R^1 = Me, E = CN
5b ; R = Hex, R^1 = Me, E = CN
5c ; R = Bu, R^1 = Me, E = CN
5d ; R = $CH_2CH_2CH_2OMe$, R^1 = Me, E = CN
5e ; R = $CH_2CH(OMe)_2$, R^1 = Me, E = CN
5f ; R = CH_2-*p*-C_6H_4Cl, R^1 = Me, E = CN
5g ; R = Bn, R^1 = Me, E = CO_2Et
5h ; R = Bn, R^1 = *i*-Pr, E = CN
5i ; R = Bn, R^1 = Bn, E = CN

Results and Discussion

The results are summarized in Table 1. In the presence of catalytic amounts of $Pd(PPh_3)_4$ (5 mol %) and triphenylphosphine oxide (10 mol %), the reaction of 1-benzyl-2-methyleneaziridine 1a (0.75 mmol) with methylmalononitrile **2a** (0.5 mmol) in THF at 120 °C for 4 h gave **5a** in 87% yield (entry 1). The catalytic system $Pd(dba)_2/PPh_3$ was less effective, and $Pd_2(dba)_3.CHCl_3$ or $Pd(PPh_3)_2Cl_2$ did not promote the reaction. The reaction using $Pd(OAc)_2/PPh_3$ as a catalyst gave **5a** in a moderate yield. The combination of $Pd(PPh_3)_4$ and monodentate phosphine ligands such as PPh_3, $P(O)Bu_3$, and P(*o*-tolyl)$_3$, gave **5a** in moderate to good yields. In the presence of only $Pd(PPh_3)_4$, without additional phosphine ligands, **5a** was obtained in good yield (80%). However, even in the presence of $Pd(PPh_3)_4$, if bidentate ligands such as bis-(diphenylphosphino)methane (dppm), 1,2-bis-(diphenylphosphino)ethane (dppe), 1,3-bis-(diphenylphosphino)propane (dppp) were used as a ligand, only small amounts of **5a** were obtained. The best results were obtained with the catalytic system, $Pd(PPh_3)_4$ and $P(O)Ph_3$. The reactions of 1-hexyl-2-methyleneaziridine **1b** with **2a**, and 1-butyl-2-methyleneaziridine **1c** with **2a** afforded **5b** and **5c** in yields of 71 and

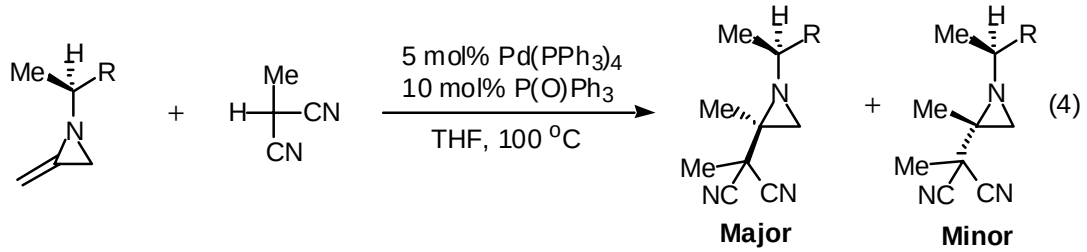
63%, respectively (entries 2, 3). The reactions of **1d** with **2a**, and **1e** with **2a** proceeded smoothly and the corresponding hydrocarbonation products **5d** and 5e were produced in 65 and 79% yield, respectively (entries 4, 5). The reaction of 1-*p*-chlorobenzyl-2-methyleneaziridine, **1f**, which has an electron withdrawing group on the nitrogen atom, with **2a** required longer reaction times and gave **5f** in a lower yield (entry 6). The reaction of **1a** with 2-cyanopropionate **2b** afforded **5g** in 63% yield (entry 7). Other activated methines such as *i*-propylmalononitrile **2c** and benzylmalononitrile **2d**, upon treatment with **1a**, gave products **5h** and **5i** in 71 and 61% yield, respectively (entries 8, 9).

