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Synthesis of Mesomeric Betaines Containing a Pyrrolo- or Imidazotriaziniumolate System and Their Cycloaddition with Acetylenic Dipolarophiles Leading to Triazocinone Derivatives

Norio Sakai, Makoto Funabashi, Takayuki Hamada, Satoshi Minakata, Ilhyong Ryu and Mitsuo Komatsu*

Department of Applied Chemistry, Graduate School of Engineering, Osaka University, Yamadaoka 2-1, Suita, Osaka 565-0871, Japan

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Abstract: A series of 2-substituted mesomeric betaines containing a cyclic azomethine imine unit were synthesized and their cycloaddition with acetylenic dipolarophiles were examined. Unexpectedly, the cycloaddition of the betaines with electron-deficient dipolarophiles gave ring-expanding adducts having a triazocinone structure. With electron-rich dipolarophiles such as ynamines, the reactions proceeded more readily leading regioselectively to the same type of triazocinones in almost quantitative yields. In particular, in the case of an imidazobetaine and an ynamine, the cycloaddition took place at room temperature to afford the initial cycloadducts exclusively and in excellent yields. The isolated tricyclic precursors were found to rearrange quantitatively to the final products on heating to 60 °C.

Keywords: Cycloadditions; Mesoionic compounds; Rearrangements; Medium-ring heterocycles

Introduction

Mesomeric betaines[1] constitute a unique class of 1,3-dipoles[2] which have long been known to be extremely important intermediates in cycloaddition reactions for the construction of a number of natural products and new heterocyclic compounds.[3] While 1,3-dipoles are highly reactive toward a variety of dipolarophiles, they are nearly all unstable and not isolable because of their highly polarized structures. Hence, these intermediates must be generated in situ and the presence of additives such as strong bases or the necessity of unfavorable conditions such as high temperatures and irradiation often poses limitation to successive cycloaddition reactions.[2] To overcome these problems, many chemists focused on a strategy in which these transient reagents are embedded into cyclic aromatic structures which afford stable and isolable 1,3-dipoles such as mesomeric betaines.[1,2a,b] A considerable number of cycloaddition reactions of this type of 1,3-dipoles with dipolarophiles have been reported, clearly demonstrating that they are quite useful for synthesis of bi- and polycyclic compounds.[2]

On the other hand, fused heterocyclic compounds containing a pyrrolo[1,2-*d*][1,2,4]triazine skeleton[4] reportedly show biological activities with respect to, for example, antihypertensive activity,[5a] blood platelet aggregation inhibition[5b] and antimicrobial activity.[5c] Hence, the development of such derivatives having a 1,3-dipolar nature in their ring systems is quite interesting from the point of view of synthetic and pharmaceutical chemistry. We previously reported synthesis of a new bicyclic betaine, 2-*tert*-butylpyrrolo[1,2-*d*][1,2,4]triazinium-4-olate (**4a**), prepared by the thermolysis of a ring-expansion reaction product **3** of a diaziridinone[6] **2** with pyrrole-2-carboxaldehyde (**1**),[7] and its cycloaddition reaction with a dipolarophile such as dimethyl acetylenedicarboxylate (DMAD: **5a**) leading to a fused ring-enlarged compound, a triazocinone derivative **6aa** (Scheme 1).[8,9] However, the 2-substituent of this type of betaine **4a** was limited to a *tert*-butyl

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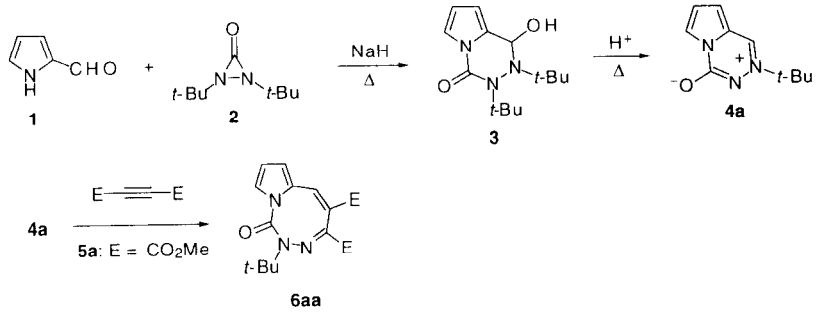
Scheme 1



group because of the stability of the starting diaziridinone, and, unfortunately, the yield of the bicyclotriazocinone derivative **6aa** was rather low. Thus, the development of facile preparation of these type of betaines by alkylation of the unsubstituted pyrrolotriazinone was examined as the first part of this investigation. Secondly, detailed research of the cycloaddition of the synthesized betaine with electron-deficient dipolarophiles was carried out to establish its generality. Thirdly, MO calculation[10] indicated that the HOMO-LUMO energy gap between the betaine and an electron-rich dipolarophile such as an ynamine is significantly smaller than that between the betaine and the electron-deficient dipolarophile, DMAD. Since few examples of cycloadditions of such mesomeric betaines with electron-rich acetylenic dipolarophiles leading to ring-enlargement products have been reported, research on the 1,3-dipolar cycloaddition with electron-rich dipolarophiles was done in detail. The introduction of another nitrogen atom to the pyrrole ring, leading to novel imidazobetaines was attempted, in order to lower the LUMO level of the betaine. Such a lowering would cause greater reactivity of the imidazobetaines in reactions with electron-rich dipolarophiles than would be observed for the pyrrolobetaines, especially.

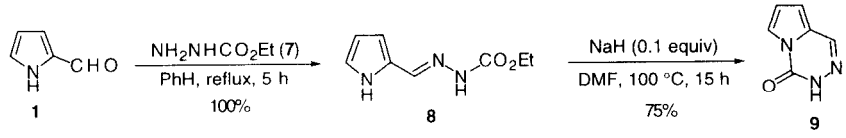
Here we wish to report a new and more general synthetic method for these types of betaines, and to demonstrate the cycloaddition reactions of the synthesized mesomeric betaines with various acetylenic dipolarophiles under several sets of conditions [Type I (HOMO controlled) and Type III (LUMO controlled) in the Sustmann classification[11]]. Furthermore, the isolation of the initial cycloadducts clarified the major features of the thermal rearrangement process leading to the final products **6**, which could not be reported in our previous report.[8]

Results and Discussion

Synthesis of Mesomeric Betaines via the Alkylation of Triazinone with Alkyl Halides.

According to the procedure in the literature,[12] dehydrative condensation of pyrrole-2-carboxaldehyde (**1**) and ethyl carbazate (**7**) was carried out to give carbethoxyhydrazone **8** in quantitative yield (Scheme 2). A cyclization of the hydrazone **8** by a stoichiometric amount of sodium hydride was then examined in DMF at

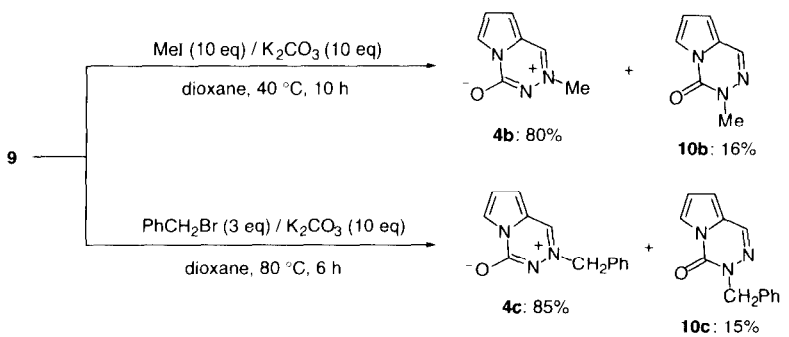
Scheme 2



100 °C for 15 h. However, a complicated mixture was obtained. It was found that pyrrolo[1,2-*d*][1,2,4]triazin-4-one (**9**) can be prepared by treatment of **8** with a catalytic amount (0.1 equiv) of the base in 75% yield. It is noteworthy that the liberated ethoxide ion which functioned as a base instead of sodium hydride provided a catalytic system.

The preparation of the mesomeric betaines was established by alkylation of the cyclization product **9**, which is based on the reported quaternization[13] of pyridazin-3-one or phthalazin-1-one with methyl *p*-toluenesulfonate, thus affording the betaine structure. After several preliminary experiments to find optimal conditions, 2-methylpyrrolo[1,2-*d*][1,2,4]triazinium-4-olate (**4b**) was obtained as the major product in 80% yield by treatment of **9** with methyl iodide (10 equiv) in the presence of potassium carbonate (10 equiv) in dioxane at 40 °C for 10 h along with a 3-methylated product, 3-methylpyrrolo[1,2-*d*][1,2,4]triazine-4-one (**10b**) in 16% yield (Scheme 3).

Scheme 3



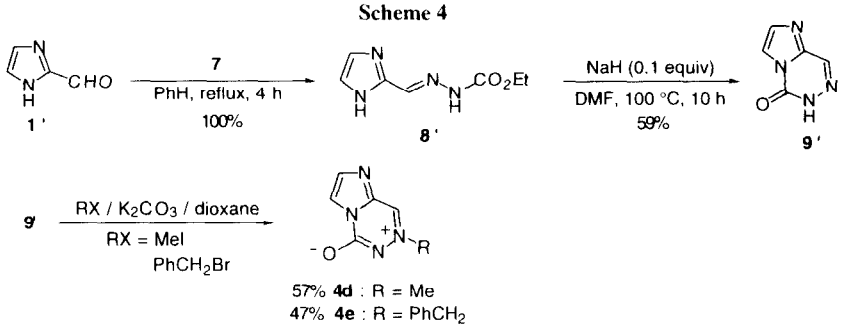
The structure of betaine **4b** was deduced from spectral data and elemental analysis. A singlet at δ 8.23 in the ^{1}H-NMR spectrum was assigned to a methine proton at C-1, the signal of which appeared at δ 127.3 in the ^{13}C-NMR spectrum. These chemical shifts were slightly shifted to lower magnetic field than those of the corresponding atoms of **9**, reflecting the mesomeric effect of the cation in **4b**. In addition, a singlet (δ 4.05) of the methyl group was observed at lower field in comparison with a methyl group attached to a neutral nitrogen-containing functional group, such as amino or amide group. This lower-field shift is caused by the quaternized immonium cation in the vicinal position. A strong absorption at 1628 cm^{-1} in the IR spectrum, which is atypical of a carbonyl group is indicative of the contribution of a single-bond character to the C=O bond. All the other spectral data were also in good agreement with the mesomeric betaine structure of the triaziniumolate derivative **4b**, in comparison with those of the 2-*tert*-butylated betaine **4a**, whose structure was unambiguously determined by X-ray crystallographic analysis.[7] While compound **10b** showed the mass number of 149 for the M$^+$ ion peak, the same as that for **4b**, other spectral features were quite different from those of **4b**. The strong absorption observed at 1700 cm^{-1} in the IR spectrum is typical of a carbonyl group in cyclic ureas. In the ^{1}H-NMR spectrum, all the signals of **10b** were shifted to higher magnetic field than those of **4b**. These data are all consistent with the lesser extent of the electron withdrawing effect in inductive and/or mesomeric manner being caused by the alkylation of triazinone **9** on the nitrogen atom at the 3-position.

