Thermal Reaction of Imidazolium *N*-Vinylimino Ylides: Formation of Mesomeric Betaines, Imidazopyridaziniumides, *via* Back-Donated 1,6-Cyclization

Yoshiro MATSUDA,* Makoto YAMASHITA, Kimitoshi TAKAHASHI, Shizuki IDE, Takahiro ITOU, Chieko MOTOKAWA, and Yasushige CHIYOMARU

School of Pharmaceutical Sciences, Nagasaki University, 1–14 Bunkyo-machi, Nagasaki 852, Japan.
Received August 16, 1993; accepted October 1, 1993

The reaction of *N*-aminoimidazolium salts (4, 5) with polarized olefins (2a—d, 3a, b) in the presence of K_2CO_3 in EtOH gave the corresponding imidazolium *N*-vinylimino ylides (6, 7). Thermolyses of the *N*-vinylimino ylides (6c—f, 7a—c) afforded mesomeric betaines (8a—d, 9a, b, 10a, b). Treatment of the salt (5) with polarized olefins (2b—d, 3c) in the presence of K_2CO_3 in EtOH directly yielded mesomeric betaines (9c—d, 10c), while in EtOH, the reaction of the salt (5) with polarized olefins (2e, 3d) in the presence of K_2CO_3 gave pyrazoles (11a, b). The formation of mesomeric betaines is suggested to proceed *via* back-donated 1,6-cyclization.

Keywords imidazopyridaziniumide; polarized olefin; imidazolium *N*-vinylimino ylide; 1,5-dipolar cyclization; back-donated 1,6-cyclization; mesomeric betaine

Polarized olefins (ethoxymethylene compounds and ketene dithioacetals) that are appropriately functionalized (cyano, methoxycarbonyl, nitro, sulfonyl, pyridyl, *etc.*) are versatile reagents which have been extensively utilized in heterocyclic synthesis.[1] As a part of our continuing interest in polarized olefins, we carried out extensive studies on the reaction of heteroaromatic compounds with various polarized olefins and their analogues.[2] In particular, it is well known that heterocyclic *N*-amino salts react with polarized olefins to produce heterocyclic *N*-vinylimino ylides (**1**). These ylides (**1**), acting as extended dipoles, are of interest in heterocyclic chemistry.[3] These *N*-vinylimino ylides may be considered to be resonance hybrids of the representative structures (**1**, **1′**, **1″**) shown in Fig. 1.

However, a number of previous studies on *N*-vinylimino ylides (**1**) have been mainly concerned with the synthesis of bicyclic compounds with bridgehead nitrogen (azaindolizine, pyrazoloimidazole, *etc.*) by 1,5-dipolar cyclization due to the resonance structure (**1″**). We have taken advantage of an alternative *N*-vinylimino ylide form (resonance structure **1′**) to realize a novel reaction which we have termed a "back-donated 1,6-cyclization." Our preliminary studies on the thermolyses of imidazolium *N*-allylides and the reaction of imidazolium *N*-amino salt with ketene dithioacetal have led to a new heterocyclic ring closure proceeding by back-donated 1,6-cyclization onto carbonyl or cyano carbon at X to produce the mesomeric betaines, imidazo[1,2-*a*]pyridiniumides[4] or imidazo[1,2-*b*]pyridaziniumides.[4a] The purpose of the present investigation was to extend back-donated 1,6-cyclization to the synthesis of 7-oxoimidazopyridaziniumides (**8**) and benzimidazopyridaziniumides (**9**, **10**), and to examine the decarboxylation of **8a**. Consequently, we obtained the hydrobromide (**12**) and the parent compound (**13**) by the decarboxylation of **8a**. The polarized olefins (**2**, **3**)[5] used in the present work are shown in Fig. 2.

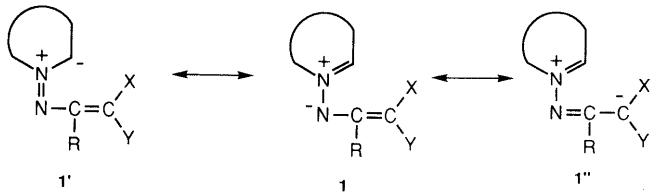
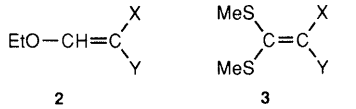


Fig. 1



	X	Y
a	COOEt	CN
b	CN	CN
c	COOEt	COOEt
d	COOEt	NO_2
e	H	CN

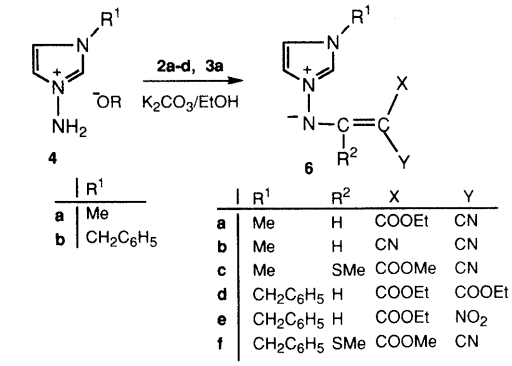
	X	Y
a	COOMe	CN
b	CN	CN
c	COOMe	COOMe
d	H	NO_2

Fig. 2

Results and Discussion

The starting materials, *N*-amino salts (**4**, **5**) were prepared by amination of *N*-alkylimidazoles or *N*-methylbenzimidazole with *O*-mesitylsulfonylhydroxylamine in CH_2Cl_2.[6] The reaction of *N*-amino salts (**4**, **5**) with polarized olefins (**2a—d**, **3a, b**) in the presence of K_2CO_3 gave *N*-vinylimino ylides (**6**, **7**) in good yields (Chart 1).

