A NOVEL 1,6-CYCLIZATION OF IMIDAZOLIUM *N*-ALLYLIDES (2)[1]: FORMATION OF THE MESOMERIC BETAINE, 7-IMINOIMIDAZO-[1,2-*a*]PYRIDINIUMIDE

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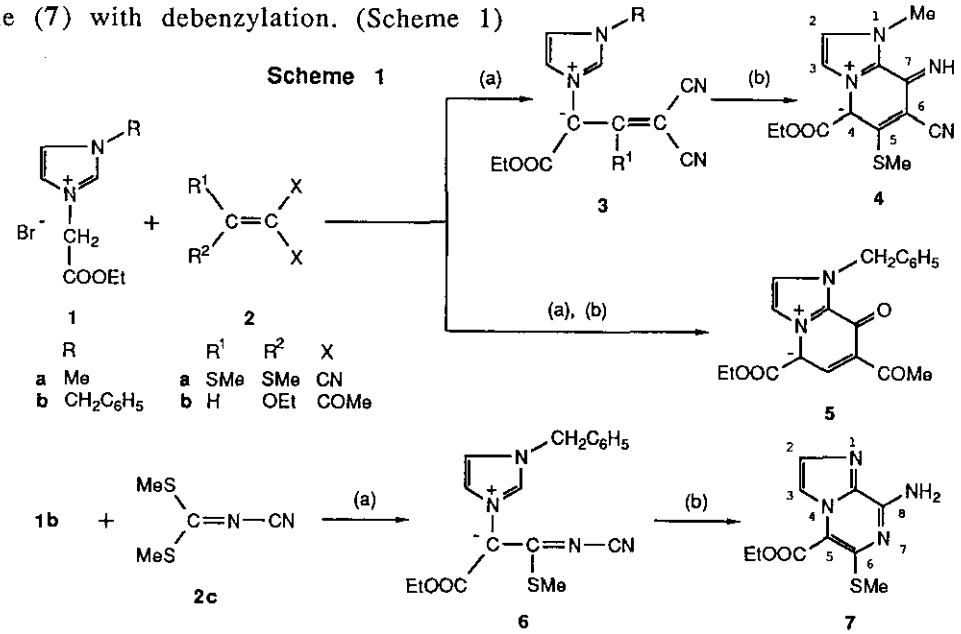
Abstract - Treatment of imidazolium *N*-allylide (**3**) in refluxing 1,2,4-trimethylbenzene resulted in 1,6-cyclization to give the mesomeric betaine, 7-iminoimidazo[1,2-*a*]pyridiniumide (**4**). On the other hand, heating of 1-cyanoimidoylmethylimidazolium *N*-ylide (**6**) in refluxing 1,2,4-trimethylbenzene underwent 1,6-cyclization and debenzylation to give 8-aminoimidazo[1,2-*a*]pyrazine (**7**). Furthermore, treatment of the imidazolium salt (**1a**) and ethyl ethoxymethylenenitroacetate (**2d**) with K_2CO_3 in DMSO afforded the mesomeric betaine, imidazo[1,2-*a*]pyridiniumide (**12**), whereas the reaction of **1a** and nitroketene dithioacetal (**2e**) with K_2CO_3 in DMSO resulted in 1,5-dipolar cyclization to produce pyrrolo[1,2-*a*]imidazole (**13**) and pyrrolo[1,2-*a*]pyrazine (**14**).

Pyridinium and imidazolium *N*-allylides are well known to undergo thermal 1,5-dipolar cyclization and aromatization giving the corresponding indolizines and pyrroloimidazoles.[2-10] With regard to imidazolium *N*-allylides, a novel 1,6-cyclization has been found in the thermolysis of imidazolium *N*-allylides in our previous

paper.[1] Thus, the thermolysis of imidazolium *N*-allylides with the ester group at the 3-position of the allyl group resulted in 1,6-cyclization to give the mesomeric betaines, 7-oxoimidazo[1,2-*a*]pyridiniumides. As a part of our continuing work on the thermolysis of imidazolium *N*-allylides, we here report the thermolysis of imidazolium *N*-allylide (**3**) with the cyano group instead of the ester group at the 3-position of the allyl group to produce the mesomeric betaine, 7-iminoimidazo[1,2-*a*]pyridiniumide (**4**) involving 1,6-cyclization.