Similarly, 2-benzylpyrrolo[1,2-*d*][1,2,4]triazinium-4-olate (**4c**) was obtained in 85% yield after the quaternization reaction of **9** with 3 equiv of benzyl bromide in the presence of potassium carbonate (10 equiv)

at 80 °C for 6 h along with a by-product, 3-benzyl-3,4-dihydropyrrolo[1,2-*d*][1,2,4]triazine-4-one (**10c**) in 15% yield (Scheme 3). The quaternization reaction with benzyl bromide having a dichloro or a carbomethoxy substituent on the benzene ring also resulted in good yields of betaines. However, the reaction with 2-iodobutane or acetyl chloride gave no betaines, because the ready elimination of 2-butene followed the quaternization reaction or the anticipated acetylated betaine is probably unstable toward hydrolysis during the silica gel column chromatography workup.

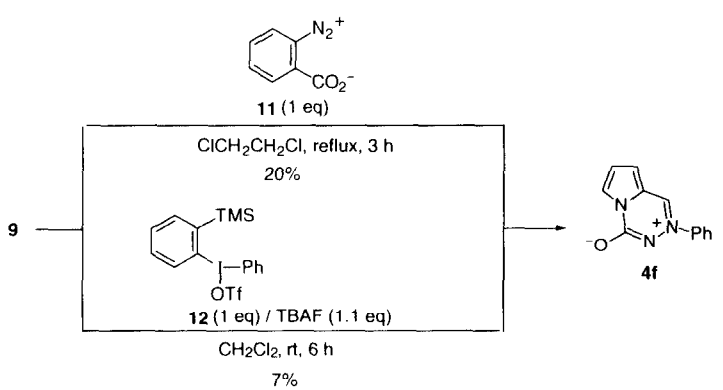
The same procedure as was used for the pyrrolo betaines was applied to the preparation of imidazobetaines **4d,e** by the quaternization of imidazotriazinone[14] **9'** with alkyl halides. Imidazotriazinone **9'** was also prepared from imidazole-2-carboxaldehyde (**1'**) by two-step procedure in 59% yield (Scheme 4). A quaternization reaction of imidazotriazinone **9'** with excess methyl iodide or benzyl bromide under similar conditions gave 57% of 2-methylimidazo[1,2-*d*][1,2,4]triazinium-4-olate (**4d**) or 47% of 2-benzylimidazo[1,2-*d*][1,2,4]triazinium-4-olate (**4e**) along with by-products. The yields of the imidazo betaines **4d,e** were lower than those of the pyrrole derivatives **4b,c** reflecting the lower solubility of imidazotriazinone **9'** in the solvent used.

Scheme 4



On the other hand, benzenediazonium-2-carboxylate[15] (a benzyne precursor) **11** and compound **9** were employed to obtain 2-phenylpyrrolo[1,2-*d*][1,2,4]triazinium-4-olate (**4f**) in 20% yield (Scheme 5). To avoid the use of a rather dangerous benzyne precursor such as benzenediazonium-2-carboxylate, the preparation of the *N*-phenyl derivative was carried out by reaction with phenyl[(*o*-trimethylsilyl)phenyl] iodonium triflate[16] (a

Scheme 5



much safer benzyne precursor) **12** in the presence of TBAF and **9** in CH_2Cl_2 at room temperature for 6 h to give the betaine **4f** in only 7% yield.

Cycloaddition of Mesomeric Betaines with Electron-deficient Dipolarophiles

The ring-enlargement reaction of 2-*tert*-butylated betaine **4a** with an electron-deficient dipolarophile, such as dimethyl acetylenedicarboxylate (DMAD: **5a**) leading to the triazocinone derivative **6aa** was found in our preliminary research.[8] Thus, further investigation of the cycloaddition of the synthesized mesomeric betaines **4** containing a different 2-substituent such as methyl, benzyl or phenyl with acetylenic dipolarophiles was undertaken to clarify the details of the reaction and to establish its generality. For example, the reaction of 2-*tert*-butyl betaine **4a** with 1.5 equiv of DMAD was carried out in toluene at 110 °C for 10 h. The isolated product was not a simple 1 : 1 adduct but an unexpected ring-enlargement adduct having a pyrrolotriazocinone skeleton, 2-*tert*-butyl-2,3-bis(methoxycarbonyl)-5,6-dihydropyrrolo[1,2-*d*][1,2,4]triazocin-6-one (**6aa**) along with its structural isomer, 1-*tert*-butyl-4-(1'-methoxycarbonyl-2'-pyrrolylmethylene)-3-methoxycarbonyl-2-pyrazolin-5-one (**13aa**), in 32% and 11% yields, respectively (recovery of **4a**: 46% / ^{1}H-NMR). The structure of **6aa** was determined by spectral analysis. In the ^{1}H-NMR spectrum, three protons on the pyrrole ring (δ 6.39, 6.40, 7.50) of **6aa** were shifted to higher magnetic field than those of betaine **4a** (δ 6.91, 7.0, 7.95), reflecting disappearance of the mesomeric effect in **6aa**. Furthermore, in the present study, crystalline **6aa** was subjected to X-ray crystallographic analysis to confirm the fused eight-membered triazocinone skeleton (Figure 1). The pyrrole ring and the triazocinone skeleton in **6aa** are not coplanar but bent to avoid steric strain. The structure of product **13aa** was also determined by spectral data and elemental analysis. The mass spectrum of **13aa** indicated that this product has the same molecular weight (M^+: *m/z* 333) with **6aa**. A strong absorption at 1704 cm^{-1} in the IR spectrum of **13aa** is assigned to a C=O stretching of cyclic amides such as pyrazolinones. In the ^{1}H-NMR spectrum, a methine proton on the bridging carbon was observed at unusually low field (δ 9.64) suggesting an anisotropic effect of the carbonyl group(s). Moreover, the proposed structure for **13aa**, as a combination of pyrrole and pyrazolinone rings, was unambiguously supported by X-ray analysis of the red crystal of an analogous product **13ba** (Figure 2). Both rings in **13ba** are nearly coplanar, indicative of extensive conjugation. The coplanar structure, including two carbonyl groups of **13ba**, explains the low chemical shift (δ 9.74) of the methine proton between the two rings, as the result of the anisotropic effect of the carbonyl groups.

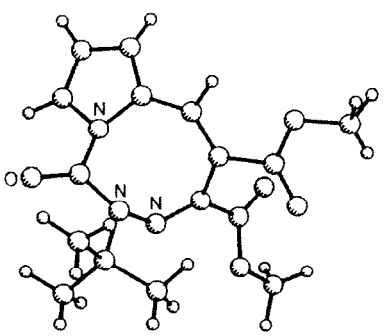


Figure 1. ORTEP view of triazocinone **6aa**

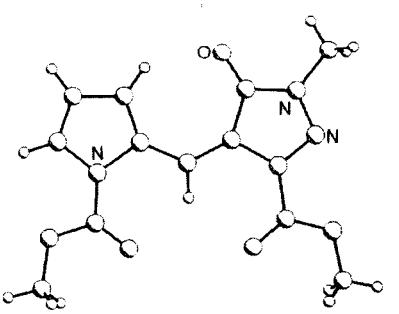
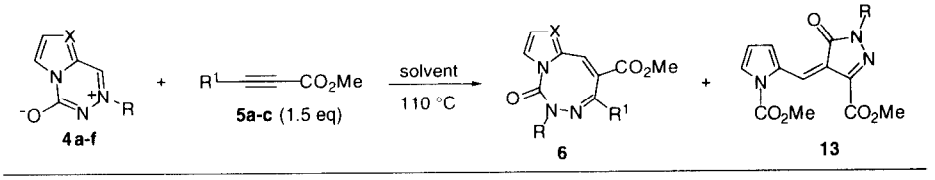


Figure 2. ORTEP view of pyrazolinone **13ba**

The detailed results of the cycloaddition of various betaine derivatives **4** with electron-deficient acetylenic dipolarophiles under several sets of conditions, leading to two types of products **6** and **13** are listed in Table 1. Treatment of betaines **4a-c** with DMAD (**5a**) in nonpolar solvents generally resulted in higher yields (entries 1-3 and 9). Under severe conditions (140 °C), the increased yield of **13ba** probably was the result of the isomerization of **6ba** to **13ba** (entry 2). The addition of some Lewis acids was then examined for accelerating the cycloaddition reaction. Interestingly, the addition of a catalytic amount (0.1 equiv) of $MgBr_2 \cdot 6H_2O$ improved the yield of triazocinone **6ba** to 54% (entry 4). It appears that magnesium bromide coordinates to the carbonyl oxygen to lower the LUMO level of **5a**, because the lower magnetic field shift of the methyl proton was observed by ^{1}H-NMR when magnesium bromide was added to a $CDCl_3$ solution of DMAD. However, other additives, such as $TiCl_4$, $AlCl_3$ and $ZnBr_2$ were not effective in improving the yield of **6**, except that $ZnBr_2$ restrained the formation of pyrazolinone **13**. In the case of polar solvents such as CH_3CN and $CHCl_3$ (entries 5 and 6), compound **6ba** was obtained in lower yields, because of a faster isomerization of triazocinone **6** to the by-product **13** in these solvents, which was confirmed by the monitoring of the reaction by ^{1}H-NMR (see Scheme 6). Hence, nonpolar solvents were employed in the other entries. As shown in entries 7 and 8, betaine **4b**, when reacted with electron-deficient dipolarophiles **5b,c** in the presence of a Lewis acid, gave only the triazocinone derivatives **6bb** and **6bc** in 20% and 35% yields, respectively. In both cases the products **6**, which have an ester group on 2-position, were formed as the main products. In contrast, the reactions of imidazo betaines **4d** and **4e** with **5a** gave no cycloadducts (entries 10 and 11), where the polymerization of **5a** was observed and the betaines remained nearly unchanged in both cases. In case of the phenyl derivative **4f**, a complex mixture of products was formed and pyrazolinone derivative **13fa** was isolated in only 5% yield (entry 12).

Table 1. Cycloaddition of Betaines 4 with Electron-deficient Dipolarophiles 5

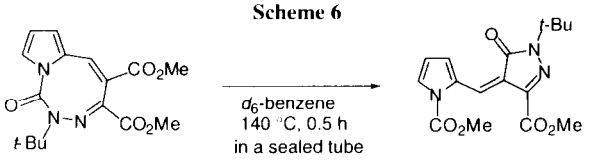


entries	betaines 4			dipolarophiles 5		solvent	time (h)	yield (%)[a]			
		R	X		R^1			6		13	
1	**4a**	t-Bu	CH	**5a**	CO_2Me	PhMe	10	**6aa**	32	**13aa**	11
2	**4b**	Me	CH	**5a**	CO_2Me	xylene[b]	10	**6ba**	33	**13ba**	17
3	**4b**	Me	CH	**5a**	CO_2Me	PhH	50	**6ba**	41	**13ba**	5
4	**4b**	Me	CH	**5a**	CO_2Me	PhH[c]	50	**6ba**	54	**13ba**	8
5	**4b**	Me	CH	**5a**	CO_2Me	CD_3CN	50	**6ba**	27[d]	**13ba**	8
6	**4b**	Me	CH	**5a**	CO_2Me	$CDCl_3$	50	**6ba**	3[d]	**13ba**	17
7	**4b**	Me	CH	**5b**	Ph	PhH[c]	100	**6bb**	20	**13bb**	—
8	**4b**	Me	CH	**5c**	H	PhH[c]	100	**6bc**	35	**13bc**	—
9	**4c**	$PhCH_2$	CH	**5a**	CO_2Me	PhH	45	**6ca**	32	**13ca**	5
10	**4d**	Me	N	**5a**	CO_2Me	PhH	50	**6da**	0[e]	**13da**	0
11	**4e**	$PhCH_2$	N	**5a**	CO_2Me	PhH	50	**6ea**	0[e]	**13ea**	0
12	**4f**	Ph	CH	**5a**	CO_2Me	PhMe	10	**6fa**	nd.[f]	**13fa**	5

[a] Isolated yields. [b] Reaction temperature: 140 °C. [c] $MgBr_2 \cdot 6H_2O$ (0.1 eq) was added. [d] Estimated by ^{1}H-NMR.
[e] Betaines **4** were recovered in almost quantitative yields. [f] nd.: not detected.