Attempts to obtain the mesomeric betaine from 3-methylimidazolium *N*-vinylimino ylides (**6a—c**) by thermolysis in refluxing xylene, trimethylbenzene or diphenylether, *etc.*, were fruitless. Thus, only unreacted material and/or unidentified decomposition products could be detected by ^{1}H-NMR spectroscopy and TLC, and these were not further studied. After much investigation, we found that heating of 3-benzylimidazolium *N*-vinylimino ylides (**6d, e**) in refluxing xylene resulted in back-donated 1,6-cyclization, giving rise to the mesomeric betaines, 7-oxoimidazo[1,2-*b*]pyridaziniumides (**8a, b**), in moder-



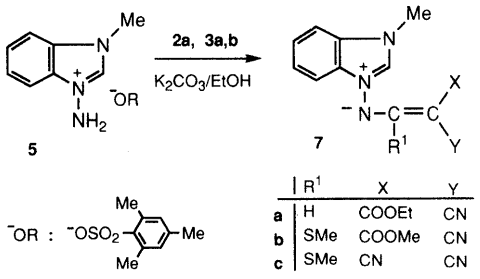


Chart 1

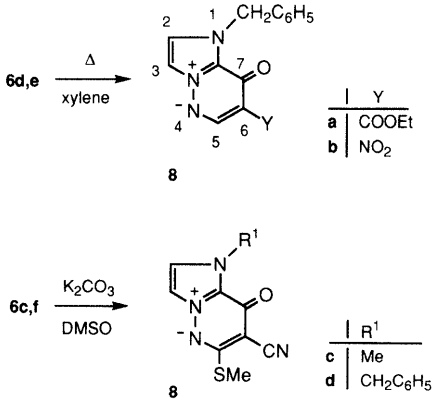


Chart 2

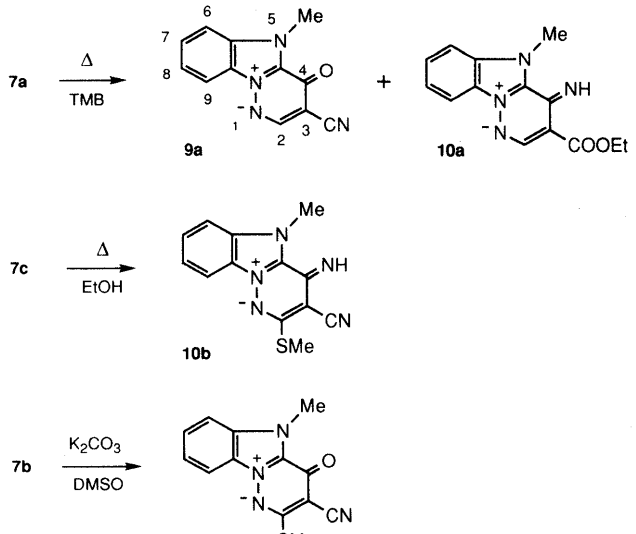


Chart 3

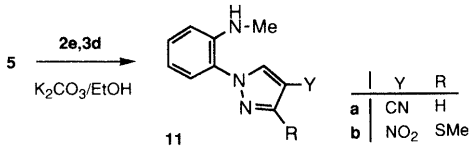


Chart 4

ate yields. On the other hand, thermolysis of **6f** in a variety of refluxing solvents did not proceed. In our previous paper we reported the synthesis of the mesomeric betaine **8d** by the reaction of the salt (**4b**) with ketene dithioacetal (**3a**) in the presence of K_2CO_3 in dimethylsulfoxide (DMSO) at room temperature for a week. Therefore we treated **6f** under similar conditions to give **8d** in good yield. Similar treatment of **6c** gave **8c** in good yield. However, other *N*-vinylimino ylides (**6a, b**, **6d, e**) did not afford the expected mesomeric betaines under the same conditions. The reasons for failure of the cyclization of **6a, b** are unclear at the present time (Chart 2).

Reactions of benzimidazolium *N*-vinylimino ylides (**7a, c**) were investigated under a variety of conditions. Thermolysis of **7a** in refluxing trimethylbenzene (TMB) proceeded, with formation of 4-oxobenzimidazopyridaziniumide (**9a**) together with 4-iminobenzimidazopyridaziniumide (**10a**). The mesomeric betaine (**10b**) was obtained by heating of **7c** in refluxing EtOH. Under conditions similar to those used in the formation of **8c** and **8d**, the mesomeric betaine (**9b**) was obtained by the reaction of **7b** in the presence of K_2CO_3. The reaction of the benzimidazolium *N*-amino salt (**5**) with polarized olefins (**2b—d**, **3c**) in the presence of K_2CO_3 did not give *N*-vinylimino ylide but directly afforded the back-donated 1,6-cyclization products, benzimidazopyridaziniumides (**9c—e**, **10c**, respectively) (Chart 3).

Similar treatment of **5** with the polarized olefins (**2e**, **3d**) afforded the 1,5-dipolar cyclization products (pyrazoles **11a, b**) (Chart 4).