Table 1. Palladium catalyzed hydrocarbonation of **1** with **2**[a]

Entry	**1**	**2**	Time(h)	**3**	Yield(%)[b]
1	**1a**	**2a**	4	**5a**	87
2	**1b**	**2a**	5	**5b**	71
3	**1c**	**2a**	5	**5c**	63
4	**1d**	**2a**	4	**5d**	65
5	**1e**	**2a**	4	**5e**	79
6	**1f**	**2a**	10	**5f**	51
7	**1a**	**2b**	15	**5g**	63(1:1)[c]
8	**1a**	**2c**	5	**5h**	71
9	**1a**	**2d**	5	**5i**	61

[a]The reaction of **1** (0.75 mmol) with **2** (0.5 mmol) was carried out in the presence of 5 mol% of $Pd(PPh_3)$ and 10 mol% of triphenyl phosphine oxide in THF at 120°C. [b]isolated yield based on **2**. [c]the diastereomeric ratio of **5g**.

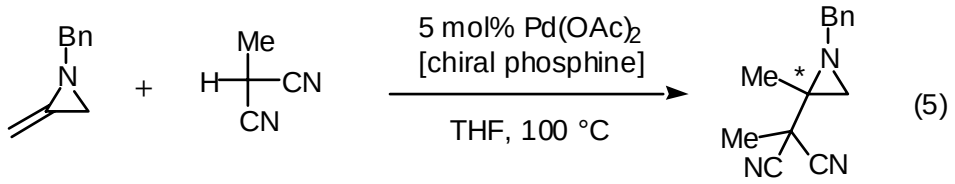
Significantly high de's (82%) were obtained in the reaction of (S)-*N*-(1-naphthylethyl)-2-methylene-aziridine **1h** with **2a**, although (S)-*N*-(1-phenylethyl)-2-methyleneaziridine **1g** produced only a moderate de (54%) (eq 4). The absolute stereochemistry of **5k** was determined unambiguously by X-ray analysis and NOE experiments.



1g ; R = Ph **2a** **5j** ; R = Ph, 83% (54% de)
1h ; R = naphthyl **5k** ; R = naphthyl, 68% (82% de)

Next, we examined the asymmetric hydrocarbonation of methyleneaziridine **1a** with **2a** using several chiral phosphine ligands (eq 5). The results are summarized in Table 2. In the presence of

5 mol.% of $Pd(OAc)_2$ and 5 mol% of 1-[1-(acetyloxy)ethyl]-1',2-bis(diphenylphosphino)ferrocene (BPPFOAc), the reaction of **1a** with **2a** afforded the hydrocarbonation product **5a** in 56% yield with the enantiomeric excess of 22% (entry 1). The reaction of **1a** with **2a** using 1-[1-(dimethylamino)ethyl]-2-(diphenylphosphino)ferrocene (BPPFA) instead of BPPFOAc gave **5a** with the same level of *ee*. The reaction of **1a** with **2a** using other ligands, such as 1,1'-bis(diphenylphosphino)-2-(1-hydroxyethyl)ferrocene (BPPFOH) and [5-methyl-2-(1-methylethyl)cyclohexyl]diphenylphosphine (NMDPP), gave the product **5a** in ~0% *ee* (entries 3 and 4).



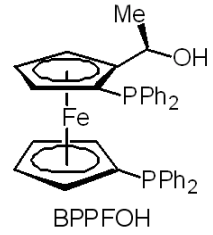
1a **2a** **5a**

A plausible mechanism for the hydrocarbonation is illustrated in Scheme 1. The oxidative addition of palladium(0) into a C-H bond of the pronucleophile **2a** would give the hydridopalladium complex **6**.[3] The hydropalladation of the methyleneaziridines **1** with **6** would be facilitated by a chelation effect of the nitrogen atom **7**, giving the H-Pd addition product **8**. Reductive elimination of palladium(0) could then give the hydrocarbonation products **5**.[4]