The starting imidazolium *N*-allylide (**3**) and 1-cyanoimidoylmethylimidazolium *N*-ylide (**6**) used in the present work were prepared by the reaction of 1-ethoxycarbonylmethylimidazolium bromides (**1a, b**) with ketene dithioacetals (**2a, c**) in the presence of K_2CO_3. A solution of **3** in 1,2,4-trimethylbenzene was refluxed to afford the mesomeric betaine, 7-iminoimidazo[1,2-*a*]pyridiniumide (**4**) with 1,6-cyclization. Interestingly, the salt (**1b**) reacted with **2b** in the presence of K_2CO_3, followed by heating in refluxing 1,2,4-trimethylbenzene to give the mesomeric betaine, 7-oxoimidazo[1,2-*a*]pyridiniumide (**5**). On the other hand, compound (**6**) was heated in refluxing 1,2,4-trimethylbenzene to produce 8-aminoimidazo[1,2-*a*]-pyrazine (**7**) with debenzylation. (Scheme 1)

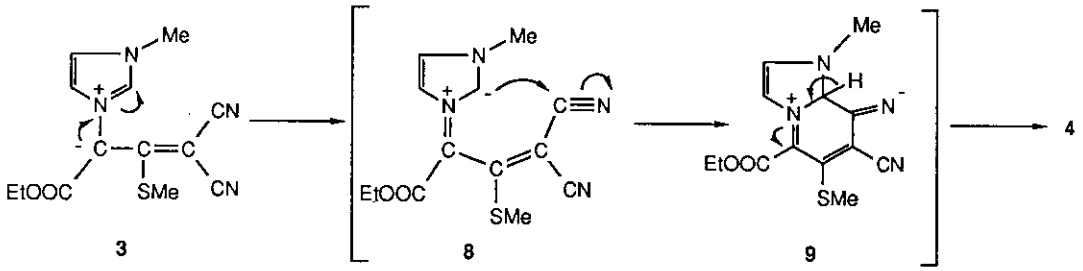
Scheme 1



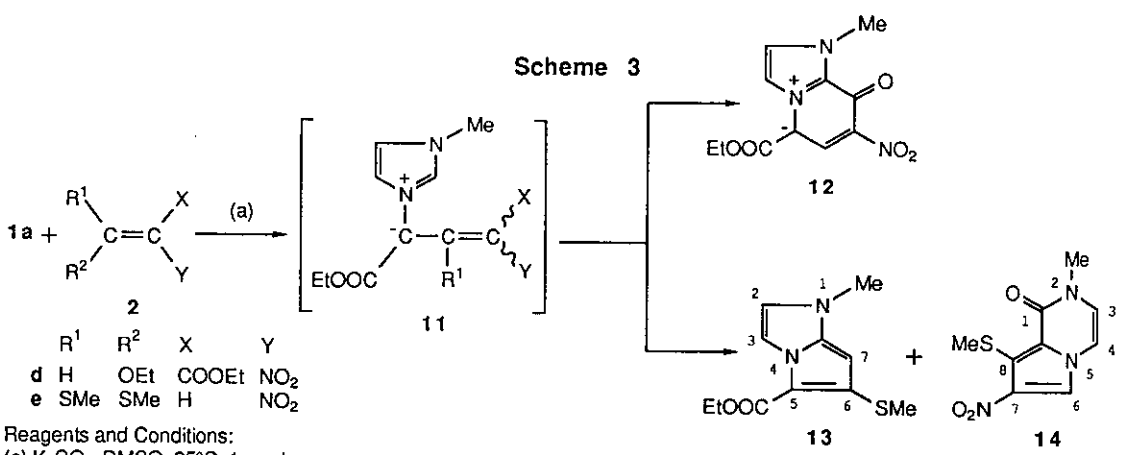
R	R^1	R^2	X
a Me	**a** SMe	SMe	CN
b $CH_2C_6H_5$	**b** H	OEt	COMe

Reagents and Conditions:
(a) K_2CO_3, $CHCl_3$, 25°C, 1 week;
(b) heating in refluxing 1,2,4-trimethylbenzene, 24 h.