In order to obtain the parent base of the imidazo[1,2-*b*]-pyridaziniumide derivative, we examined various conditions for removal of the methoxycarbonyl or cyano groups, and succeeded in isolation of 1-benzylimidazo[1,2-*b*]-pyridaziniumide (**13**). The methoxycarbonyl group of **8a** could be easily removed upon treatment with 47% hydrobromic acid under reflux to give the hydrobromide

(**12**), which was converted to the free base (**13**) by the use of K_2CO_3. However, attempts to produce the parent base of the benzo analogue were fruitless (Chart 5).

Physical Properties of Mesomeric Betaines The thermal stability of most of the mesomeric betaines (**8**, **9**, **10**) is shown by the fact that the mesomeric betaines melt over 159 °C, except for the parent free base (**13**). The parent base (**13**) was so unstable and hygroscopic that it decomposed within a week on exposure to air at room temperature.

Infrared (IR) Absorption Spectra The 7-carbonyl absorption maxima for the mesomeric betaines (**8a—d**, **13**) vary from 1575 to 1620 cm^{-1}. This result indicates that, in certain cases, the carbonyl absorption maxima for the mesomeric betaines are influenced by the electronic properties of the substituent group at the 6-position. The mesomeric betaines (**8a—d**, **13**) can be described to a first approximation by the resonance structures A and B as shown below. Comparison of the 7-carbonyl absorption maximum (1575 cm^{-1}) of the parent base (**13**) with those (1575—1620 cm^{-1}) of the other mesomeric betaines (**8a—d**) left no doubt that at least the parent base (**13**) has the dipolar form B (Fig. 3).

NMR Spectra of Mesomeric Betaines The chemical shifts (7.91—8.27 ppm) of the C_2- and C_3-protons in the ^{1}H-NMR spectra of the mesomeric betaines (**8a—d**, **13**) are little influenced by the electronic properties of the substituent groups on the pyridazine moiety.

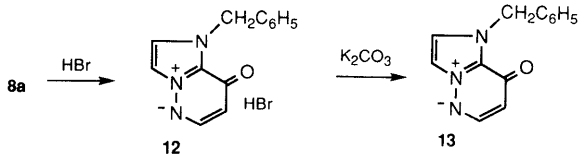


Chart 5

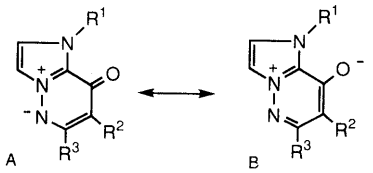


Fig. 3

^{13}C-NMR spectra of mesomeric betaines (**8a**, **12**, **13**) were measured in DMSO-d_6. The C-7 signal appears at 160.3 ppm in **8a**, 154.4 ppm in **12**, and 161.2 ppm in the free base (**13**). Those values are similar to the chemical shifts[3k] (159.5, 157.8 ppm) of the carbonyl carbons in the mesomeric betaines, triazolopyridazines.

Mechanistic Overview As pointed out in our previous paper,[4] a reasonable mechanism for the formation of the back-donated 1,6-cyclization product (**8a**) involves the resonance structure (**6d'**), as outlined in Chart 6.

As pointed out by Acheson and Elmore[3d] and Meth-Cohn,[3m] the formation of **11** may be rationalized as outlined in Chart 7.

In conclusion, the *N*-vinylimino ylides (**15**) with hydrogen at the 3-position of the vinylimino group underwent 1,5-dipolar cyclization to give the pyrazole derivatives (**11**), whereas the other *N*-vinylimino ylides (**6**, **7**) which had two electron-withdrawing groups at the 3-position of the vinylimino group participated in back-donated 1,6-cyclization to produce the mesomeric betaines (**8**, **9**, **10**). The high efficiency of the back-donated 1,6-cyclization, due to the resonance structure **1'**, in thermolysis of the *N*-vinylimino ylide of the resulting mesomeric betaine, imidazo[1,2-*b*]pyridaziniumide, presents interesting synthetic possibilities.

Experimental

Melting points were determined with a Mitamura Mel-Temp and are uncorrected. IR spectra were recorded in KBr pellets on a JASCO IRA-2 spectrophotometer. Ultraviolet (UV) spectra were recorded on a Hitachi 323 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were obtained on JNM-FX-90Q and JNM-GX400 spectrometers with tetramethylsilane as an 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.

General Procedure for the Preparation of 6 and 7 A mixture of a salt (**4**, **5**) (4 mmol), a polarized olefin (**2a—d**, **3a**, **b**) (4 mmol) and K_2CO_3 (8 mmol) in EtOH (50 ml) was stirred at room temperature for a week and the mixture was then evaporated under reduced pressure. The residue was taken up in ice-water (100 ml). The precipitate was collected by filtration, washed with water, dried and recrystallized from $CHCl_3$–MeOH to give the corresponding product (**6a—f**, **7a—c**, respectively).

6a: mp 188—190 °C (36%). IR (KBr) cm^{-1}: 2180 (CN), 1645 (CO). UV λ_{max}^{EtOH} nm (log ε): 222 (4.14), 311 (4.32). ^{1}H-NMR (DMSO-d_6) δ: 1.16 (3H, t, J=7 Hz, $OCH_2\underline{CH_3}$), 3.79 (3H, s, NMe), 4.02 (2H, q, J=7 Hz, $OC\underline{H_2}CH_3$), 7.58 (1H, t, J=2 Hz, C_4-H), 7.83 (1H, t, J=2 Hz,