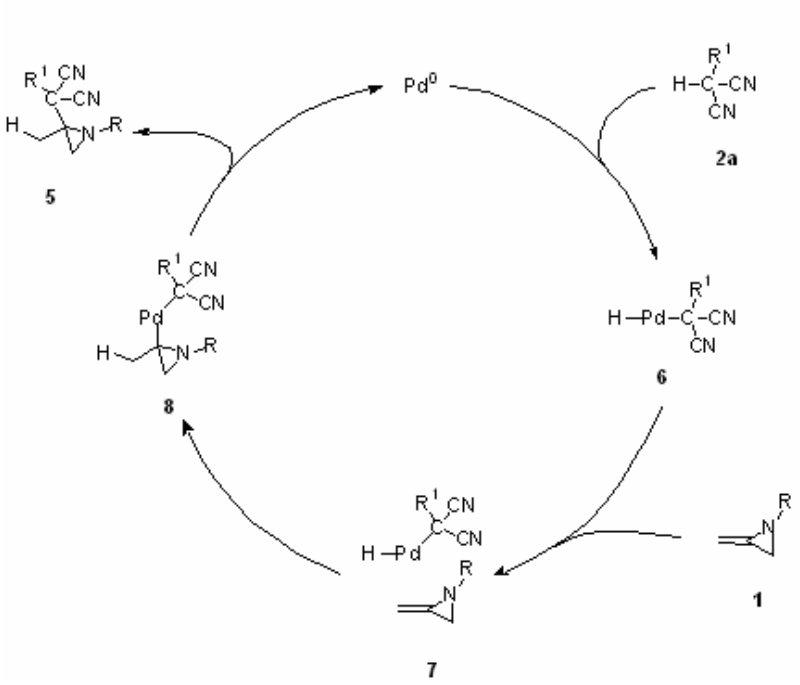
Table 2. Asymmetric hydrocarbonation of **1a** with **2a**[a]

Entry	Ligand	Yield/ %[b]	ee/ %[c]
1	BPPFOH	56	22
2	BPPFA	55	23
3	BPPFOH	66	0
4	NMDPP[d]	64	0

[a]The reaction of **1a** (0.75 mmol) with **2a** (0.5 mmol) was carried out in the presence of 5 mol% of $Pd(OAc)_2$ and 10 mol% of chiral phosphine in THF at 100°C. [b]NMR yield based on **2** using p-xylene as an internal standard. [c]Determined by a chiral HPLC analysis (column: Daicel, chiralcel OD-R). [d]Ten mol% of NMDPP was used.

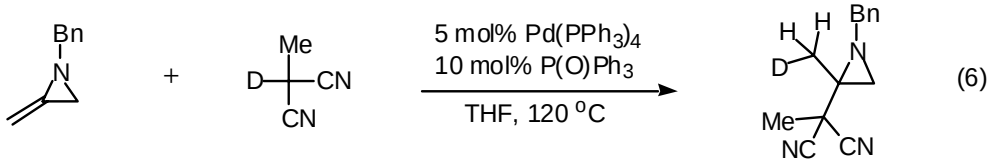


BPPFOH



Scheme 1

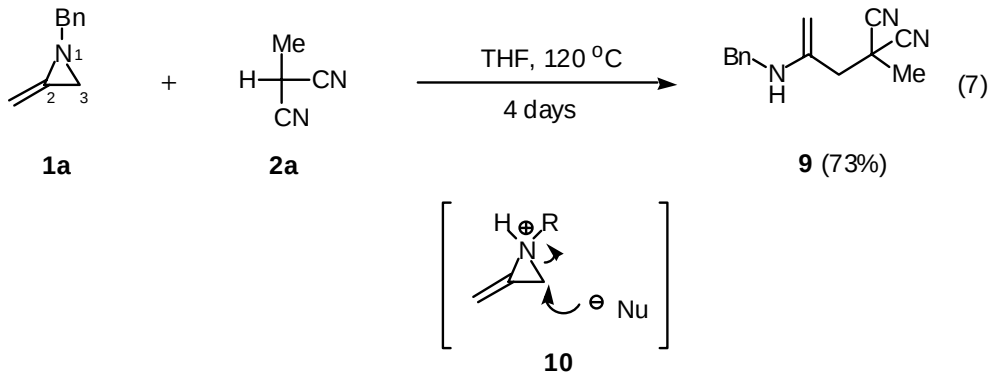
The reaction with deuterated methylmalononitrile (**2a**-*d*, 90% D) substantiated the proposed mechanism. The reaction of **1a** with **2a**-*d* under the same reaction conditions as above gave **5a**-*d* in 82% yield, in which the deuterium content was 76% (eq 6).