The in situ thermal transformation of the triazocinone derivative **6** to the by-product **13** was confirmed by heating a solution of the isolated **6aa** in d_6-benzene in an NMR tube at 140 °C for 0.5 h. As a result, the skeletal isomerization to **13aa** was observed in 21% yield (recovery of **6aa**: 37%) (Scheme 6).

Scheme 6



In general the reactivity and the regioselectivity of the 1,3-dipolar cycloaddition can be predicted, based on MO calculation.[11,17] For the case of entry 10, for example, calculation by the PM3 method indicates that the HOMO-LUMO energy gap (ΔE = 8.47 eV) between imidazo betaine **4d** and DMAD (**5a**) is larger than that (ΔE = 7.83 eV) between pyrrolo betaine **4b** and **5a** (vide infra). The orbital correlation suggests the lower reactivity of **4d** toward **5a** than that of **4b**. The regioselectivity of the cycloaddition will be discussed later in connection with the results of reactions with electron-rich dipolarophiles.

Cycloaddition of Mesomeric Betaines with Electron-rich Dipolarophiles.

The synthesized betaines **4** showed 1,3-dipolar characteristics in the presence of electron-deficient dipolarophiles to give triazocinone derivatives **6**. However, the yields of **6** were not high (~54%) and the mechanism for the formation of **6** could not be confirmed. Thus, the application of these betaines **4** to an inverse electron-demand type cycloaddition (Type III; LUMO controlled[11]) was then attempted. The orbital correlations calculated by PM3 method, which indicated that the HOMO-LUMO energy gap (ΔE = 7.57 eV) between **4b** and an electron-rich dipolarophile such as ynamine **14a** is smaller than that (ΔE = 7.83 eV) between **4b** and DMAD (**5a**), suggest a higher reactivity of ynamines **14** toward **4** (Figure 3). In the case of imidazo betaine **4d**, a lowering of the HOMO by 0.12 eV should allow the cycloaddition to proceed under milder conditions.

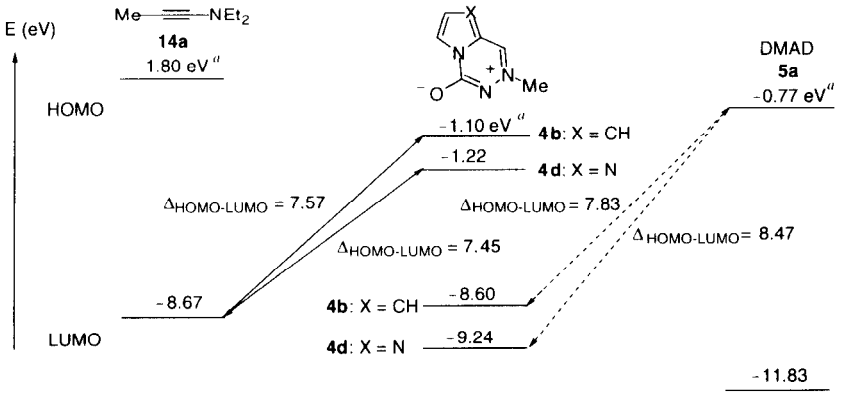


Figure 3. Orbital Correlation between the Betaines **4b,d** and Acetylenic Dipolarophiles**14a** and **5a**. [a] Calculated by PM3.

Initially, a suspension of 2-*tert*-butylbetaine **4a** and 1-(*N*,*N*-diethylamino)-1-propyne[18] **14a** in benzene was heated at 110 °C for 20 h to give only a ring-enlarged adduct having a pyrrolotriazocinone skeleton, 5-*tert*-butyl-3-diethylamino-2-phenyl-5,6-dihydropyrrolo[1,2-*d*][1,2,4]triazocin-6-one (**16aa**) in 85% yield after purification by silica gel column chromatography. The structure of the bicyclic product **16aa** was determined by spectral data and elemental analysis. In the ^{1}H-NMR spectrum, a vinylic proton (δ 6.40) on C1 atom was shifted to lower magnetic field than the β-vinilic protons of normal enamines, suggesting that the electron-donating diethylamino group is not located on the C2 atom. Formation of the urea-type carbonyl group of **16aa** was indicated by both ^{13}C-NMR (δ 170.2) and IR spectra (1680 cm^{-1}). The mass spectrum (CI) indicated a molecular weight of **16aa** as 303 (M^+ +1), which corresponds to a 1 : 1 adduct of **4a** and **14a**. Furthermore, the proposed structure for **16aa** as the bicyclic triazocinone was fully supported by X-ray analysis of a colorless crystal of the analogous compound **16ca** (Figure 4).

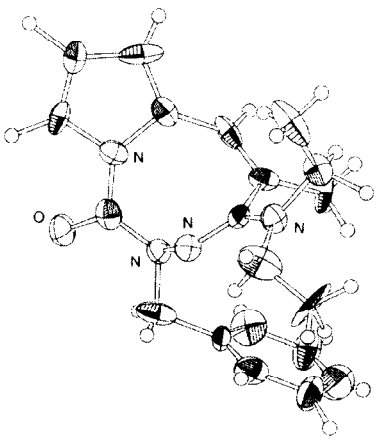
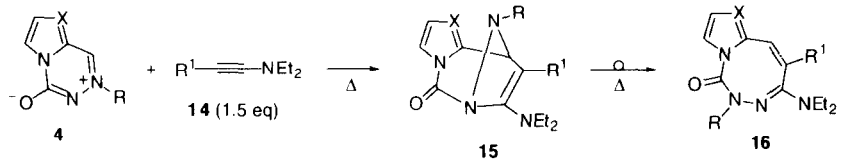


Figure 4. ORTEP view of triazocinone derivative **16ca**

Table 2 represents the results of the cycloaddition of various betaines **4a-e** with ynamines **14a,b**. Treatments of the cyclic azomethine imines **4a-c** with excess (1.5 eq) of **14a,b** at high temperature (110 °C) in benzene gave only triazocinone derivatives **16** in nearly quantitative yields (entries 1, 2, 4, 5, 7 and 8). In the presence of stoichiometric amounts of **14**, the cycloaddition provided the final products in low yields because of polymerization of **14** (entries 7-9). The cycloaddition was then carried out in CH_2Cl_2 at 60 °C in the hope of higher yields of the products, since CH_2Cl_2 is a better solvent for **4** than benzene and, furthermore, the isomerization corresponding to that from **16** to the by-product **13** does not proceed at all for the cycloadducts **16** even in polar solvents. Contrary to our expectation, the reaction of **4a** with **14b** in CH_2Cl_2 at 60 °C gave only **16ab** in 6% yield (entry 3). On the other hand, the betaine **4b**, which has a substituent smaller than a *tert*-butyl group, reacted with **14b** in CH_2Cl_2 at 60 °C to give a presumed 1 : 1 initial adduct **15bb** in 43% yield (entry 6). Similarly, in cases of **4c** and **14a,b**, the cycloaddition reactions took place smoothly to afford [3+2] tricyclic adducts, 6,9-benzylimino-7-diethylamino-8-methyl-5,6-dihydropyrrolo[1,2-*c*][1,3]diazepine-5-one (**15ca**) and 6,9-benzylimino-7-diethylamino-8-phenyl-5,6-dihydropyrrolo[1,2-*c*][1,3]diazepine-5-one (**15cb**) in 84% and 82% yields, respectively after purification by preparative GPC using chloroform as an eluent (entries 8 and 10). The reaction of imidazo betaine **4d** and **14b** in CH_2Cl_2 at 60 °C also provided the

Table 2. Cycloaddition of Betaines 4 with Ynamines 14[a,b]



entries	betaines 4			ynamines 14	solvent	temp. (°C)	yield (%)[c]			
		R	X	R^1			15		16	
1	**4a**	*t*-Bu	CH	**14a** Me	C_6D_6	110	**15aa**	0	**16aa**	85 (100)
2	**4a**	*t*-Bu	CH	**14b** Ph	C_6D_6	110	**15ab**	0	**16ab**	85 (100)
3	**4a**	*t*-Bu	CH	**14b** Ph	CD_2Cl_2	60	**15ab**	0	**16ab**	(6)
4	**4b**	Me	CH	**14a** Me	C_6D_6	110	**15ba**	0	**16ba**	69 (100)
5	**4b**	Me	CH	**14b** Ph	C_6D_6	110	**15bb**	0	**16bb**	89 (100)
6	**4b**	Me	CH	**14b** Ph	CD_2Cl_2	60	**15bb**	(43)	**16bb**	(9)
7	**4c**	$PhCH_2$	CH	**14a** Me	C_6D_6	110	**15ca**	0	**16ca**	81 (100)
8	**4c**	$PhCH_2$	CH	**14a** Me	CD_2Cl_2	60	**15ca**	84	**16ca**	0
9	**4c**	$PhCH_2$	CH	**14b** Ph	C_6D_6	110	**15cb**	0	**16cb**	68 (100)
10	**4c**	$PhCH_2$	CH	**14b** Ph	CD_2Cl_2	60	**15cb**	82	**16cb**	(10)
11	**4d**	Me	N	**14b** Ph	C_6D_6	110	**15db**	(1)	**16db**	86 (99)
12	**4d**	Me	N	**14b** Ph	CD_2Cl_2	60	**15db**	(40)	**16db**	(8)
13	**4e**	$PhCH_2$	N	**14a** Me	C_6D_6	110	**15ea**	0	**16ea**	71
14	**4e**	$PhCH_2$	N	**14b** Ph	C_6D_6	110	**15eb**	0	**16eb**	91 (100)
15	**4e**	$PhCH_2$	N	**14b** Ph	CD_2Cl_2	r.t.	**15eb**	89	**16eb**	0

[a] In sealed tubes. [b] Reaction time = 20 h. [c] Isolated yields (^{1}H-NMR yields are given in parentheses.).

tricyclic adduct **15db** (entry 12), while **16db** was obtained in high yield from a reaction at 110 °C in benzene (entry 11). It should be emphasized that the cycloaddition reaction of **4e** with **14b** in CH_2Cl_2 proceeded at room temperature to give only imidazodiazepinone **15eb** in 89% yield (entry 15).

The structure of **15ca** was determined by spectral data and HR-Mass spectrum. In the NMR spectra of **15ca** (C_6D_6 as a solvent), a singlet peak was observed at δ 3.85 which was characterized as a proton on the carbon atom at bridgehead (δ = 67.4). The carbonyl absorption (1754 cm^{-1}) in the IR spectrum is shifted to higher wave numbers than those of carbonyl groups of typical cyclic ureas. It seems that a lone pair of electrons on the nitrogen atom at the bridgehead can not be involved in conjugation with the vicinal carbonyl group because of steric strain. In the EI mass spectrum, an M^+ ion peak was observed at *m/z* 336, indicating that **15ca** is a isomer of **16ca**. All spectral data strongly support the conclusion that the isolated product is the tricyclic diazepinone compound containing nitrogen atom at bridgehead position. The isolated compounds **15** were air-stable below room temperature, but hydrolyzed on alumina or silica gel to give the pyrrole derivatives. The tricyclic structures for **15cb** and **15eb** were also defined by spectral analysis and HR-MS analysis.