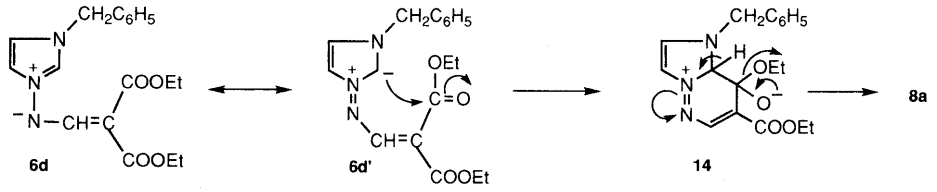


Chart 6

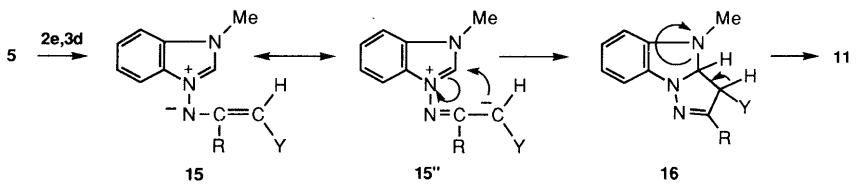


Chart 7

C_5-H), 8.33 (1H, s, –CH=), 9.10 (1H, t, J=2 Hz, C_2-H). *Anal.* Calcd for $C_{10}H_{12}N_4O_2$: C, 54.54; H, 5.49; N, 25.44. Found: C, 54.48; H, 5.54; N, 25.13

6b: mp 223—225 °C (10%). IR (KBr) cm^{-1}: 2200 (CN), 2180 (CN). UV λ_{max}^{EtOH} nm (log ε): 312 (3.82). ^{1}H-NMR (DMSO-d_6) δ: 3.79 (3H, s, NMe), 7.58 (1H, t, J=2 Hz, C_5-H), 7.90 (1H, t, J=2 Hz, C_4-H), 8.09 (1H, s, –CH=), 9.10 (1H, t, J=2 Hz, C_2-H). *Anal.* Calcd for $C_8H_7N_5$: C, 55.48; H, 4.07; N, 40.44. Found: C, 55.34; H, 4.14; N, 40.40.

6c: mp 142—143 °C (52%). IR (KBr) cm^{-1}: 2180 (CN), 1660 (CO). UV λ_{max}^{EtOH} nm (log ε): 217 (3.89), 263 (3.70). ^{1}H-NMR (DMSO-d_6) δ: 2.29 (3H, s, SMe), 3.36 (3H, s, OMe), 3.78 (3H, s, NMe), 7.49 (1H, br s, C_4-H or C_5-H), 7.51 (1H, br s, C_4-H or C_5-H), 8.94 (1H, br s, C_2-H). *Anal.* Calcd for $C_{10}H_{12}N_4O_2S$: C, 47.61; H, 4.79; N, 22.21; S, 12.71. Found: C, 47.44; H, 4.73; N, 22.11; S, 12.76.

6d: mp 157—158 °C (83%). IR (KBr) cm^{-1}: 1650 (CO), 1630 (CO). UV λ_{max}^{EtOH} nm (log ε): 202 (4.20), 236 (4.11), 310 (4.34). ^{1}H-NMR ($CDCl_3$) δ: 1.26 (6H, t, J=7 Hz, 2×$OCH_2C\underline{H}_3$), 4.15 (4H, q, J=7 Hz, 2×$OC\underline{H}_2CH_3$), 5.32 (2H, s, $C\underline{H}_2Ph$), 6.96 (1H, t, J=2 Hz, C_4-H), 7.20—7.45 (6H, m, C_5-H and ArH), 8.64 (1H, s, –CH=), 9.16 (1H, t, J=2 Hz, C_2-H). *Anal.* Calcd for $C_{18}H_{21}N_3O_4$: C, 62.96; H, 6.16; N, 12.24. Found: C, 62.75; H, 6.10; N, 12.24.

6e: mp 176—178 °C (47%). IR (KBr) cm^{-1}: 1675 (CO). UV λ_{max}^{EtOH} nm (log ε): 276 (4.34), 360 (4.56). ^{1}H-NMR ($CDCl_3$) δ: 1.32 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 4.29 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 5.42 (2H, s, $C\underline{H}_2Ph$), 7.04 (1H, br s, C_4-H), 7.27—7.41 (5H, m, Ar-H), 7.49 (1H, br s, C_5-H), 9.07 (1H, s, –CH=), 9.29 (1H, br s, C_2-H). *Anal.* Calcd for $C_{15}H_{16}N_4O_4$: C, 56.96; H, 5.10; N, 17.71. Found: C, 56.70; H, 5.04; N, 17.41.

6f: mp 154—155 °C (50%). IR (KBr) cm^{-1}: 2180 (CN), 1660 (CO). UV λ_{max}^{EtOH} nm (log ε): 207 (4.02), 236 (3.77) sh, 256 (3.77) sh, 307 (3.63). ^{1}H-NMR ($CDCl_3$) δ: 2.35 (3H, s, SMe), 3.57 (3H, s, OMe), 5.24 (2H, s, –$C\underline{H}_2$Ph), 7.03 (1H, t, J=2 Hz, C_4-H), 7.26 (1H, t, J=2 Hz, C_5-H), 7.40—7.50 (5H, m, Ar-H), 8.14 (1H, t, J=2 Hz, C_2-H). *Anal.* Calcd for $C_{16}H_{16}N_4O_2S$: C, 58.52; H, 4.91; N, 17.06. Found: C, 58.43; H, 4.91; N, 17.11.