Scheme 2



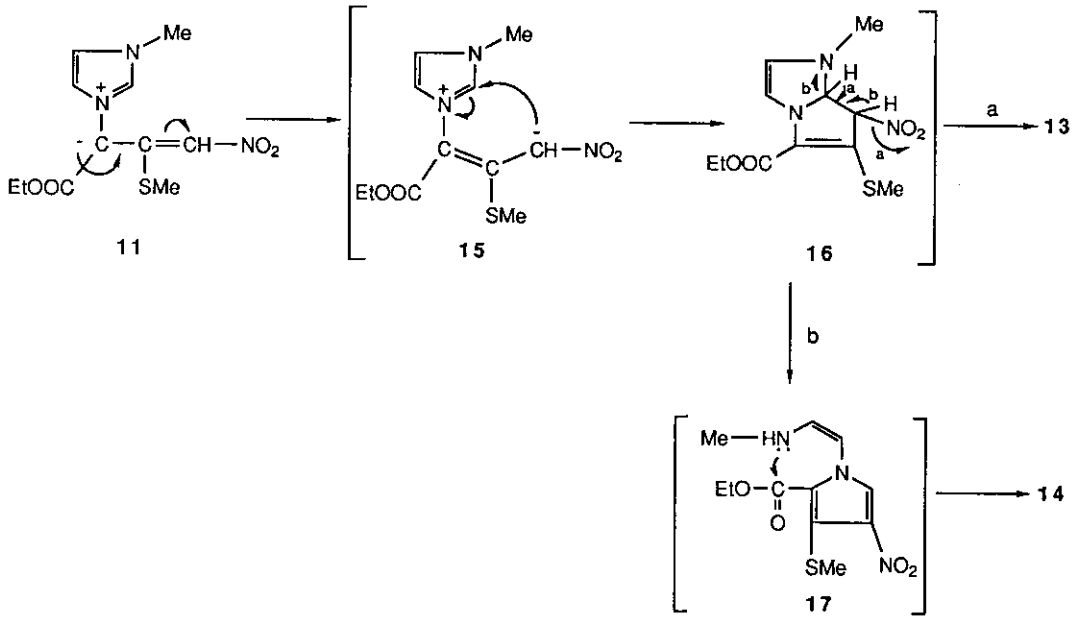
Scheme 3



	R^1	R^2	X	Y
d	H	OEt	COOEt	NO_2
e	SMe	SMe	H	NO_2

Reagents and Conditions:
(a) K_2CO_3, DMSO, 25°C, 1 week.

Scheme 4



The formation of **4** may be rationalized by the outline in Scheme 2. As pointed out in our previous paper,[1] the mechanism for the formation of **4** may proceèd *via* intermediate (**8**). Thus, the intermediate (**8**) may cyclize to give **4** *via* intermediate (**9**).

Next, we attempted the reaction of **1a** with ethyl ethoxymethylenenitroacetate (**2d**) or nitroketene dithioacetal (**2e**). The treatment of **1a** and **2d** with K_2CO_3 in DMSO did not give imidazolium *N*-allylide (**11**) but afforded the mesomeric betaine (**12**). On the other hand, the reaction of **1a** with **2e** in the presence of K_2CO_3 in DMSO produced pyrrolo[1,2-*a*]imidazole (**13**) and pyrrolo[1,2-*a*]pyrazine (**14**) with 1,5-dipolar cyclization (Scheme 3). As pointed out by Acheson[5] and Meth-Cohn,[10] the formation of **13** and **14** may be rationalized as outlined in Scheme 4.