By employing the ynamines **14** as a dipolarophile, the yield of the triazocinone derivatives **16** was nearly quantitative at 110 °C and the formation of the diazepinone derivatives **15** was successfully confirmed in CH_2Cl_2 at 60°C. In the case of *tert*-butylated betaine **4a**, however, the tricyclic adduct **15ab** was not obtained (entry 3). The failure to observe the formation of **15ab** at 60 °C may be accounted for by slow cycloaddition and rapid isomerization reaction. In the first cycloaddition step the approach of **14** to **4a** would be hindered by the bulky *tert*-butyl substituent, and the successive rearrangement of **15** to **16** would be accelerated by the

steric repulsion between a pyrrolo ring and a *tert*-butyl substituent on the bridged nitrogen atom in **15**. Unfortunately, the betaines **4** did not give cycloadducts with various olefinic dipolarophiles involving enamines, vinyl ethers, electron-deficient alkenes.

Thermal Rearrangement of Initial Adduct to Final Product

To develop a better understanding of the reaction mechanism of the cycloaddition, the time course of the thermal isomerization of the isolated **15cb** to **16cb** was monitored by ^{1}H-NMR at 95 °C (Figure 5). The gradual conversion of **15cb** to **16cb** was observed and was complete in 10 h, revealing the reaction route via **15** to **16** of the present 1,3-dipolar cycloaddition (Scheme 7). This transformation is analogous to the thermal rearrangement of a tricyclic compound into a benzazocine derivative reported by Padwa et al.[19]

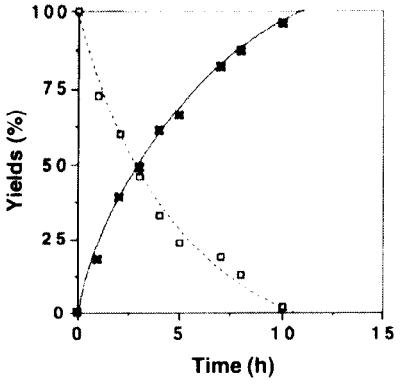
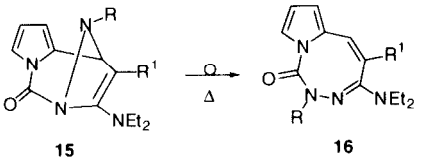


Figure 5. Time course of the thermal rearrangement of **15cb** to **16cb** in C_6D_6 at 95 °C (in a sealed tube).

Scheme 7



The activation energy of the isomerization of **15cb** to **16cb** was also estimated. From the slope of the Arrhenius plot (Figure 6), the value of activation energy (*Ea*) of the rearrangement was calculated to be 22 kcal/mol (92 kJ/mol).[20] The magnitude of the activation energy for the present thermal isomerization was comparable to those of intramolecular thermal rearrangements of some other heterocyclic compounds.[21]

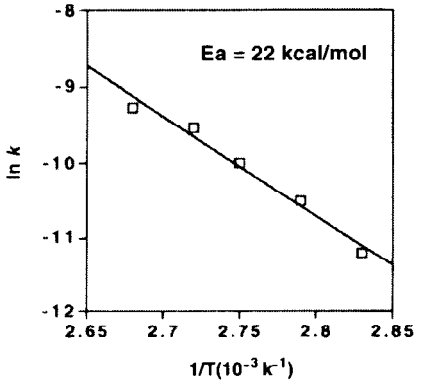


Figure 6. Arrhenius plot of ln *k* vs. 1/T for the thermal isomerization of **15cb** to **16cb**.

Regioselectivity of 1,3-Dipolar Cycloaddition

It is well known that the regioselectivity of 1,3-dipolar cycloaddition reactions is governed by the orbital coefficients of the bond-forming atoms in the HOMO and LUMO of the both reactants.[17] To clarify the regioselectivity of the present 1,3-dipolar cycloaddition, the orbital coefficients of betaines **4** and dipolarophiles **5** and **14** were calculated by the PM3 method and some of the values obtained are listed in Table 3.

Table 3. Coefficient Values[a] for FMOs of Betaine 4b andDipolarophiles 5b and 14a

reactants	MO	4b		5b		14a	
		C1	N3	C1[b]	C2	C1[b]	C2
4b	HOMO	0.36	-0.54				
	LUMO	-0.53	0.33				
5b	LUMO			-0.44	0.34		
14a	HOMO					-0.38	0.12

[a] Calculated by PM3 method. [b] C1 denotes the carbons next to phenyl substituent (**5b**) or methyl group (**14a**).

In the case of the cyclic azomethine imine **4b** and the acetylene **5b**, the N3 atom has a lager orbital coefficient than the C1 atom in **4b** (HOMO), and in **5b** the C1 atom has a larger one (LUMO). The predicted approach of **4b** to **5b** and subsequent intramolecular rearrangement affording the final products **6bb** are depicted in Figure 7, and the calculated prediction and the experimental result are in good agreement. As for

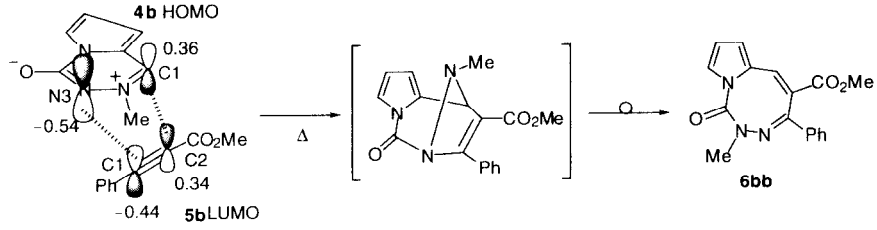


Figure 7. The Orientation of Betaine **4b** (HOMO) and Dipolarophile **5b** (LUMO) Leading to Triazocinone **6bb**.

the reaction of betaine **4b** and ynamine **14a**, the favored overlap of the lobes of both C1 atoms in **4b** (LUMO) and in **14a** (HOMO) dominates the regioselectivity of the cycloaddition (Figure 8).

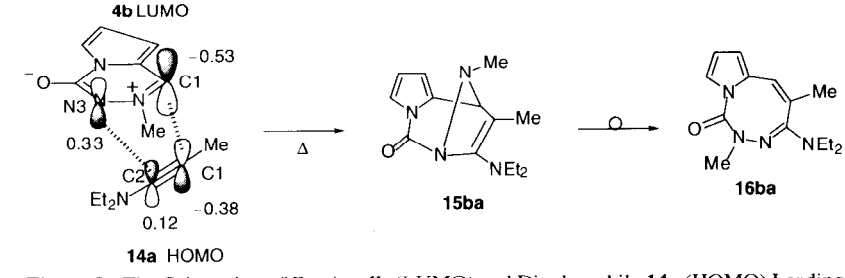


Figure 8. The Orientation of Betaine **4b** (LUMO) and Dipolarophile **14a** (HOMO) Leading to Triazocinone **16ba**.

Conclusion

Mesomeric betaines containing a pyrrolo- or imidazotriaziniumolate unit were readily synthesized by quaternization of pyrrolo- or imidazotriazinones with alkyl halides. The betaines were found to act as cyclic azomethine imines in the presence of acetylenic dipolarophiles to give unusual ring-expanding adducts containing bicyclic triazocinone structure in good to high yields. With electron-rich dipolarophiles such as ynamines, the formation of the initial 1 : 1 adducts, which could not be detected in the reactions with the electron-deficient dipolarophiles, was successfully observed as the precursors of the triazocinones. In particular, the imidazobetaines reacted with an ynamine even at room temperature to provide only the initial cycloadducts, the thermal isomerization of which proved to be a part of the pathway leading to the fused triazocinones. The reactivity and regioselectivity of the cycloaddition were in agreement with the results of MO calculations. Thus, the results herein show that the mesomeric betaines are isolable and highly tractable bicyclic 1,3-dipoles because of aromatic stability and should be good building blocks for the preparation of a variety of heteromulticyclic compounds. Further development of novel mesomeric betaines having a 1,3-dipolar nature is under investigation.

Experimental Section

General Procedure. Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were obtained on a HITACHI 270-30 infrared spectrophotometer. ^{1}H and ^{13}C-NMR spectra were recorded on a JEOL FT-NMR JNM EX 270 spectrometer (^{1}H-NMR, 270 MHz; ^{13}C-NMR, 68 MHz) and a JEOL FT-NMR JNM EX 90 spectrometer (^{1}H-NMR, 90 MHz; ^{13}C-NMR, 23 MHz), respectively, with tetramethylsilane as an internal standard. Mass spectra were measured on Shimadzu Model GCMS-QP2000 and GCMS-QP5000 spectrometers. High-resolution mass spectral data were obtained on a JEOL DX-303 mass spectrometer. Flash column chromatography (FCC) was performed using silica gel BW-300 (Fuji Silysia Chemical Co.). Preparative gel permeation liquid chromatography (GPLC) was performed on a JAI (Japan Analytical Industry) LC-908 instrument with JAIGEL 1H-2H columns and chloroform as an eluent. X-Ray crystallographic data for **6aa**, **13ba** and **16ca** were collected on a Rigaku four-cycle diffractometer AFC6R and AFC5R, respectively. The structures of **6aa** and **13ba** were solved by the direct method (MITHRIL).[22] The structure of **16ca** was also solved by the direct method (MULTAN88).[23] All calculations were performed using teXsan crystallographic software package of Molecular Structure Corporation.[24] All reactions were carried out under a nitrogen atmosphere, unless otherwise noted. Organic solvents were dried and distilled prior to use.

2-*tert*-Butylpyrrolo[1,2-*d*][1,2,4]triazinium-4-olate (**4a**). Preparation and spectral data of **4a** are reported in our previous report.[7]

Pyrrolo[1,2-*d*][1,2,4]triazin-4-one (**9**). Compound **8** was prepared via procedures described in the literature.[12] All of the spectroscopic data for **8** were in complete agreement with the reported data. Compound **9** was prepared as follows. A solution of **8** (5.2 g, 28.7 mmol) in DMF (50 mL) was added dropwise to NaH (60 wt % dispersion in mineral oil was washed with dry hexane three times, 115 mg, 2.86 mmol) at 0 °C and then heated at 100 °C for 15 h. After cooling the solvent was removed in vacuo and the

residue was subjected to silica gel column chromatography (hexane-EtOAc) to give 2.9 g (75%) of **9** as a white solid.

Imidazo[1,2-*d*][1,2,4]triazin-4-one (9'). A solution of imidazole-2-aldehyde **1'** (2.3 g, 24 mmol) and ethyl carbazate **7** (2.5 g, 24 mmol) in benzene (60 mL) was refluxed for 4 h and the solvent was removed under reduced pressure to afford 4.37 g (100%) of carbethoxyhydrazone **8'** as a white solid. A solution of the resulting **8'** (4.37 g, 24 mmol) in DMF (60 mL) was then added dropwise to NaH (60 wt % dispersion in mineral oil was washed with dry hexane three times, 96 mg, 2.4 mmol) at 0 °C and heated at 100 °C for 10 h. After cooling the solvent was removed and the crude products were separated on a silica gel column (hexane-EtOAc) to afford 1.93 g (59%) of **9'** as a white solid. **9'**: m.p. 248 °C (colorless prisms from hexane-CH_2Cl_2); IR (KBr) 1700 (C=O) cm $^{-1}$; ^{1}H-NMR (d_6-DMSO, 270 MHz) δ 7.65 (d, 1H, *J* = 3.6 Hz, H-7), 8.06 (d, 1H, *J* = 3.6 Hz, H-6), 8.47 (s, 1H, H-1), 12.92 (S, 1H, NH); ^{13}C-NMR (d_6-DMSO, 68 MHz) δ 114.0, 131.4, 134.1, 140.0, 144.9; MS (EI) *m/z* 136 (M^+); Anal. Calcd for $C_5H_4N_4O$: C, 44.12; H, 2.96; N, 41.16%. Found: C, 44.25; H, 3.03; N, 41.00%.