7a: mp 191—193 °C (62%). IR (KBr) cm^{-1}: 2190 (CN), 1635 (CO). UV λ_{max}^{EtOH} nm (log ε): 216 (4.28), 274 (4.22), 281 (4.30), 289 (4.27), 318 (4.05). ^{1}H-NMR (DMSO-d_6) δ: 1.17 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 4.02 (3H, s, NMe), 4.04 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.55—7.99 (4H, m, $C_{4,5,6,7}$-H), 8.51 (1H, s, –CH=), 9.74 (1H, s, C_2-H). *Anal.* Calcd for $C_{14}H_{14}N_4O_2$: C, 62.21; H, 5.22; N, 20.73. Found: C, 62.22; H, 5.26; N, 20.77.

7b: mp 131—132 °C (52%). IR (KBr) cm^{-1}: 2170 (CN), 1675 (CO). UV λ_{max}^{EtOH} nm (log ε): 274 (4.26), 280 (4.27), 320 (3.74). ^{1}H-NMR ($CDCl_3$) δ: 2.48 (3H, s, SMe), 3.52 (3H, s, OMe), 4.07 (3H, s, NMe), 7.34—7.77 (4H, m, $C_{4,5,6,7}$-H), 8.57 (1H, s, C_2-H). *Anal.* Calcd for $C_{14}H_{14}N_2O_2S$: C, 55.61; H, 4.67; N, 18.53. Found: C, 55.49; H, 4.65; N, 18.47.

7c: mp 180—182 °C (70%). IR (KBr) cm^{-1}: 2190 (CN), 2150 (CN). UV λ_{max}^{EtOH} nm (log ε): 273 (4.35), 279 (4.34). ^{1}H-NMR (DMSO-d_6) δ: 2.53 (3H, s, SMe), 4.04 (3H, s, NMe), 7.71—8.04 (4H, m, $H_{4,5,6,7}$-H), 9.68 (1H, s, C_2-H). *Anal.* Calcd for $C_{13}H_{11}N_5S$: C, 57.97; H, 4.12; N, 26.00. Found: C, 57.86; H, 4.14; N, 25.94.

General Procedure for the Preparation of 8a, b A solution of an *N*-vinylimino ylide (**6d, e**) (2 mmol) in xylene (60 ml) was refluxed for 24 h and the solution was then evaporated under reduced pressure. The residue was taken up in ice-water (50 ml) and the mixture was extracted with $CHCl_3$ (4×30 ml). The combined extracts were washed with water (50 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was submitted to column chromatography on silica gel. From a benzene–$CHCl_3$ (1:20) fraction, the corresponding product (**8a, b**) was obtained.

8a: mp 181—182 °C (58%). IR (KBr) cm^{-1}: 1705 (CO), 1580 (CO). UV λ_{max}^{EtOH} nm (log ε): 205 (4.32), 237 (4.29), 244 (4.23) sh, 273 (3.80) sh, 283 (3.85) sh, 315 (4.24), 323 (4.21). ^{1}H-NMR (DMSO-d_6) δ: 1.26 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 4.19 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 6.00 (2H, s, $C\underline{H}_2$Ph), 7.32—7.41 (5H, m, Ar-H), 8.08 (1H, d, J=2 Hz, C_2-H), 8.19 (1H, d, J=2 Hz, C_3-H), 8.48 (1H, s, C_5-H). ^{13}C-NMR (DMSO-d_6) δ: 14.3, 51.4, 59.1, 106.3, 117.6, 123.8, 127.7, 128.0, 128.7, 135.2, 136.5, 150.5, 160.3, 164.7. *Anal.* Calcd for $C_{16}H_{15}N_3O_3$: C, 64.64; H, 5.09; N, 14.13. Found: C, 64.52; H, 5.16; N, 14.02.

8b: mp 208—210 °C (50%). IR (KBr) cm^{-1}: 1620 (CO). UV λ_{max}^{EtOH} nm (log ε): 204 (4.23), 246 (4.16), 276 (3.69), 286 (3.64) sh, 355 (4.13). ^{1}H-NMR (DMSO-d_6) δ: 5.98 (2H, s, $C\underline{H}_2$Ph), 7.29—7.38 (5H, m, Ar-H), 8.12 (1H, d, J=2 Hz, C_2-H), 8.27 (1H, d, J=2 Hz, C_3-H), 8.89 (1H, s, C_5-H). *Anal.* Calcd for $C_{13}H_{10}N_4O_3$: C, 57.78; H, 3.73; N, 20.73. Found: C, 57.77; H, 3.86; N, 20.77.

General Procedure for the Preparation of 8c, d A mixture of an *N*-vinylimino ylide (**6c, f**) (4 mmol) and K_2CO_3 (8 mmol) in DMSO (30 ml) was stirred at room temperature for a week and then evaporated under reduced pressure. The residue was taken up in ice-water (100 ml). The precipitate was filtered, washed with water, dried and recrystallized from $CHCl_3$–MeOH to give the corresponding product (**8c, d**, respectively).

8c: mp 288—290 °C (95%). IR (KBr) cm^{-1}: 2200 (CN), 1595 (CO). UV λ_{max}^{EtOH} nm (log ε): 242 (3.97), 309 (3.66), 322 (3.60) sh. ^{1}H-NMR (DMSO-d_6) δ: 2.52 (3H, s, SMe), 4.19 (3H, s, NMe), 7.91 (1H, d, J=2 Hz, C_2-H), 8.08 (1H, d, J=2 Hz, C_3-H). *Anal.* Calcd for $C_9H_8N_4OS$: C, 49.08; H, 3.66; N, 25.44. Found: C, 49.00; H, 3.47; N, 25.63.