EXPERIMENTAL

Melting points were determined with a Mitamura Mel-Temp and are uncorrected. Infrared (ir) spectra were recorded as KBr pellets on a JASCO IRA-2 spectrophotometer. Ultraviolet (uv) spectra were recorded on a Hitachi 323 spectrophotometer. Proton nuclear magnetic resonance (^{1}H-nmr) spectra were obtained on a JMN-FX-90Q (90 MHz) spectrometer with tetramethylsilane as internal standard. Chemical shifts are reported in parts per million (δ). Elemental analyses (C, H, N) of all compounds described here were performed on a Yanagimoto MT-2 CHN recorder. Mass spectra (ms) were measured on a JMS-DX-303G spectrometer.

1-Methylimidazolium *N*-(3,3-dicyano-1-ethoxycarbonyl-2-methylthio)-allylide (3)

A mixture of **1a** (1.00 g, 4 mmol), **2a** (0.68 g, 4 mmol), and K_2CO_3 (1.10 g, 8 mmol) in $CHCl_3$ (40 ml) was stirred at room temperature for a week and the mixture was then evaporated under reduced pressure. To the residue was added ice-water (100 ml). The precipitate was filtered, washed with water, dried and recrystallized from $CHCl_3$-MeOH to give **3**.

3, mp 189 °C, 1.11 g (96%); ^{1}H-nmr ($CDCl_3$) δ 1.28(3H, t, *J*=7 Hz, $CH_2C\underline{H}_3$), 2.53(3H, s, SCH_3), 3.95(3H, s, NCH_3), 4.18(2H, t, *J*=7 Hz, $C\underline{H}_2CH_3$), 7.14-7.19(2H, m, $C_{4,5}$-H), 8.17(1H, t, *J*=2 Hz, C_2-H); ir(KBr) 1670(CO), 2170(CN), 2200(CN) cm^{-1}; uv(EtOH) λmax(log ε) 299(3.83), 370(4.35) nm. *Anal.* Calcd for $C_{13}H_{14}N_4O_2S$: C, 53.78; H, 4.86; N, 19.30. Found: C, 53.70; H, 4.87; N, 19.14.

6-Cyano-1,7-dihydro-4-ethoxycarbonyl-7-imino-1-methyl-5-methylthio-imidazo[1,2-*a*]pyridin-3a-ium-4-ide (4)

A solution of **3** (0.58 g, 2 mmol) in 1,2,4-trimethylbenzene (60 ml) was refluxed for 24 h and the solution was then evaporated under reduced pressure. To the residue was added ice-water (50 ml). The precipitate was filtered, washed with water, dried and recrystallized from EtOH give **4**.

4, mp 150 °C, 0.17 g (30%); ^{1}H-nmr ($CDCl_3$) δ 1.41(3H, t, *J*=7 Hz, $CH_2C\underline{H}_3$), 2.55(3H, s, SCH_3), 4.38(2H, q, *J*=7 Hz, $C\underline{H}_2CH_3$), 4.48(3H, s, NCH_3), 7.18(1H, d, *J*=2 Hz, C_2-H), 8.50(1H, d, *J*=2 Hz, C_3-H); ir(KBr) 1670(CO), 2190(CN), 3260(NH) cm^{-1}; uv(EtOH) λmax(log ε) 243(4.14), 260(4.17), 360(4.27) nm. *Anal.* Calcd for $C_{13}H_{14}N_4O_2S$: C, 53.78; H, 4.86; N, 19.30. Found: C, 54.05; H, 4.96; N, 19.00.

1-Benzyl-1,7-dihydro-4-ethoxycarbonyl-6-acetyl-7-oxoimidazo[1,2-*a*]-pyridin-3a-ium-4-ide (5)

A mixture of **1b** (1.30 g, 4 mmol), **2b** (0.62 g, 4 mmol), and K_2CO_3 (1.10 g, 8 mmol) in $CHCl_3$ (40 ml) was stirred at room temperature for a week and ice-water (100 ml) was added. The mixture was separated and the aqueous layer was extracted with $CHCl_3$ (2x30 ml). The combined organic phase was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was heated in refluxing 1,2,4-trimethylbenzene (60 ml) for 24 h and the solution was then evaporated under reduced pressure. To the residue was added ice-water (50 ml) and the mixture was extracted with $CHCl_3$ (3x30 ml). The combined extracts were washed with water (50 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The tarry residue was submitted to column chromatography on silica gel. From a $CHCl_3$-acetone (10:1) fraction, compound (**5**) was obtained.