2-Methylpyrrolo[1,2-*d*][1,2,4]triazinium-4-olate (4b) and 3-Methyldihydropyrrolo[1,2-*d*][1,2,4]triazin-4-one (10b). To a suspension of pyrrolotriazinone **9** (134.5 mg, 0.99 mmol) and potassium carbonate (1.38 g, 10 mmol) in 1,4-dioxane (5 mL) was added methyl iodide (640 μL, 10.3 mmol) via a syringe. The solution was heated at 40 °C for 10 h and the solvent was removed under reduced pressure. The residue was poured into a mixture of water (100 mL) and CH_2Cl_2 (100 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (100 mL x 5). The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was washed with hexane (100 mL) and the remaining solid was dried in vacuo to give 119.2 mg (80%) of **4b** as a white solid and the filtrate was concentrated to afford 24.1 mg (16%) of **10b** as a white solid. **4b**: m.p. 250-253 °C (colorless prisms from hexane-CH_2Cl_2); IR (KBr) 1626 (C=O) cm $^{-1}$; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 4.05 (s, 3H, Me), 6.91 (dd, 1H, *J* = 4 Hz, *J* = 2.6 Hz, H-7), 7.00 (dd, 1H, *J* = 4 Hz, *J* = 1.3 Hz, H-8), 7.95 (dd, 1H, *J* = 2.6 Hz, *J* = 1.3 Hz, H-6), 8.23 (s, 1H, H-1); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 49.7, 112.7, 116.8, 118.7, 123.8, 127.3, 150.2; MS (EI) *m/z* 149 (M^+); Anal. Calcd for $C_7H_7N_3O$: C, 56.37; H, 4.73; N, 28.17%. Found: C, 55.99; H, 4.53; N, 28.17%. **10b**: m.p. 115-119 °C (colorless prisms from hexane); IR (KBr) 1700 (C=O) cm $^{-1}$; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 3.77 (s, 3H, Me), 6.68 (dd, 1H, *J* = 3.8 Hz, *J* = 3 Hz, H-7), 6.73 (dd, 1H, *J* = 3.8 Hz, *J* = 1.3 Hz, H-8), 7.75 (dd, 1H, *J* = 3 Hz, *J* = 1.3 Hz, H-6), 7.96 (s, 1H, H-1); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 38.6, 108.8, 115.4, 117.1, 125.6, 131.7, 145.0; MS (CI) *m/z* 150 (M^+ + 1); Anal. Calcd for $C_7H_7N_3O$: C, 56.37; H, 4.73; N, 28.17%. Found: C, 56.01; H, 4.63; N, 28.17%.

2-Benzylpyrrolo[1,2-*d*][1,2,4]triazinium-4-olate (4c) and 3-Benzyl-3,4-dihydropyrrolo [1,2-*d*][1,2,4]triazin-4-one (10c). The same procedure as above with pyrrolotriazinone **9** (135.2 mg, 1 mmol), benzyl bromide (360 μL, 3.03 mmol) and potassium carbonate (1.38 g, 10 mmol) in 1,4-dioxane (5 mL) gave 191.3 mg (85%) of **4c** as a white solid and 34.4 mg (15%) of **10c** as a white solid. **4c**: m.p. 212-214 °C (colorless prisms from hexane-CH_2Cl_2); IR (KBr) 1638 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 5.30 (s, 2H, $PhCH_2$), 6.89 (dd, 1H, *J* = 4 Hz, *J* = 2.6 Hz, H-7), 6.95 (dd, 1H, *J* = 4 Hz, *J* = 1.3 Hz, H-8),

7.4-7.5 (m, 5H), 7.95 (dd, 1H, J = 2.6 Hz, J = 1.3 Hz, H-6), 8.09 (s, 1H, H-1); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 66.1, 113.0, 116.9, 118.6, 124.0, 126.4, 129.3, 129.4, 129.6, 132.6, 150.4; MS (EI) *m/z* 225 (M^+); Anal. Calcd for $C_{13}H_{11}N_3O$: C, 69.31; H, 4.93; N, 18.66%. Found: C, 69.04; H, 4.90; N, 18.81%. **10c**: m.p. 73-74 °C (colorless prisms from hexane); IR (KBr) 1686 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 5.29 (s, 2H, $PhCH_2$), 6.67 (dd, 1H, J = 3.6 Hz, J = 1.3 Hz, H-8), 6.72 (dd, 1H, J = 3.6 Hz, J = 3 Hz, H-7), 7.2-7.5 (m, 5H), 7.76 (dd, 1H, J = 3 Hz, J = 1.3 Hz, H-6), 7.99 (s, 1H, H-1); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 54.4, 109.0, 115.6, 117.4, 125.5, 127.9, 128.5, 128.6, 132.1, 136.5, 144.9; MS (CI) *m/z* 225 (M^+); Anal. Calcd for $C_{13}H_{11}N_3O$: C, 69.32; H, 4.92; N, 18.66%. Found: C, 69.51; H, 4.96; N, 18.68%.

2-Methylimidazo[1,2-*d*][1,2,4]triazinium-4-olate (**4d**). The same procedure as above with imidazotriazinone **9'** (1 g, 7.3 mmol), methyl iodide (4.54 mL, 73 mmol) and potassium carbonate (10 g, 73 mmol) in 1,4-dioxane (100 mL) gave 0.62 g (57%) of **4d** as a white solid. **4d**: m.p. >300 °C (colorless prisms from hexane-CH_2Cl_2); IR (KBr) 1650 (C=O) cm^{-1}; ^{1}H-NMR (d_6-DMSO, 270 MHz) δ 4.10 (s, 3H, Me), 7.84 (d, J = 3.6 Hz, 1H, H-7), 8.02 (d, J = 3.6 Hz, 1H, H-6), 9.31 (s, 1H, H-1); ^{13}C-NMR (d_6-DMSO, 68 MHz) δ 44.2, 107.9, 122.7, 130.6, 133.5, 143.7; MS (EI) *m/z* 150 (M^+); Anal. Calcd for $C_6H_6N_4O$: C, 48.00; H, 4.03; N, 37.32%. Found: C, 47.87; H, 3.95; N, 37.51%.

2-Benzylimidazo[1,2-*d*][1,2,4]triazinium-4-olate (**4e**). The same procedure as above with imidazotriazinone **9'** (0.57 g, 4.2 mmol), benzyl bromide (0.87 mL, 7.3 mmol) and potassium carbonate (10 g, 73 mmol) in 1,4-dioxane (100 mL) gave 0.77 g (47%) of **4e** as a white solid. **4e**: m.p. 231 °C (colorless prisms from hexane-CH_2Cl_2); IR (KBr) 1656 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 5.43 (s, 2H, $PhCH_2$), 7.4-7.5 (m, 5H, Ph), 7.8 (d, 1H, J = 3.6 Hz, H-7), 7.99 (d, 1H, J = 3.6 Hz, H-6), 8.37 (s, 1H, H-1); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 67.7, 114.4, 125.6, 129.6, 129.8, 130.2, 131.4, 137.4, 139.0, 150.2; MS (EI) *m/z* 226 (M^+); Anal. Calcd for $C_{12}H_{10}N_4O$: C, 63.71; H, 4.46; N, 24.77%. Found: C, 63.65; H, 4.50; N, 24.49%

2-Phenylpyrrolo[1,2-*d*][1,2,4]triazinium-4-olate (**4f**). A 1,2-dichloroethane solution (10 mL) of **9** (95.1 mg, 1 mmol) and benzenediazonium-2-carboxylate **11** (247.5 mg, 1.67 mmol) was refluxed for 3 h and the solvent was removed in vacuo. The residue was subjected to silica gel column chromatography (hexane-EtOAc-MeOH) to give 19 mg (20%) of **4f** as a white solid. **4f**: m.p. 240-243 °C (colorless prisms from CH_2Cl_2); IR (KBr) 1638 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 7.00 (dd, 1H, J = 4 Hz, J = 2.6 Hz, H-7), 7.18 (dd, 1H, J = 4 Hz, J = 1.3 Hz, H-8), 7.5-7.6 (m, 3H, Ph), 7.8-7.9 (m, 2H, Ph), 8.05 (dd, 1H, J = 2.6 Hz, J = 1.3 Hz, H-6), 8.67 (s, 1H, H-1); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 114.6, 117.7, 119.3, 122.4, 124.5, 125.8, 129.6, 130.1, 144.0, 150.1; MS (EI) *m/z* 211 (M^+); Anal. Calcd for $C_{12}H_9N_3O$: C, 68.24; H, 4.29; N, 19.89%. Found: C, 68.28; H, 4.34; N, 19.82%.

5-*tert*-Butyl-2,3-bis(methoxycarbonyl)-5,6-dihydropyrrolo[1,2-*d*][1,2,4]triazocin-6-one (6aa) and 1-*tert*-Butyl-4-(1'-methoxycarbonyl-2'-pyrrolylmethylene)-3-methoxycarbonyl-2-pyrazolin-5-one (**13aa**). A mixture of 114.9 mg (0.601 mmol) of **4a** and 111.0 μL (0.902 mmol) of DMAD in toluene (5 mL) was treated to give 63.8 mg (32%) of **6aa** as a yellow solid, along with 22.0 mg

(11%) of **13aa** as a red solid and the recovery of 46% (^{1}H-NMR) of **4a**. **6aa**: m.p. 111-112 °C (yellow prisms from Et_2O-hexane); IR (KBr) 1740 (COOMe), 1704 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 90 MHz) δ 1.45 (s, 9H, *t*-Bu), 3.83 (s, 3H, Me), 3.85 (s, 3H, Me), 6.39 (dd, 1H, *J* = 3.5 Hz, *J* = 3.2 Hz, H-9), 6.39 (dd, 1H, *J* = 3.5 Hz, *J* = 1.7 Hz, H-10), 7.50 (dd, 1H, *J* = 3.2 Hz, *J* = 1.7 Hz, H-8), 7.96 (s, 1H, H-1); ^{13}C-NMR ($CDCl_3$, 23 MHz) δ 27.0, 52.4, 53.3, 61.4, 113.5, 120.8, 121.0, 129.3, 130.5, 137.7, 151.5, 162.7, 164.2, 167.1; MS (EI) *m/z* 333 (M^+); Anal. Calcd for $C_{16}H_{19}N_3O_5$: C, 57.65; H, 5.75; N, 12.61%. Found: C, 57.43; H, 5.71; N, 12.40%. **13aa**: m.p. 133-134 °C (red prisms from Et_2O); IR (KBr) 1758 (COOMe), 1712 (COOMe), 1704 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 90 MHz) δ 1.61 (s, 9H, *t*-Bu), 3.93 (s, 3H, Me), 4.04 (s, 3H, Me), 6.45 (dd, 1H, *J* = 3.9 Hz, *J* = 3.4 Hz, H-4'), 7.70 (dd, 1H, *J* = 3.4 Hz, *J* = 1.5 Hz, H-5'), 8.91 (dd, 1H, *J* = 3.9 Hz, *J* = 1.5 Hz, H-3'), 9.64 (s, 1H, -CH=); ^{13}C-NMR ($CDCl_3$, 23 MHz) δ 28.1, 52.0, 54.6, 58.6, 113.6, 120.2, 129.2, 130.1, 131.1, 135.7, 137.1, 150.6, 161.7, 163.2; MS (EI) *m/z* 291 (M^+); Anal. Calcd. for $C_{16}H_{19}N_3O_5$: C, 57.65; H, 5.75; N, 12.61%. Found: C, 57.60; H, 5.70; N, 12.59%.