1a **2a**-*d* 90% D **5a**-*d* 76% D (6)

Interestingly, the thermal reaction of **1a** with **2a** without any palladium catalyst in THF at 120 °C for 4 days gave the vinylic amine **9** in 73% yield (eq 7). These ring opening reactions of the methyleneaziridine most probably occurred by the nucleophilic addition of the carbanion derived from **2a** to the C-3 position of the protonated methyleneaziridine, **10**.[1] It is now clear that

the palladium catalyzed and thermal reactions of **2a** with **1a** take totally different reaction courses; the Lewis acidic Pd(II)-nitrogen interaction (**7**) leads to **5a** while the Brønsted acid H^+-nitrogen interaction (**10**) gives **9**. The addition of carbon pronucleophiles to *activated alkenes* catalyzed by transition metals, that is the Michael addition, is known.[5] Recently, we and other groups reported the palladium catalyzed addition of carbon pronucleophiles **2** to *unactivated olefins* such as allenes,[6] enynes,[7] methylenecyclopropanes,[8] and 1,3-dienes.[9] The driving force for these reactions originates in the formation of stable π-allylpalladium complexes. The present hydrocarbonation reaction does not proceed through the formation of a π-allylpalladium intermediate, but most probably proceeds via a chelation effect of the nitrogen atom of the aziridine moiety.



Conclusions

We have developed the direct hydrocarbonation of methyleneaziridines[9] using carbon pronucleophiles in the presence of a palladium catalyst. The palladium-catalyzed reaction provides geminally disubstituted functionalized aziridines, while traditional reactions give ring-opening products upon treatment with nucleophiles.

Experimental Section

General Procedures. Spectroscopic measurements were carried out with the following instruments: JEOL JNM LA-300 and JEOL α-500 (^{1}H- and ^{13}C NMR), SHIMADZU FTIR-8200A (FT-IR), HITACHI M-2500s (HRMS). All methyleneaziridines were prepared following the reported procedure.[10] Daicel Chiralcel OD-R was used to analyze the enantiomeric excess of **5a**.

General procedure for the addition of the active methyne 1 to methyleneaziridines 4

To a solution of $Pd(PPh_3)_4$ (28.9 mg, 0.025 mmol), triphenylphosphine oxide (13.9 mg, 0.05 mmol) and active methyne **1** (0.5 mmol) in THF (1 mL) was added methyleneaziridine **4** (0.75 mmol) under Ar atmosphere in pressure vial. After heating at 120 °C for 4-15 hours, the reaction mixture was filtered through a short Florisil column using ethyl acetate as an eluent. Separation by passing through a Florisil column using *n*-hexane-ethyl acetate as eluent.

2-(1-Benzyl-2-methylaziridin-2-yl)-2-methylmalononitrile (5a). Pale yellow oil: IR (neat) 3062, 3031, 2997, 2935, 2858, 2250, 1496, 1454, 1392, 1342, 1245, 1182, 1159, 1126, 1076, 1028, 736, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.48 (s, 1H), 1.53 (s, 3H), 1.64 (s, 3H), 2.31 (s, 1H), 3.70 (d, *J* = 2.5 Hz, 2H), 7.25-7.39 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ11.64, 20.79, 37.14, 39.64, 41.87, 56.49, 115.03, 115.22, 127.34, 127.91, 128.44, 138.50. HRMS (EI) Calcd for $C_{14}H_{15}N_3$; *m/z* 225.1266: found, 225.1271.

2-(1-Hexyl-2-methylaziridin-2-yl)-2-methylmalononitrile (5b). Pale yellow oil: IR (neat) 2931, 2858, 2250, 1456, 1392, 1377, 1342, 1182, 1164, 1126 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, *J* = 6.9 Hz, 3H), 1.29-1.57 (m, 12H), 1.72 (s, 3H), 2.19 (s, 1H), 2.47 (td, *J* = 6.6 and 2.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) 11.22, 13.98, 20.64, 22.54, 26.83, 30.25, 31.61, 36.97, 39.68, 41.37, 52.91, 115.30, 115.34. HRMS (EI) Calcd for $C_{13}H_{21}N_3$; *m/z* 219.1735: found, 219.1727.

2-(1-Butyl-2-methylaziridin-2-yl)-2-methylmalononitrile (5c). Pale yellow oil: IR (neat) 2958, 2935, 2864, 2252, 1456, 1392, 1377, 1340, 1244, 1184, 1168, 1145, 1126, 1070, 1045 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, *J* = 6.9 Hz, 3H), 1.29 (s, 1H), 1.32-1.62 (m, 7H), 1.72 (s, 3H), 2.19 (s, 1H), 2.48 (t, *J* = 6.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.13, 13.86, 20.27, 20.60, 32.33, 36.92, 39.68, 41.31, 52. 52, 115.26, 115.30. HRMS (EI) Calcd for $C_{11}H_{17}N_3$; *m/z* 191.1422: found, 191.1422.