8d: mp 226—228 °C (95%) (lit.[4a] mp 227 °C).

Thermolysis of 7a A solution of **7a** (2 mmol) in TMB (60 ml) was refluxed for 24 h and the solution was then evaporated under reduced pressure. The residue was taken up in ice-water (50 ml) and the mixture was extracted with $CHCl_3$ (4×30 ml). The combined extracts were washed with water (50 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was submitted to column chromatography on silica gel. From a benzene–$CHCl_3$ (2:1) fraction, **9a** was obtained. From a $CHCl_3$ fraction, **10a** was obtained.

9a: mp 257—260 °C (6%). IR (KBr) cm^{-1}: 2240 (CN), 1660 (CO). UV λ_{max}^{EtOH} nm (log ε): 204 (4.55), 229 (4.41), 257 (4.12), 263 (4.12), 327 (4.21). ^{1}H-NMR ($CDCl_3$) δ: 3.77 (3H, s, NMe), 7.27—7.57 (3H, m, $C_{6,7,8}$-H), 8.20 (1H, s, C_2-H), 8.31—8.42 (1H, m, C_9-H). *Anal.* Calcd for $C_{12}H_8N_4O$: C, 64.28; H, 3.60; N, 24.99. Found: C, 64.25; H, 3.80; N, 24.80.

10a: mp 159—160 °C (5%). IR (KBr) cm^{-1}: 1700 (CO), 1600 (C=NH). UV λ_{max}^{EtOH} nm (log ε): 215 (4.20), 253 (3.81), 358 (3.98). ^{1}H-NMR ($CDCl_3$) δ: 1.39 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 3.81 (3H, s, NMe), 4.34 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.31—7.57 (3H, m, $C_{6,7,8}$-H), 8.48 (1H, s, C_2-H), 8.95 (1H, m, C_9-H), 9.25 (1H, br s, C=NH). *Anal.* Calcd for $C_{14}H_{14}N_4O_2$: C, 62.21; H, 5.22; N, 20.73. Found: C, 62.20; H, 5.22; N, 20.72.

3-Cyano-4,5-dihydro-4-imino-5-methyl-2-methylthiobenzimidazo[1,2-*b*]pyridazin-9b-ium-1-ide (10b) A solution of **7c** (2 mmol) in EtOH (60 ml) was refluxed for 24 h and the solution was then evaporated under reduced pressure. The residue was taken up in ice-water (50 ml) and the mixture was extracted with $CHCl_3$ (4×30 ml). The combined extracts were washed with water (50 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was submitted to column chromatography on silica gel. From a $CHCl_3$ fraction, **10b** was obtained.

10b: mp 267—270 °C (20%). IR (KBr) cm^{-1}: 2180 (CN). UV λ_{max}^{EtOH} nm: 202, 235 sh, 246, 268 sh, 276, 298 sh, 310 sh, 375, 390. ^{1}H-NMR (DMSO-d_6) δ: 2.60 (3H, s, SMe), 4.54 (3H, s, NMe), 7.33 (1H, br s, C=NH), 7.53—8.14 (4H, m, $C_{6,7,8,9}$-H). *Anal.* Calcd for $C_{13}H_{11}N_5S$: C, 57.97; H, 4.12; N, 26.00. Found: C, 57.97; H, 4.20; N, 25.90.

3-Cyano-4,5-dihydro-5-methyl-2-methylthio-4-oxobenzimidazo[1,2-*b*]pyridazin-9b-ium-1-ide (9b) A mixture of **7b** (4 mmol) and K_2CO_3 (8 mmol) in DMSO (30 ml) was stirred at room temperature for a week and the mixture was then evaporated under reduced pressure. The residue was taken up in ice-water (100 ml). The precipitate was filtered, washed with water, dried and recrystallized from $CHCl_3$–MeOH to give **9b**.

9b: mp >300 °C (95%). IR (KBr) cm^{-1}: 2200 (CN), 1590 (CO). UV λ_{max}^{EtOH} nm (log ε): 236 (3.76), 253 (3.89), 259 (3.92), 265 (3.89), 297 (2.96), 332 (3.48), 346 (3.61), 364 (3.58). ^{1}H-NMR (DMSO-d_6) δ: 2.69 (3H, s, SMe), 4.41 (3H, s, NMe), 7.67 (4H, m, $C_{6,7,8,9}$-H). *Anal.* Calcd for $C_{13}H_{10}N_4OS$: C, 57.76; H, 3.73; N, 20.73. Found: C, 57.94; H, 3.84; N, 20.74.

General Procedure for the Preparation of 9c—d and 10c A mixture of the salt **5** (4 mmol), a polarized olefin (**2b—d, 3c**) (4 mmol) and K_2CO_3 (8 mmol) in EtOH (50 ml) was stirred at room temperature for a week and the mixture was then evaporated under reduced pressure. The residue was taken up in ice-water (100 ml). The precipitate was collected by filtration, washed with water, dried and recrystallized from $CHCl_3$–MeOH to give the corresponding product (**9c—e**, **10c**, respectively).

9c: mp 270—272 °C (10%). IR (KBr) cm^{-1}: 1710 (CO), 1690 (CO). UV λ_{max}^{EtOH} nm (log ε): 232 (4.34), 259 (4.40), 264 (4.45), 295 (3.59), 306 (3.65), 328 (3.95), 344 (4.21), 361 (4.21). ^{1}H-NMR ($CDCl_3$) δ: 1.44 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 4.43 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 4.63 (3H, s, NMe), 7.60—7.75 (4H, m, $C_{6,7,8,9}$-H), 8.83 (1H, s, C_2-H). *Anal.* Calcd for $C_{14}H_{13}N_3O_3$: C, 61.99; H, 4.83; N, 15.49. Found: C, 61.92; H, 4.97; N, 15.35.