2,3-Bis(methoxycarbonyl)-5-methyl-5,6-dihydropyrrolo[1,2-*d*][1,2,4]triazocin-6-one (6ba) and 1-Methyl-4-(1'-methoxycarbonyl-2'-pyrrolylmethylene)-3-methoxycarbonyl-2-pyrazolin-5-one (13ba). To a xylene solution (5 mL) of **4b** (114.9 mg, 0.998 mmol) was added 184.1 μL (1.5 mmol) of DMAD. The solution was refluxed for 10 h and the solvent was then removed under reduced pressure. The residue was subjected to silica gel column chromatography (hexane-EtOAc-MeOH) to give 97.5 mg (33%) of **6ba** as a yellow solid along with 49.9 mg (17%) of **13ba** as a red solid and the recovery of 6% (^{1}H-NMR) of **4b**. **6ba**: m.p. 120-121 °C (yellow prisms from hexane-Et_2O); IR (KBr) 1768 (COOMe), 1718 (COOMe), 1682 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 3.31 (s, 3H, N-Me), 3.83 (s, 3H, Me), 3.87 (s, 3H, Me), 6.34 (dd, 1H, *J* = 3.5 Hz, *J* = 3.3 Hz, H-9), 6.60 (dd, 1H, *J* = 3.5 Hz, *J* = 1.7 Hz, H-10), 7.46 (dd, 1H, *J* = 3.3 Hz, *J* = 1.7 Hz, H-8), 7.98 (s, 1H, H-1); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 38.6, 52.6, 53.5, 114.2, 120.6, 121.2, 128.9, 130.6, 138.0, 152.7, 162.5, 164.1, 164.9; MS (EI) *m/z* 291 (M^+); Anal. Calcd for $C_{13}H_{13}N_3O_5$: C, 53.61; H, 4.50; N, 14.43%. Found: C, 53.44; H, 4.43; N, 14.38%. **13ba**: m.p. 197-198 °C (red prisms from Et_2O); IR (KBr) 1758 (COOMe), 1716 (COOMe), 1668 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 90 MHz) δ 3.53 (s, 3H, N-Me), 3.95 (s, 3H, Me), 4.05 (s, 3H, Me), 6.48 (dd, 1H, *J* = 4.0 Hz, *J* = 3.5 Hz, H-4'), 7.73 (dd, 1H, *J* = 3.3 Hz, *J* = 1.6 Hz, H-5'), 9.01 (dd, 1H, *J* = 4.0 Hz, *J* = 1.6 Hz, H-3'), 9.74 (s, 1H, -CH=); ^{13}C-NMR ($CDCl_3$, 23 MHz) δ 32.1, 52.3, 54.8, 113.9, 118.2, 130.1, 130.9, 131.4, 137.1, 138.4, 150.6, 161.4, 162.9; MS (EI) *m/z* 291 (M^+); Anal. Calcd for $C_{13}H_{13}N_3O_5$: C, 53.61; H, 4.50; N, 14.43%. Found: C, 53.46; H, 4.45; N, 14.40%.

5-Benzyl-2,3-bis(methoxycarbonyl)-5,6-dihydropyrrolo[1,2-*d*][1,2,4]triazocin-6-one (6ca) and 1-Benzyl-4-(1'-methoxycarbonyl-2'-pyrrolylmethylene)-3-methoxycarbonyl-2-pyrazolin-5-one (13ca). A mixture of 227.3 mg (1.01 mmol) of **4c** and 185 μL (1.5 mmol) of DMAD in toluene (5 mL) was heated at 110 °C for 45 h and treated in a manner similar to that of **4a** to give 118 mg (32%) of **6ca** as a yellow solid along with 49.9 mg (17%) of **13ca** as a red solid. **6ca**: m.p. 120-121 °C (yellow prisms from hexane-CH_2Cl_2); IR (KBr) 1740 (COOMe), 1730 (COOMe), 1688 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 3.53 (s, 3H, Me), 3.72 (s, 3H, Me), 4.47 (d, 1H, *J* = 14 Hz, PhC<u>H</u>H), 5.41 (d, 1H, *J* = 14 Hz, PhCH<u>H</u>), 6.49 (t, 1H, *J* = 3.3 Hz, H-9), 6.70 (d, 1H, *J* = 3.3 Hz, H-10), 7.26-7.28 (m, 5H), 7.50

(d, 1H, J = 3.3 Hz, H-8), 7.96 (s, 1H, H-1); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 52.3, 53.5, 54.1, 114.2, 121.0, 121.5, 127.7, 128.4, 129.1, 129.4, 130.4, 135.0, 137.6, 152.0, 162.2, 163.5, 166.8; MS (CI) *m/z* 368 (M^+ + 1); Anal. Calcd for $C_{19}H_{17}N_3O_3$: C, 62.12; H, 4.66; N, 11.44%. Found: C, 62.10; H, 4.62; N, 11.45%. **13ca**: m.p. 156-158 °C (red prisms from CH_2Cl_2); IR (KBr) 1758 (COOMe), 1712 (COOMe) 1704 (C=O) cm $^{-1}$; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 3.96 (s, 3H, Me), 4.07 (s, 3H, Me), 5.11 (s, 2H, $PhCH_2$), 6.50 (dd, 1H, J = 3.9 Hz, J = 3 Hz, H-4'), 7.26-7.36 (m, 5H, Ph), 7.76 (d, 1H, J = 3 Hz, H-5'), 9.03 (d, 1H, J = 3.9 Hz, H-3'), 9.79 (s, 1H, -CH=); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 49.0, 52.4, 54.8, 114.0, 118.2, 127.7, 128.0, 128.6, 130.2, 130.9, 131.4, 136.4, 137.3, 138.9, 150.6, 161.6, 162.8; MS (CI) *m/z* 368 (M^++1); Anal. Calcd for $C_{19}H_{17}N_3O_5$: C, 62.12; H, 4.66; N, 11.44%. Found: C, 62.16; H, 4.81; N, 11.20%.

1-Phenyl-4-(1'-methoxycarbonyl-2'-pyrrolylmethylene)-3-methoxycarbonyl-2-pyrazolin-5-one (13fa). A mixture of 147.8 mg (0.7 mmol) of **4f** and 129 μL (1.05 mmol) of DMAD in toluene (7 mL) was heated at 110 °C for 10 h and treated in a manner similar to that of **4a** to give 12 mg (5%) of **13fa** as a red solid. **13fa**: m.p. 166-168 °C (red prisms from Et_2O); IR (KBr) 1768 (COOMe), 1732 (COOMe) 1684 (C=O) cm $^{-1}$; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 4.01 (s, 3H, Me), 4.09 (s, 3H, Me), 6.53 (dd, 1H, J = 4 Hz, J = 3.3 Hz, H-4'), 7.2-7.3 (m, 2H, Ph), 7.4-7.5 (m, 1H, Ph), 7.79 (d, 1H, J = 3.3 Hz, H-5'), 7.9-8.0 (m, 2H, Ph), 9.04 (d, 1H, J = 4 Hz, H-3'), 9.85 (s, 1H, -CH=); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 52.4, 54.8, 114.1, 118.6, 120.6, 126.1, 128.8, 130.6, 131.2, 131.3, 137.5, 137.9, 140.0, 150.6, 161.7, 161.9; MS (EI) *m/z* 353 (M^+); Anal. Calcd for $C_{18}H_{15}N_3O_5$: C, 61.19; H, 4.28; N, 11.89%. Found: C, 61.10; H, 4.22; N, 11.83%.

2-Methoxycarbonyl-5-methyl-3-phenyl-5,6-dihydropyrrolo[1,2-*d*][1,2,4]triazocin-6-one (6bb). A mixture of 149 mg (1 mmol) of **4b**, magnesium bromide hexahydrate (24 mg, 0.1 mmol) and 261 mg (1.5 mmol) of **5b** in benzene (1.2 mL) was heated at 110 °C for 100 h and treated as above to give 64.3 mg (20%) of **6bb** as a yellow solid. **6bb**: m.p. 97 °C (yellow prisms from hexane-CH_2Cl_2); IR (KBr) 1711 (COOEt), 1674 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 3.25 (t, 3H, CH_3), 3.87 (s, 3H, N-Me), 6.37 (t, 1H, J = 3.6 Hz, H-9), 6.53 (d, 1H, J = 3.6 Hz, H-10), 7.33-7.62 (m, 6H, H-8 and Ph), 8.08 (s, 1H, H-1); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 13.7, 37.6, 61.2, 113.9, 118.7, 124.8, 127.6, 128.5, 128.7, 128.7, 131.3, 134.8, 136.3, 153.6, 164.3, 172.9; MS (EI) *m/z* 309 (M^+); Anal. Calcd for $C_{17}H_{15}N_3O_3$: C, 66.01; H, 4.89; N, 13.58%. Found: C, 66.30; H, 5.09; N, 13.51%.

2-Methoxycarbonyl-5-methyl-5,6-dihydropyrrolo[1,2-*d*][1,2,4]triazocin-6-one (6bc). In a dry glass tube were placed 149 mg (1 mmol) of **4b** and 24 mg (0.1 mmol) of magnesium bromide hexahydrate and a solution of 126.1 mg (1.5 mmol) of **5c** in benzene (1.2 mL) was added to the tube via a syringe. The tube was then sealed under a N_2 atmosphere and heated at 110 °C for 100 h. The solvent was removed in vacuo and the residue subjected to silica gel column chromatography (hexane-AcOEt-MeOH) to yield 82 mg (35%) of **6bc** as yellow oil. **6bc**: yellow oil; IR (KBr) 1750 (COOMe), 1700 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 3.21 (s, 3H, Me), 3.87 (s, 3H, N-Me), 6.42 (t, 1H, J = 3.6 Hz, H-9), 6.57 (d, 1H, J = 3.6 Hz, H-10), 7.56 (d, 1H, J = 3.6 Hz, H-8), 7.84 (s, 1H, H-1) , 8.17 (s, 1H, H-3); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 38.1, 52.5, 113.9, 120.2, 121.7, 129.9, 130.1, 137.1, 153.6, 163.8, 164.7; MS (EI)

m/z 233 (M^+). Anal. Calcd for $C_{11}H_{11}N_3O_3$: C, 56.65; H,4.75; N, 18.02%. Found: C, 56.87; H, 4.71; N, 18.12%.