5, mp 182 °C, 0.04 g (3%); ^{1}H-nmr ($CDCl_3$) δ 1.39(3H, t, *J*=7 Hz, $CH_2C\underline{H}_3$), 2.78(3H, s, $COCH_3$), 4.35(2H, q, *J*=7 Hz, $C\underline{H}_2CH_3$), 6.25(2H, s, CH_2), 7.20(1H, d, *J*=2 Hz, C_2-H), 7.37(5H, s, Ar-H), 8.65(1H, s, C_6-H), 8.97(1H, d, *J*=2 Hz, C_3-H); ir(KBr) 1630(CO), 1690(CO) cm^{-1}; uv(EtOH) λmax(log ε) 243(4.06), 259(4.16), 268(4.15), 331(4.26), 359(4.17), 372(4.15) nm. High resolution ms Calcd for $C_{19}H_{18}N_2O_4$: 338.1266. Found: 338.1256.

1-Benzylimidazolium *N*-[(*N*-cyano-1-methylthioimidoyl)-1-ethoxycarbonyl]methylide (6)

Compound (**6**) was prepared by the reaction of **1b** (1.30 g, 4 mmol), **2c** (0.58 g, 4 mmol), and K_2CO_3 (1.10 g, 8 mmol) in $CHCl_3$ (40 ml) using procedure above for the synthesis of **3**.

6, mp 223 °C, 1.09 g (80%); ^{1}H-nmr ($CDCl_3$) δ 1.15(3H, t, *J*=7 Hz, $CH_2C\underline{H}_3$), 2.30(3H, s, SCH_3), 4.08(2H, q, *J*=7 Hz, $C\underline{H}_2CH_3$), 5.31(2H, s, CH_2), 7.12(1H, t, *J*=2 Hz, C4-H or C_5-H), 7.20(1H, t, *J*=2 Hz, C4-H or C_5-H), 7.42(5H, s, Ar-H) 8.08(1H, t, *J*=2 Hz, C_2-H); ir(KBr) 1650(CO), 2140(CN) cm^{-1}; uv(EtOH) λmax(log ε) 265(4.12), 310(4.37) nm. *Anal.* Calcd for $C_{17}H_{18}N_4O_2S$: C, 59.63; H, 5.30; N, 16.36. Found: C, 59.50; H, 5.33; N, 16.21.

8-Amino-5-ethoxycarbonyl-6-methylthioimidazo[1,2-*a*]pyrazine (7)

Compound (**7**) was prepared from refluxing of **6** (0.68 g, 2 mmol) in 1,2,4-trimethylbenzene (60 ml) using procedure above for the synthesis of **4**. The tarry residue was submitted to column chromatography on silica gel. From a $CHCl_3$-acetone (10:1) fraction, compound (**7**) was obtained.

7, mp 171 °C, 0.015 g (3%); ^{1}H-nmr ($CDCl_3$) δ 1.49(3H, t, *J*=7 Hz, $CH_2C\underline{H}_3$), 2.51(3H, s, SCH_3), 4.49(2H, q, *J*=7 Hz, $C\underline{H}_2CH_3$), 5.95(2H, br s, NH_2), 7.55(1H, d, *J*=1 Hz, C_2-H), 8.59(1H, d, *J*=1 Hz, C_3-H); ir(KBr) 1660(CO), 3300(NH), 3400(NH) cm^{-1}; uv(EtOH) λmax(log ε) 220(4.02), 266(4.49), 272(4.53), 330(3.98), 343(4.06), 356(3.93) nm. High resolution ms Calcd for $C_{10}H_{12}N_4O_2S$: 252.0681. Found: 252.0679.