2-[1-(3-Methoxypropyl)-2-methylaziridin-2-yl]-2-methylmalononitrile (5d). Pale yellow oil: IR (neat) 2931, 2873, 2831, 2249, 1452, 1392, 1342, 1245, 1224, 1186, 1164, 1043 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.33 (s, 1H), 1.50 (s, 3H), 1.73 (s, 3H), 1.78-1.89 (m, 2H), 2.22 (s, 1H), 2.47-2.66 (m, 2H), 3.34 (s, 3H), 3.51 (t, *J* = 6.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.23, 20.68, 30.34, 37.13, 39.74, 41.41, 49.55, 58.59, 70.11, 115.27, 115.29. HRMS (EI) Calcd for $C_{11}H_{17}N_3O$, *m/z* 207.1372: found, 207.1376.

2-[1-(2,2-Dimethoxyethyl)-2-methylaziridin-2-yl]-2-methylmalononitrile (5e). Pale yellow oil: IR (neat) 2993, 2945, 2912, 2835, 1454, 1888, 1346, 1313, 1247, 1188, 1166, 1134, 1076, 968, 854 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.41 (s, 1H), 1.48 (s, 3H), 1.74 (s, 3H), 2.25 (s, 1H), 2.57-2.72 (m, 2H), 3.43 (d, *J* = 2.4 Hz, 6H), 4.54 (t, *J* = 5.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.86, 20.64, 36.81, 39.59, 41.21, 54.14, 54.54, 54.73, 104.44, 115.06, 115.16. HRMS (EI) Calcd for $C_{11}H_{17}N_3O_2$, *m/z* 223.1321: found, 223.1327.

2-[1-(4-Chloro-benzyl)-2-methylaziridin-2-yl]-2-methylmalononitrile (5f). Pale yellow oil: IR (neat) 2977, 2937, 2860, 2250, 1596, 1492, 1454, 1409, 1340, 1245, 1182, 1161, 1087, 1014,

842, 806, 773 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.48 (s, 1H), 1.54 (s, 3H), 1.67 (s, 3H), 2.32 (s, 1H), 3.67 (q, *J* = 13.7 Hz, 2H), 7.32 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.60, 20.83, 37.12, 39.65, 41.92, 55.75, 114.93, 115.08, 128.58, 129.17, 133.04, 136.98. HRMS (EI) Calcd for $C_{14}H_{14}N_3Cl$, *m/z* 259.0876: found, 259.0873.

(1-Benzyl-2-methylaziridin-2-yl)-cyanomethylacetic acid ethyl ester (5g). Diastereoisomer A. Pale yellow oil: IR (neat) 2985, 2240, 1741, 1452, 1257, 1174, 1153, 1114, 1064, 1016, 736, 698cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.29 (t, *J* = 7.1 Hz, 3H), 1.34 (s, 1H), 1.39 (s, 3H), 1.49 (s, 3H), 2.30 (s, 1H), 3.53-3.82 (m, 2H), 4.18-4.27 (m, 2H), 7.23-7.41 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.34, 13.96, 19.10, 37.28, 41.94, 50.69, 56.41, 62.56, 119.01, 126.99, 127.86, 128.27, 139.36, 167.55; HRMS (EI) Calcd for $C_{16}H_{20}N_2O_2$: *m/z* 272.1525: found, 272.1528.

Diastereoisomer B. Pale yellow oil: IR (neat) 2932, 2241, 1741, 1452, 1259, 1153, 1114, 1066, 1018, 734, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.29 (t, *J* = 7.1 Hz, 3H), 1.34 (s, 1H), 1.43 (s, 3H), 1.51 (s, 3H), 2.25 (s, 1H), 3.56 (d, *J* = 13.9 Hz, 1H), 3.80 (d, *J* = 13.9 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 7.24-7.41 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.94, 13.90, 19.03, 36.87, 41.78, 50.42, 56.45, 62.62, 119.16, 126.99, 127.88, 128.27, 139.33, 168.20; HRMS (EI) Calcd for $C_{16}H_{20}N_2O_2$: *m/z* 272.1525: found, 272.1529.