5-*tert*-Butyl-3-diethylamino-2-methyl-5,6-dihydropyrrolo[1,2-*d*][1,2,4]triazocin-6-one (16aa). In a dry NMR tube was placed 54.5 mg (0.28 mmol) of **4a** and a solution of 61 mg (0.9 mmol) of **14a** in d_6-benzene (400 μL) containing mesitylene (3.5 mg, 0.029 mmol) as an internal standard was added to the tube, which was then sealed under a N_2 atmosphere. The tube was heated at 110 °C for 20 h and monitored by ^{1}H-NMR. The solvent was removed in vacuo and the residue was subjected to flash column chromatography on silica gel (hexane : EtOAc = 7 : 3) to give 72.5 mg (85%) of **16aa** as a white solid. **16aa**: m.p. 117-120 °C (colorless prisms from hexane-CH_2Cl_2); IR (KBr) 1680 (C=O), 1558 (C=N) cm^{-1}; ^{1}H-NMR (C_6D_6, 270 MHz) δ 0.74 (t, 6H, *J* = 7.3 Hz, ($CH_2C\underline{H}_3$)x2), 1.58 (s, 9H, *t*-Bu), 1.60 (s, 3H, Me) 2.62 (q, 2H, *J* = 7.3 Hz, -CH_2-), 3.01 (brs, 2H, -CH_2-), 5.95 (d, 1H, *J* = 3.3 Hz, H-10), 6.14 (t, 1H, *J* = 3.3 Hz, H-9), 6.16 (s, 1H, H-1), 7.41 (d, 1H, *J* = 3.3 Hz, H-8); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 13.1, 20.5, 27.5, 41.8, 59.6, 110.3, 110.7, 122.7, 124.7, 128.6, 131.8, 153.5, 170.2; MS (CI) *m/z* 303 (M^+ + 1); Anal. Calcd for $C_{17}H_{26}N_4O$: C, 67.52; H, 8.67; N, 18.53%. Found: C, 67.14; H, 8.66; N, 18.28%.

5-*tert*-Butyl-3-diethylamino-2-phenyl-5,6-dihydropyrrolo[1,2-*d*][1,2,4]triazocin-6-one (16ab). The same procedure as above with 66.1 mg (0.34 mmol) of **4a** and 155.1 mg (0.89 mmol) of **14b** in d_6-benzene (700 μL) containing mesitylene (9 mg, 0.075 mmol) as an internal standard at 110 °C for 20 h gave 105 mg (85%) of **16ab** as a white solid. **16ab**: m.p. 158-160 °C (colorless prisms from hexane-CH_2Cl_2); IR (KBr) 1670 (C=O), 1556 (C=N) cm^{-1}; ^{1}H-NMR (C_6D_6, 270 MHz, 80 °C) δ 0.82 (t, 6H, *J* = 7.3 Hz, ($CH_2C\underline{H}_3$)x2), 1.49 (s, 9H, *t*-Bu), 2.76 (q, 2H, *J* = 7.3 Hz, -CH_2-), 3.23 (brs, 2H, -CH_2-), 6.10 (d, 1H, *J* = 3.3 Hz, H-10), 6.20 (t, 1H, *J* = 3.3 Hz, H-9), 6.98 (s, 1H, H-1), 7.03-7.13 (m, 3H), 7.35-7.37 (m, 2H), 7.46 (d, 1H, *J* = 3.3 Hz, H-8); ^{13}C-NMR ($CDCl_3$, 68 MHz, 60 °C) δ 13.0, 27.4, 29.7, 59.6, 110.9, 112.4, 121.3, 123.6, 125.4, 128.4, 128.8, 129.1, 134.0, 134.6, 153.4, 166.9; MS (CI) *m/z* 365 (M^+ + 1); Anal. Calcd for $C_{22}H_{28}N_4O$: C, 72.50; H, 7.74; N, 15.37%. Found: C, 72.38; H, 7.71; N, 15.35%.

3-Diethylamino-2,5-dimethyl-5,6-dihydropyrrolo[1,2-*d*][1,2,4]triazocin-6-one (16ba). A reaction similar to that above, with 179.3 mg (1.2 mmol) of **4b** and 193.2 mg (1.73 mmol) of **14a** in benzene (5 mL) solution at 110 °C for 20 h afforded a pale yellow solid. The crude solid was then subjected to preparative GPC using chloroform as an eluent to yield 214 mg (69%) of **16ba** as a white solid. **16ba**: m.p. 84-86 °C (colorless prisms from hexane-CH_2Cl_2); IR (KBr) 1672 (C=O), 1552 (C=N) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 1.03 (t, 6H, *J* = 7.3 Hz, ($CH_2C\underline{H}_3$)x2), 2.00 (s, 3H, Me), 3.07 (q, 2H, *J* = 7.3 Hz, -CH_2-), 3.1-3.3 (brs, 2H, -CH_2-), 3.21 (s, 3H, N-Me), 6.01 (d, 1H, *J* = 3.3 Hz, H-10), 6.22 (t, 1H, *J* = 3.3 Hz, H-9), 6.56 (s, 1H, H-1), 7.02 (d, 1H, *J* = 3.3 Hz, H-8); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 13.0, 20.7, 38.1, 42.1, 110.7, 110.9, 122.3, 124.0, 128.5, 132.7, 154.1, 169.8; MS (CI) *m/z* 261 (M^+ + 1); Anal. Calcd for $C_{14}H_{20}N_4O$: C, 64.59; H, 7.74; N, 21.52%. Found: C, 64.48; H, 7.72; N, 21.44%.

3-Diethylamino-5-methyl-2-phenyl-5,6-dihydropyrrolo[1,2-*d*][1,2,4]triazocin-6-one (**16bb**). The same procedure as above with 70 mg (0.47 mmol) of **4b** and 155.5 mg (0.9 mmol) of **14b** in d_6-benzene (500 μL) containing mesitylene (3.9 mg, 0.032 mmol) as an internal standard at 110 °C for 20 h gave 134 mg (89%) of **16bb** as a white solid. **16bb**: m.p. 95-96 °C (colorless prisms from hexane-CH_2Cl_2); IR (KBr) 1676 (C=O), 1564 (C=N) cm^{-1}; ^{1}H-NMR (C_6D_6, 270 MHz, 80 °C) δ 0.82 (t, 6H, *J* = 7.3 Hz, ($CH_2C\underline{H}_3$)x2), 2.77 (q, 2H, *J* = 7.3 Hz, -CH_2-), 3.06-3.10 (brs, 2H, -CH_2-), 3.22 (s, 3H, N-Me), 6.09 (d, 1H, *J* = 3.3 Hz, H-10), 6.21 (t, 1H, *J* = 3.3 Hz, H-9), 6.88 (s, 1H, H-1), 7.03-7.13 (m, 3H, Ph), 7.24-7.27 (m, 2H, Ph), 7.33 (d, 1H, *J* = 3.3 Hz, H-8); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 11.9, 13.6, 38.4, 41.5, 44.6, 111.3, 111.7, 122.1, 123.1, 125.3, 128.4, 128.6, 129.1, 135.6, 154.1, 167.1; MS (CI) *m/z* 323 (M^+ + 1); Anal. Calcd for $C_{19}H_{22}N_4O$: C,70.78; H, 6.88; N, 17.38%. Found: C, 70.67; H, 6.86; N, 17.38%.

5-Benzyl-3-diethylamino-2-methyl-5,6-dihydropyrrolo[1,2-*d*][1,2,4]triazocin-6-one (**16ca**). The same procedure as above with 113.3 mg (0.5 mmol) of **4c** and 117.1 mg (0.89 mmol) of **14a** in benzene (3 mL) solution at 110 °C for 20 h gave 138 mg (81%) of **16ca** as a white solid. **16ca**: m.p. 116-117 °C (colorless prisms from hexane-CH_2Cl_2); IR (KBr) 1662 (C=O), 1556 (C=N) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 0.97 (t, 6H, *J* = 7.3 Hz, ($CH_2C\underline{H}_3$)x2), 1.14 (s, 3H, Me), 2.93 (q, 2H, *J* = 7.3 Hz, -CH_2-), 3.26 (brs, 2H, -CH_2-), 4.19 (d, 1H, *J* = 13.9 Hz, PhC$\underline{H}$H), 5.49 (d, 1H, *J* = 13.9 Hz, PhCH$\underline{H}$), 5.97 (d, 1H, *J* = 3.3 Hz, H-10), 6.21 (t, 1H, *J* = 3.3 Hz, H-9), 6.40 (s, 1H, H-1), 7.08 (d, 1H, *J* = 3.3 Hz, H-8), 7.27-7.32 (m, 5H, Ph); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 13.0, 19.5, 42.1, 53.9, 110.7, 110.9, 122.3, 124.0, 127.5, 128.3, 128.7, 130.2, 133.2, 137.1, 154.3, 169.8; MS (CI) *m/z* 337 (M^+ + 1); Anal. Calcd for $C_{20}H_{24}N_4O$: C, 71.40; H, 7.19; N, 16.65%. Found: C, 71.47; H, 7.27; N, 16.59%.

5-Benzyl-3-diethylamino-2-phenyl-5,6-dihydropyrrolo[1,2-*d*][1,2,4]triazocin-6-one (**16cb**). The same procedure as above with 218.8 mg (0.97 mmol) of **4c** and 179.2 mg (1.04 mmol) of **14b** in toluene (15 mL) at 110 °C for 17 h gave 247.1 mg (68%) of **16cb** as a white solid. **16cb**: m.p. 133-134 °C (colorless prisms from hexane-CH_2Cl_2); IR (KBr) 1660 (C=O), 1560 (C=N) cm^{-1}; ^{1}H-NMR (C_6D_6, 270 MHz, 80 °C) δ 0.70 (t, 6H, *J* = 7.3 Hz, ($CH_2C\underline{H}_3$)x2), 2.66 (q, 2H, *J* = 7.3 Hz, -CH_2-), 3.08 (brs, 2H, -CH_2-), 4.62 (d, 1H, *J* = 14 Hz, PhC$\underline{H}$H), 5.32 (d, 1H, *J* = 14 Hz, PhCH$\underline{H}$), 6.09 (d, 1H, *J* = 3.3 Hz, H-10), 6.22 (t, 1H, *J* = 3.3 Hz, H-9), 6.83-6.86 (m, 2H), 6.92 (s, 1H, H-1), 6.96-6.98 (m, 6H), 7.24-7.27 (m, 2H), 7.36 (d, 1H, *J* = 3.3 Hz, H-8); ^{13}C-NMR ($CDCl_3$, 68 MHz, 60 °C) δ 12.7, 42.9, 55.1, 111.4, 112.3, 121.9, 123.7, 125.4, 127.3, 128.0, 128.1, 128.7, 129.8, 130.7, 135.3, 135.4, 136.7, 155.0, 166.8; MS (CI) *m/z* 399 (M^+ + 1); Anal. Calcd for $C_{25}H_{26}N_4O$: C, 75.35; H, 6.58; N, 14.06%. Found: C, 75.38; H, 6.57; N, 14.08%.

3-Diethylamino-5-methyl-2-phenyl-5,6-dihydroimidazo[1,2-*d*][1,2,4]triazocin-6-one (**16db**). The same procedure as above with 25 mg (0.167 mmol) of **4d** and 43.3 mg (0.25 mmol) of **14b** in benzene (2 mL) at 110 °C for 20 h gave 47 mg (86%) of **16db** as a white solid. **16db**: m.p. 97-99 °C (colorless prisms from hexane-C_6H_6); IR (KBr) 1692 (C=O) cm^{-1}; ^{1}H-NMR (C_6D_6, 270 MHz) δ 0.99 (t, 6H, *J* = 6.9 Hz, ($CH_2C\underline{H}_3$)x2), 1.19 (q, 2H, *J* = 6.9 Hz, -CH_2-), 3.25 (brs, 2H, -CH_2-), 3.5 (s, 3H, N-Me),

7.07 (s, 1H, H-1), 7.2-7.3 (m, 7H, Ph and imidazole protons); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 11.6, 13.5, 38.4, 41.3, 44.5, 119.7, 120.2, 125.5, 129.3, 129.5, 130.4, 134.6, 139.6, 142.8, 152.0, 166.4; MS (EI) *m/z* 323 (M^+); Anal. Calcd for $C_{18}H_{21}N_5O$: C, 66.85; H, 6.55; N, 21.66%. Found: C, 67.01; H, 6.57; N, 21.52%.