9d: mp 297—300 °C (11%). IR (KBr) cm^{-1}: 1635 (CO). UV λ_{max}^{EtOH} nm: 228, 238, 270, 277, 301, 313, 372, 382. ^{1}H-NMR (DMSO-d_6) δ: 3.83 (3H, s, NMe), 7.07—7.84 (4H, m, $C_{6,7,8,9}$-H), 8.11 (1H, s, C_2-H). *Anal.* Calcd for $C_{11}H_8N_4O_3$: C, 54.10; H, 3.30; N, 22.94. Found: C, 53.90; H, 3.43; N, 22.82.

9e: mp 182—184 °C (7%). IR (KBr) cm^{-1}: 1735 (CO), 1670 (CO). UV λ_{max}^{EtOH} nm (log ε): 212 (4.41), 220 (4.41), 251 (4.51), 273 (3.88), 345 (4.19), 360 (4.05). ^{1}H-NMR ($CDCl_3$) δ: 2.69 (3H, s, SMe), 3.73 (3H, s, OMe), 3.98 (3H, s, NMe), 7.27—8.38 (4H, m, $C_{6,7,8,9}$-H). *Anal.* Calcd for $C_{14}H_{13}N_3O_3S$: C, 55.43; H, 4.32; N, 13.85. Found: C, 55.35; H, 4.45; N, 13.64.

10c: mp 247—249 °C (23%). IR (KBr) cm^{-1}: 2200 (CN). UV λ_{max}^{EtOH} nm (log ε): 234 (4.32), 237 (4.32), 264 (4.28), 273 (4.42), 290 (4.14), 306 (3.93), 310 (3.88), 318 (3.74), 382 (3.99), 392 (3.97). ^{1}H-NMR (DMSO-d_6) δ: 4.58 (3H, s, NMe), 7.42 (1H, br s, C=NH), 7.45—8.20 (4H, m, $C_{6,7,8,9}$-H), 9.75 (1H, s, C_2-H). *Anal.* Calcd for $C_{12}H_9N_5$: C, 64.56; H, 4.06; N, 31.37. Found: C, 64.40; H, 4.19; N, 31.35.

General Procedure for the Preparation of 11 A mixture of the salt **5** (4 mmol), a polarized olefin (**2e**, **3d**) (4 mmol) and K_2CO_3 (8 mmol) in EtOH (50 ml) was stirred at room temperature for a week and the mixture was then evaporated under reduced pressure. The residue was taken up in ice-water (100 ml). The precipitate was collected by filtration, washed with water, dried and recrystallized from $CHCl_3$–MeOH to give the corresponding product (**11a**, **b**).

11a: mp 81—82 °C (10%). IR (KBr) cm^{-1}: 3400 (NH), 2250 (CN). UV λ_{max}^{EtOH} nm (log ε): 235 (4.30), 315 (3.66). ^{1}H-NMR ($CDCl_3$) δ: 2.86 (3H, d, J=5 Hz, NMe), 5.20 (1H, br s, NH), 6.65—7.44 (4H, m, Ar-H), 8.02 (1H, d, J=2 Hz, C_3-H or C_5-H), 8.06 (1H, d, J=2 Hz, C_3-H or C_5-H). *Anal.* Calcd for $C_{11}H_{10}N_4$: C, 66.65; H, 5.09; N, 28.26. Found: C, 66.62; H, 5.12; N, 28.11.

11b: mp 178—180 °C (57%). IR (KBr) cm^{-1}: 3400 (NH). UV λ_{max}^{EtOH} nm (log ε): 242 (3.99). ^{1}H-NMR ($CDCl_3$) δ: 2.58 (3H, s, SMe), 2.88 (3H, d, J=5 Hz, NMe), 5.20 (1H, br s, NH), 6.65—7.45 (4H, m, Ar-H), 8.37 (1H, s, C_5-H). *Anal.* Calcd for $C_{11}H_{12}N_4O_2S$: C, 49.99; H, 4.58; N, 21.20. Found: C, 50.13; H, 4.55; N, 21.28.

1,7-Dihydro-1-benzyl-7-oxoimidazo[1,2-*b*]pyridazin-3a-ium-4-ide Hydrobromide (12) A solution of **8a** (4 mmol) in 47% HBr (20 ml) was refluxed for 1 h. The reaction mixture was evaporated under reduced pressure. The residue was recrystallized from MeOH to give **12**.

12: mp 278—280 °C (82%). IR (KBr) cm^{-1}: 1575 (CO). UV λ_{max}^{EtOH} nm (log ε): 203 (4.35), 233 (4.16), 240 (4.14) sh, 297 (4.11). ^{1}H-NMR (DMSO-d_6) δ: 5.90 (2H, s, C$\underline{H}_2$Ph), 6.68 (1H, d, J=6 Hz, C_6-H), 7.36 (5H, br s, Ar-H), 8.26 (1H, d, J=2 Hz, C_2-H), 8.43 (1H, d, J=6 Hz, C_5-H), 8.45 (1H, d, J=2 Hz, C_3-H). ^{13}C-NMR (DMSO-d_6) δ: 52.1, 95.3, 106.0, 118.4, 124.9, 127.6, 128.2, 128.7, 132.3, 135.9, 148.9, 154.4. *Anal.* Calcd for $C_{14}H_{11}BrN_3O$: C, 51.00; H, 3.95; Br, 26.10; N, 13.72. Found: C, 50.69; H, 3.98; Br, 26.05; N, 13.65.