2-(1-Benzyl-2-methylaziridin-2-yl)-2-isopropyl-malononitrile (5h). Pale yellow oil: IR (neat) 3087-2858, 2249, 1497, 1454, 1394, 1340, 1242, 1147, 734, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.17-1.23 (m, 6H), 1.45 (s, 1H), 1.48 (s, 3H), 2.29-2.38 (m, 2H), 3.45 (d, *J* = 13.8 Hz, 1H), 3.95 (d, *J* = 14.1 Hz, 1H), 7.24-7.42 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ11.12, 17.95, 18.77, 33.44, 37.81, 40.32, 53.01, 56.01, 113.45, 113.99, 127.17, 127.85, 128.31, 138.30. HRMS (EI) Calcd for $C_{16}H_{19}N_3$, *m/z* 253.1579: found, 253.1581.

2-Benzyl-2-(1-benzyl-2-methyl-aziridin-2-yl)-malononitrile (5i). White solid: IR (KBr) 3085-2889, 2253, 1604, 1496, 1456, 1398, 1359, 1336, 1249, 1228, 1151, 1028, 740, 704 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.50 (s, 1H), 1.62 (s, 3H), 2.26 (s, 1H), 2.92 (d, *J* = 13.5 Hz, 1H), 3.12 (d, *J* = 13.5 Hz, 1H), 3.73 (s, 2H), 7.23-7.43 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ12.20, 37.73, 39.36, 41.94, 48.11, 56.45, 113.83, 114.15, 127.41, 128.00, 128.45, 128.50, 128.77, 130.08, 132.41, 138.51. HRMS (EI) Calcd for $C_{20}H_{19}N_3$, *m/z* 301.1579: found, 301.1583.

2-Methyl-2-[2-methyl-1-(1-Phenyl-ethyl)-aziridine-2-yl]-malononitrile(5j).

Major diastereoisomer. Pale yellow oil: IR (neat) 2974, 2250, 1492, 1450, 1394, 1373, 1340, 1168, 1128, 1110, 1089, 1028, 1158, 702; ^1H NMR (500 MHz, $CDCl_3$) δ 1.28 (s, 1H), 1.41 (d, *J* = 6.6 Hz, 3H), 1.63 (s, 3H), 1.79(s, 3H), 2.10 (s, 1H), 3.19 (q, *J* = 6.5 Hz, 1H), 7.24-7.41 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.38, 20.74, 25.13, 35.80, 39.96, 42.95, 61.42, 115.30, 115.31, 126.75, 127.28, 128.43, 144.04; HRMS (EI) Calcd for $C_{15}H_{17}N_3$: *m/z* 239.1422; found 239.1420.

Minor diastereoisomer. Pale yellow oil: IR (neat) 2974, 2250, 1492, 1452, 1392, 1377, 1340, 1163, 1128, 1099, 1068, 1028, 758, 702; ^1H NMR (300 MHz, $CDCl_3$) δ 1.34 (s, 3H), 1.41 (d, *J* = 6.4 Hz, 3H), 1.46 (s, 1H), 1.48 (s, 3H), 2.29 (s, 1H), 3.18 (q, *J* = 6.4 Hz, 1H), 7.21-7.38 (m, 5H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 11.67, 21.09, 24.07, 35.89, 39.91, 42.40, 62.30, 114.89, 115.30, 126.80, 127.54, 128.57, 144.47; HRMS (EI) Calcd for $C_{15}H_{17}N_3$: *m/z* 239.1422; found 239.1419.

The stereochemistry of **5j** was determined by NOE experiment as shown in Figure 1.

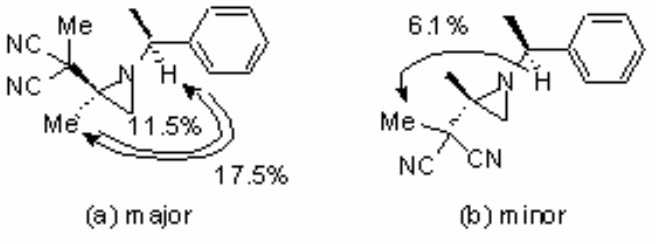


Figure 1. NOE experimet of **5j**.