5-Benzyl-3-diethylamino-2-methyl-5,6-dihydroimidazo[1,2-*d*][1,2,4]triazocin-6-one (16ea). The same procedure as above with 200 mg (0.88 mmol) of **4e** and 147 mg (1.33 mmol) of **14a** in benzene (9 mL) at 110 °C for 20 h gave 210 mg (71%) of **16ea** as a white solid. **16ea**: m.p. 98-100 °C (colorless prisms from hexane-C_6H_6); IR (KBr) 1686 (C=O) cm^{-1}; ^{1}H-NMR (C_6D_6, 270 MHz) δ 0.99 (t, 6H, *J* = 6.9 Hz, ($CH_2C\underline{H}_3$)x2), 1.18 (q, 2H, *J* = 6.9 Hz, -CH_2-), 3.25 (brs, 2H, -CH_2-), 3.7 (s, 3H, N-Me), 4.2 (d, 1H, *J* = 14 Hz, PhC$\underline{H}$H), 5.48 (d, 1H, *J* = 14 Hz, PhCH$\underline{H}$), 7.07 (s, 1H, H-1), 7.27-7.32 (m, 7H, Ph and imidazole protons); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 13.0, 19.7, 42.3, 53.9, 119.3, 122.6, 127.9, 128.4, 129.1, 130.2, 136.4, 137.7, 142.9, 152.1, 168.9; MS (EI) *m/z* 337 (M^+); Anal. Calcd for $C_{19}H_{23}N_5O$: C, 67.63; H, 6.87; N, 20.76%. Found: C, 67.52; H, 6.62; N, 20.54%.

5-Benzyl-3-diethylamino-2-phenyl-5,6-dihydroimidazo[1,2-*d*][1,2,4]triazocin-6-one (16eb). The same procedure as above with 53 mg (0.24 mmol) of **4e** and 61 mg (0.35 mmol) of **14b** in benzene (4 mL) at 110 °C for 20 h gave 87 mg (91%) of **16eb** as a white solid. **16eb**: m.p. 173-174 °C (colorless prisms from hexane-PhH); IR (KBr) 1676 (C=O) cm^{-1}; ^{1}H-NMR (C_6D_6, 270 MHz) δ 0.8-1.0 (brs, 6H, ($CH_2C\underline{H}_3$)x2), 2.8-3.4 (brs, 4H, (CH_2)x2), 4.48 (d, 1H, *J* = 14 Hz, PhC$\underline{H}$H), 5.22 (d, 1H, *J* = 14 Hz, PhCH$\underline{H}$), 6.9 (s, 1H, H-1), 6.93 (d, 1H, *J* = 1.3 Hz, H-9), 7.10-7.26 (m, 10H, Ph), 7.35 (d, 1H, *J* = 1.3 Hz, H-8); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 12.1, 13.2, 41.1, 44.5, 55.1, 119.2, 120.1, 125.7, 127.8, 128.3, 128.9, 129.1, 129.7, 129.9, 134.0, 135.6, 140, 142.9, 152.3, 165.9; MS (EI) *m/z* 399 (M^+); Anal. Calcd for $C_{24}H_{25}N_5O$: C, 72.16; H, 6.31; N, 17.53%. Found: C, 72.25; H, 6.37; N, 17.49%.

6,9-Benzylimino-7-diethylamino-8-methyl-5,6-dihydropyrrolo[1,2-*c*][1,3]diazepin-5-one (15ca). In a dry NMR tube was placed 83.5 mg (0.1 mmol) of **4c** and a solution of 86.4 mg (0.72 mmol) of **14a** in d_2-dichloromethane (500 μL) containing mesitylene (7.8 mg, 0.065 mmol) as an internal standard was added to the tube via a syringe and the tube was then sealed under a N_2 atmosphere. The tube was heated at 60 °C for 20 h and monitored by ^{1}H-NMR. The tube was opened and the solvent was removed in vacuo and the residue was subjected to preparative GPC using chloroform as an eluent to give 54 mg (43%) of **15ca** as pale yellow oil and the starting **4c** (14.9 mg). **15ca**: IR (KBr) 1754 (C=O) cm^{-1}; ^{1}H-NMR (C_6D_6, 270 MHz) δ 0.88 (t, 6H, *J* = 6.9 Hz, ($CH_2C\underline{H}_3$)x2), 1.52 (s, 3H, Me), 2.74 (q, 2H, *J* = 6.9 Hz, -CH_2-), 3.31 (q, 2H, *J* = 6.9 Hz, -CH_2-), 3.76 (d, 1H, *J* = 12.9 Hz, PhC$\underline{H}$H), 3.85 (s, 1H, H-9), 4.09 (d, 1H, *J* = 12.9 Hz, PhCH$\underline{H}$), 5.58 (dd, 1H, *J* = 3.3 Hz, *J* = 1.7 Hz, H-1), 5.80 (t, 1H, *J* = 3.3 Hz, H-2), 7.07-7.16 (m, 3H, Ph), 7.21 (dd, 1H, *J* = 3.3 Hz, *J* = 1.7 Hz, H-3), 7.28-7.31 (m, 2H, Ph); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 10.6, 13.8, 44.3, 57.2, 67.4, 101.5, 104.8, 110.4, 117.4, 127.4, 128.4, 129.1, 135.3, 136.9, 146.2, 155.6; MS (CI) *m/z* 337 (M^+ + 1); HR-MS. Calcd for $C_{20}H_{24}N_4O$: 336.1950 Found: 336.1950.

6,9-Benzylimino-7-diethylamino-8-phenyl-5,6-dihydropyrrolo[1,2-*c*][1,3]diazepin-5-one (15cb). A similar reaction as above with 23.3 mg (0.10 mmol) of **4c** and 61 mg (0.55 mmol) of **14b** in d_6-benzene (400 μL) containing mesitylene (3.5 mg, 0.029 mmol) as an internal standard at 60 ℃ for 24 h gave 33.8 mg (82%) of **15cb** as pale yellow oil and the starting **4c** (4 mg). **15cb**: IR (KBr) 1754 (C=O), 1642 (C=N) cm^{-1}; ^{1}H-NMR (C_6D_6, 270 MHz) δ 0.76 (t, 6H, J = 7.3 Hz, ($CH_2C\underline{H}_3$)x2), 2.69 (q, 2H, J = 7.3 Hz, -CH_2-), 3.43 (q, 2H, J = 7.3 Hz, -CH_2-), 3.88 (d, 1H, J = 12.9 Hz, PhC$\underline{H}$H), 4.14 (d, 1H, J = 12.9 Hz, PhCH$\underline{H}$), 4.59 (s, 1H, H-9), 5.68 (t, 1H, J = 3.3 Hz, H-2), 5.83 (d, 1H, J = 3.3 Hz, H-1), 7.04 (m, 5H, Ph), 7.19 (m, 6H, Ph and H-3); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 13.6, 44.4, 57.5, 66.8, 104.0, 105.1, 110.9, 117.1, 125.4, 125.9, 127.4, 128.1, 129.2, 135.1, 136.1, 136.6, 147.8, 155.0; MS (CI) *m/z* 399 (M^+ + 1); HR-MS. Calcd. for $C_{25}H_{26}N_4O$: 398.2107 Found: 398.2082.

6,9-Benzylimino-7-diethylamino-8-phenyl-5,6-dihydroimidazo[1,2-*c*][1,3]diazepin-5-one (15eb). A similar reaction as above with 11.1 mg (0.05 mmol) of **4e** and 86.4 mg (0.72 mmol) of **14b** in d_6-benzene (500 μL) containing mesitylene (1.9 mg, 0.016 mmol) as an internal standard at room temperature for 20 h gave 17.7 mg (89%) of **15eb** as pale yellow oil. **15eb**: IR (KBr) 1770 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 0.94 (t, 6H, J = 6.9 Hz, ($CH_2C\underline{H}_3$)x2), 3.0 (q, 2H, J = 6.9 Hz, -CH_2-), 3.43 (q, 2H, J = 6.9 Hz, -CH_2-), 3.96 (d, 1H, J = 12.6 Hz, PhC$\underline{H}$H), 4.16 (d, 1H, J = 12.6 Hz, PhCH$\underline{H}$), 4.79 (s, 1H, H-9), 6.85 (d, 1H, J = 3.3 Hz, H-8), 7.16-7.32 (m, 11H, Ph and one proton on imidazole ring); ^{13}C-NMR ($CDCl_3$, 68 MHz) δ 13.6, 44.4, 57.4, 68.0, 102.0, 114.0, 125.9, 126.1, 127.7, 127.8, 128.2, 128.5, 129.2, 134.1, 135.8, 147.7, 153.0, 154.2; MS (EI) *m/z* 399 (M^+); HR-MS. Calcd for $C_{24}H_{25}N_5O$: 339.2059 Found: 339.2072.

X-Ray crystallographic analysis of 6aa: $C_{16}H_{19}N_3O_5$, M = 333.34, pale yellow prismatic, monoclinic, space group $P2_1/a$ (#14), a = 16.643 (7) Å, b = 10.655 (3) Å, c = 20.680 (6) Å, β = 110.05 (3)°, V = 3445 (2) Å^3, Z = 8, Dc = 1.285 g/cm^{-1}, F(000) = 1408, μ(Mo Kα) = 0.91 cm^{-1}, graphite monochromated MoKα (λ = 0.71069 Å), T = 25 °C. Final discrepancy factor: R = 0.060 and R_w = 0.050.

X-Ray crystallographic analysis of 13ba: $C_{13}H_{13}N_3O_5$, M = 291.16, red prismatic, monoclinic, space group $P2_1/c$ (#14), a = 7.825 (2) Å, b = 18.319 (2) Å, c = 9.769 (2) Å, β = 111.56 (2)°, V = 1302.4 (4) Å^3, Z = 4, Dc = 1.485 g/cm^{-1}, F(000) = 608, μ(Cu Kα) = 9.42 cm^{-1}, graphite monochromated CuKα (λ = 1.54178 Å), T = 23 °C. Final discrepancy factor: R = 0.072 and R_w = 0.102.

X-Ray crystallographic analysis of 16ca: $C_{20}H_{24}N_4O$, M = 336.44, colorless prismatic, triclinic, space group $P\bar{1}$ (#2), a = 9.654 (1) Å, b = 12.316 (2) Å, c = 7.971 (2) Å, α = 96.21 (2)°, β = 94.49 (2)°, γ = 82.58 (1)°, V = 923.7 (3) Å^3, Z = 2, Dc 1.210 g/cm^{-1}, F(000) = 360.00, μ(Mo Kα) = 0.77 cm^{-1}, graphite monochromated MoKα (λ = 0.71069 Å), T = 23 °C. Final discrepancy factor: R = 0.141 and R_w = 0.130.

Kinetic measurements of the thermal isomerization of 15cb to 16cb. A solution of **15ca** (1.8 mg, 0.015 mmol) in C6D6 (550 μL) containing of mesitylene (2 mg, 0.017 mmol) as an internal standard

was sealed in a series of NMR tubes and heated at several temperatures (353, 358, 363, 368 and 373 K), independently. The rate (k) of isomerization at each temperature was determined by the plots of ln (C/C0) vs. 1/T (K^{-1}).[25]: ln$k$ = -11.2 (353 K), ln$k$ = -10.5 (358 K), ln$k$ = -10.0 (363 K), ln$k$ = -9.61 (368 K), ln$k$ = -9.26 (373 K).

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25. C_0 and C denote the initial concentration of **15ca** and the concentration at each time, respectively.