1,7-Dihydro-1-benzyl-7-oxoimidazo[1,2-*b*]pyridazin-3a-ium-4-ide (13) A solution of **12** (2 mmol) in water (20 ml) was made basic to litmus with K_2CO_3 and immediately extracted with $CHCl_3$ (3 × 10 ml). The extract was dried (Na_2SO_4) and evaporated under reduced pressure. The residue was dried under vacuum in a desiccator (2 mmHg) for 10 min. The NMR, IR, UV, HRMS spectra of the crude free base (**13**) were recorded.

13: mp 117—120 °C (95%), (hygroscopic). IR (KBr) cm^{-1}: 1575 (CO). UV λ_{max}^{EtOH} nm: 234, 240, 298. ^{1}H-NMR (DMSO-d_6) δ: 5.98 (2H, s, C$\underline{H}_2$Ph), 6.00 (1H, d, J=6 Hz, C_6-H), 7.29—7.42 (5H, m, Ar-H), 7.99 (1H, d, J=6 Hz, C_5-H), 8.00 (1H, d, J=2 Hz, C_2-H), 8.10 (1H, d, J=2 Hz, C_3-H). ^{13}C-NMR (DMSO-d_6) δ: 51.0, 106.2, 116.9, 122.4, 127.9, 128.1, 128.7, 135.9, 136.9, 148.5, 161.2. HRMS Calcd for $C_{13}H_{11}N_3O$: 225.0902. Found: 225.0911.

References

1) *a*) Y. Tominaga, Y. Matsuda, *J. Heterocycl. Chem.*, **22**, 937 (1985); *b*) M. Kolb, *Synthesis*, **1990**, 171.
2) *a*) Y. Tominaga, Y. Matsuda, *Yuki Gosei Kagaku Kyokai Shi*, **43**, 669 (1985); *b*) Y. Matsuda, H. Gotou, *Heterocycles*, **26**, 2757 (1987); *c*) Y. Matsuda, H. Gotou, M. Yamashita, K. Takahashi, S. Ide, K. Furuno, K. Torisu, T. Itou, C. Motokawa, *ibid.*, **34**, 899 (1992).
3) *a*) K. Matsumoto, *Yuki Gosei Kagaku Kyokai Shi*, **32**, 731 (1974); *b*) T. Uchida, K. Matsumoto, *Synthesis*, **1976**, 209; *c*) F. J. Swinbourene, J. H. Hunt, G. Klinkert, *Adv. Heterocycl. Chem.*, **23**, 103 (1978); *d*) R. M. Acheson, N. F. Elmore, *ibid.*, **23**, 263 (1978); *e*) Y. Tamura, M. Ikeda, *ibid.*, **29**, 71 (1981); *f*) E. C. Taylor, I. J. Turchi, *Chem. Rev.*, **79**, 181 (1979); *g*) Y. Tamura, Y. Sumida, S. Haruki, M. Ikeda, *J. Chem. Soc., Perkin Trans. 1*, **1975**, 575; *h*) A. Kakehi, S. Ito, T. Funahashi, Y. Ota, *J. Org. Chem.*, **41**, 1570 (1976); *i*) A. Kakehi, S. Ito, K. Uchiyama, Y. Konno, K. Kondo, *ibid.*, **42**, 443 (1977); *j*) H. G. O. Becker, D. Nagel, H. J. Timpe, *J. Prakt. Chem.*, **315**, 97 (1973); *k*) H. J. Timpe, H. G. O. Becker, R. Radeglia, *ibid.*, **319**, 945 (1977); *l*) V. Boekelheide, N. A. Fedoruk, *J. Am. Chem. Soc.*, **90**, 3830 (1968); *m*) O. Meth-Cohn, *Tetrahedron Lett.*, **1975**, 413.
4) *a*) Y. Matsuda, H. Gotou, K. Katou, H. Matsumoto, M. Yamashita, K. Takahashi, S. Ide, *Heterocycles*, **31**, 977 (1990); *b*) Y. Matsuda, H. Gotou, K. Katou, H. Matsumoto, M. Yamashita, K. Takahashi, S. Ide, K. Furuno, K. Torisu, *ibid.*, **32**, 2217 (1991); *c*) Y. Matsuda, M. Yamashita, K. Takahashi, S. Ide, K. Torisu, K. Furuno, *ibid.*, **33**, 295 (1992).
5) *a*) E. G. de Bollemount, *Bull. Soc. Chim. Fr.*, **25**, 20 (1902); *b*) O. Diels, H. Gärtner, R. Kaack, *Ber.*, **55**, 3439 (1922); *c*) R. Gompper, W. Töpfl, *ibid.*, **95**, 2861 (1962); *d*) M. Prystas, J. Gut, *Coll. Czech. Chem. Commun.*, **28**, 2501 (1963); *e*) B. S. Thyagarajan, P. V. Gopalakrishnan, *Tetrahedron*, **20**, 1051 (1964).
6) *a*) Y. Tamura, J. Minamikawa, K. Sumoto, S. Fujii, M. Ikeda, *J. Org. Chem.*, **38**, 1239 (1973); *b*) Y. Tamura, H. Hayashi, J. Minamikawa, M. Ikeda, *J. Heterocycl. Chem.*, **11**, 781 (1974).