2-Methyl-2-[2-methyl-1-(1-naphthalen-1-yl-ethyl)-aziridine-2-yl]-malononitrile (5k)

Major diastereoisomer. White solid: IR (KBr) 2977, 2931, 2247, 1596, 1473, 1452, 1340, 1230, 118, 1110, 779; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (s, 1H), 1.59 (d, *J* = 6.4 Hz, 3H), 1.75 (s, 3H), 1.87 (s, 3H), 2.22 (s, 1H), 3.97 (s, 1H), 7.46-7.54 (m, 4H), 7.78(d, *J* = 8.2 Hz, 1H), 7.87-8.08 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) 11.37, 20.97, 24.47, 36.16, 40.29, 43.59, 57.54, 115.37, 115.38, 122.82, 124.32, 125.40, 125.89, 125.93, 127.69, 129.12, 130.58, 133.87, 139.66; HRMS (EI) Calcd for $C_{19}H_{19}N_3$: *m/z* 289.1579; found 289.1580.

Minor diastereoisomer. Pale yellow oil: IR (neat) 2972, 2952, 2247, 1596, 1450, 1394, 1340, 1247, 1178, 1155, 802, 779; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (s, 3H), 1.56-1.60 (m, 7H), 2.43 (s, 1H), 3.92 (s, 1H), 7.46-7.54 (m, 4H), 7.77-7.90 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 11.71, 21.34, 23.43, 36.35, 40.17, 42.80, 57.69, 115.22, 115.30, 122.91, 124.86, 125.42, 125.57, 125.92, 127.84, 129.07, 129.97, 133.92, 140.08; HRMS (EI) Calcd for $C_{19}H_{19}N_3$: m/z 289.1579; found 289.1582.

The stereochemistry of **5k** was determined by NOE experiment as shown in Figure 2.

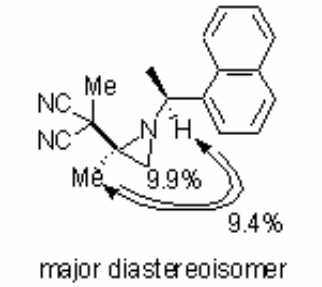


Figure 2. NOE experiment of **5k**.

We could not measure an NOE experiment for the minor diastereoisomer of **5k** because of overlap of the peaks. The ORTEP drawing of the major diastereomer of **5k** is shown in Figure 3.

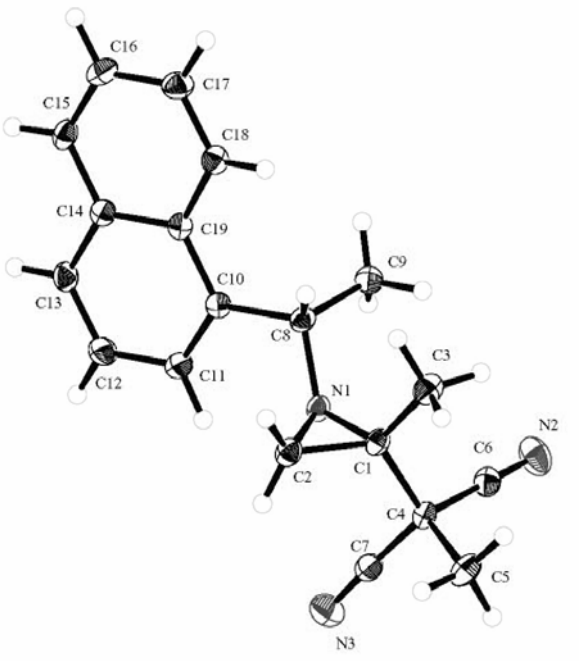


Figure 3. ORTEP drawing of the major isomer of **5k**.

2-[1-(Benzylamino-methyl)-vinyl]-2-methyl-malononitrile (9). Pale yellow oil: IR (neat) 3307, 2931, 2247, 1651, 1496, 1454, 1404, 1344, 1201, 1114, 981, 808, 727, 696; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.67 (s, 1H), 2.71 (td, *J* = 1.5 and 15.5 Hz, 1H), 3.21 (td, *J* = 1.5 and 15.5 Hz, 1H), 4.14 (ddd, *J* = 2.0, 3.5 and 39.0 Hz, 2H), 4.76 (d, *J* = 4.2 Hz, 2H), 7.21-7.33 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ24.64, 39.16, 39.46, 44.89, 84.59, 120.57, 126.16, 126.75, 127.42, 128.67, 128.82, 142.64; HRMS (EI) Calcd for $C_{14}H_{15}N_3$: *m/z* 225.1266. found: 225.1261.

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