1,7-Dihydro-4-ethoxycarbonyl-1-methyl-6-nitro-7-oxoimidazo[1,2-*a*]-pyridin-3a-ium-4-ide (12)

A mixture of **1a** (1.00 g, 4 mmol), **2d** (0.76 g, 4 mmol), and K_2CO_3 (1.10 g, 8 mmol) in DMSO (20 ml) was stirred at room temperature for 3 days and the mixture was added to ice-water (100 ml) and extracted with $CHCl_3$ (3x30 ml). The combined extracts were washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was recrystallized from EtOH-$CHCl_3$ to give **12**.

12, mp 298 °C, 0.63 g (59%); ^{1}H-nmr ($CDCl_3$) δ 1.42(3H, t, *J*=7 Hz, $CH_2C\underline{H}_3$), 4.40(2H, q, *J*=7 Hz, $C\underline{H}_2CH_3$), 4.52(3H, s, NCH_3), 7.33(1H, d, *J*=2 Hz, C_2-H), 8.84(1H, s, C_5-H), 9.03(1H, d, *J*=2 Hz, C_3-H); ir(KBr) 1690(CO), 1700(CO) cm^{-1}; uv(EtOH) λmax(log ε) 240(4.09), 265(4.16), 272(4.18), 317(4.21), 328(4.30), 390(4.10) nm. *Anal.* Calcd for $C_{11}H_{11}N_3O_5$: C, 49.81; H, 4.18; N, 15.84. Found: C, 49.83; H, 4.18; N, 15.86.

5-Ethoxycarbonyl-1-methyl-6-methylthio-1*H*-pyrrolo[1,2-*a*]imidazole (13) and 1,2-Dihydro-2-methyl-8-methylthio-7-nitro-1-oxopyrrolo[1,2-*a*]-pyrazine (14)

Compounds (**13**, **14**) were prepared by the reaction of **1a** (1.00 g, 4 mmol), **2e** (0.60 g, 4 mmol), and K_2CO_3 (1.10 g, 8 mmol) in DMSO (20 ml) using procedure above for the synthesis of **12**. The residue was submitted to column chromatography on silica gel. From a benzene-$CHCl_3$ (20:1) fraction, product (**13**) was obtained. From a benzene-$CHCl_3$ (1:20) fraction, product (**14**) was obtained.

13, mp 123 °C, 0.29 g (30%); ^{1}H-nmr ($CDCl_3$) δ 1.40(3H, t, *J*=7 Hz, $CH_2C\underline{H}_3$), 2.48(3H, s, SCH_3), 3.60(3H, s, NCH_3), 4.35(2H, q, *J*=7 Hz, $C\underline{H}_2CH_3$), 5.47(1H, s, C_7-H), 6.63(1H, d, *J*=2 Hz, C_2-H), 7.53(1H, d, *J*=2 Hz, C_3-H); ir(KBr) 1660(CO) cm^{-1}; uv(EtOH) λmax(log ε) 318(3.73) nm. *Anal.* Calcd for $C_{11}H_{14}N_2O_2S$: C, 55.44; H, 5.92; N, 11.76. Found: C, 55.32; H, 5.89; N, 11.62.

14, mp 236 °C, 0.29 g (30%); ^{1}H-nmr ($CDCl_3$) δ 2.61(3H, s, SCH_3), 3.45(3H, s, NCH_3), 6.58(1H, d, *J*=6 Hz, C_5-H or C_6-H), 6.87(1H, d, *J*=6 Hz, C_5-H or C_6-H), 7.84(1H, s, C_3-H); ir(KBr) 1640(CO) cm^{-1}; uv(EtOH) λmax(log ε) 219(3.90), 231(3.86), 287(3.91), 380(3.62) nm. *Anal.* Calcd for $C_9H_9N_3O_3S$: C, 45.18; H, 3.79; N, 17.56. Found: C, 44.99; H, 3.77; N, 17.48.

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