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

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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. @ 1999 Elsevier Science Ltd. All rights reserved.

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Introduction

Mesomeric betaines¹ constitute a unique class of 1,3-dipoles² 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 skeleton⁴ 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 diaziridinone⁶ 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



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 calculation¹⁰ 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 classification¹¹]. 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



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 quaternization¹³ 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).



The structure of betaine 4b was deduced from spectral data and elemental analysis. A singlet at δ 8.23 in the ¹H-NMR spectrum was assigned to a methine proton at C-1, the signal of which appeared at δ 127.3 in the ¹³C-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 nitrogencontaining 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 '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 imidazotriazinone¹⁴ **9'** with alkyl halides. Imidazotriazinone **9'** was also prepared from imidazote-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.



On the other hand, benzenediazonium-2-carboxylate¹⁵ (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 triflate¹⁶ (a



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 2tert-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-2pyrazolin-5-one (13aa), in 32% and 11% yields, respectively (recovery of 4a: 46% / ¹H-NMR). The structure of **6aa** was determined by spectral analysis. In the ¹H-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** (8 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 ¹H-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 MgBr₂-6H₂O 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 ¹H-NMR when magnesium bromide was added to a CDCl₃ solution of DMAD. However, other additives, such as TiCl₄, AlCl₃ and ZnBr₂ were not effective in improving the yield of $\mathbf{6}$, except that ZnBr₂ restrained the formation of pyrazolinone 13. In the case of polar solvents such as CH₃CN and CHCl₃ (entries 5 and 6), compound **6ba** was obtained in lower yields, because of a faster isomerization of triazocinone $\mathbf{6}$ to the by-product 13 in these solvents, which was confirmed by the monitoring of the reaction by ¹H-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 $\mathbf{6}$, 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).

	/	+ R	R¹ <u>−</u>	⊑CO ₂ ; (1.5 eq	Me <u>solven</u>) 110 °C		CO ₂ M	Ле +		Me CC	∙ N D₂Me
entries		betaines 4			larophiles 5			yield (%)"			
		R	x		R ¹	solvent	time (h)	6		1:	3
1	4a	⊁Bu	СН	5a	CO ₂ Me	PhMe	10	6aa	32	13aa	11
2	4b	Me	СН	5a	CO ₂ Me	xylene ^b	10	6ba	33	13ba	17
3	4b	Me	СН	5a	CO ₂ Me	PhH	50	6ba	41	13ba	5
4	4b	Me	СН	5a	CO ₂ Me	PhH	50	6ba	54	13ba	8
5	4b	Me	СН	5a	CO ₂ Me	CD ₃ CN	50	6ba	27 ^J	13ba	8
6	4b	Me	СН	5a	CO ₂ Me	CDCb	50	6ba	3 ^{<i>d</i>}	13ba	17
7	4b	Me	СН	5 b	Ph	PhH ^c	100	6bb	20	13bb	_
8	4b	Me	СН	5c	н	PhH'	100	6bc	35	13bc	
9	4 c	PhCH ₂	СН	5a	CO ₂ Me	PhH	45	6ca	32	13ca	5
10	4d	Me	N	5a	CO ₂ Me	PhH	50	6da	0 ^e	13da	0
11	4e	PhCH₂	N	5a	CO ₂ Me	PhH	50	6ea	۴ 0	13ea	0
12	4f	Ph	СН	5a	CO ₂ Me	PhMe	10	6fa	nd. /	13fa	5

D

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

" Isolated yields. "Reaction temperature: 140 °C. ' MgBr₂-6H₂O (0.1 eq) was added. "Estimated by H-NMR.

^e Betaines 4 were recovered in almost quantitative yields. ¹nd.: 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).



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 ($\Delta E = 8.47 \text{ eV}$) 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 controlled¹¹) was then attempted. The orbital correlations calculated by PM3 method, which indicated that the HOMO-LUMO energy gap ($\Delta E = 7.57 \text{ eV}$) between 4b and an electron-rich dipolarophile such as ynamine 14a is smaller than that ($\Delta E = 7.83 \text{ eV}$) 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-propyne¹⁸ **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 ¹H-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 ¹³C-NMR (δ 170.2) and IR spectra (1680 cm⁻¹). The mass spectrum (C1) 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 CH₂Cl₂ at 60 °C in the hope of higher yields of the products, since CH₂Cl₂ 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 CH₂Cl₂ 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 CH₂Cl₂ 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-5one (**15ca**) and 6,9-benzylimino-7-diethylamino-8-phenyl-5,6-dihydropyrrolo[1,2-c][1,3]diazepine-5one (**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 CH₂Cl₂ at 60 °C also provided the __X N^{-R}

[−X

-0	4	⁺ R	R¹≡ 14 (1	=_NEt ₂ .5 eq)			Δ	O R	N-N 16	-R ¹ NEt ₂
		betaines	4	ynamines 14	<i>3-4</i>			y	ield (%) ^c	
entries		R	x	R ¹	solvent	temp. (°C)	1	5		16
1	4a	t-Bu	сн	14a Me	C ₆ D ₆	110	15 aa	0	16aa	85 (100)
2	4a	t-Bu	СН	14b Ph	C ₆ D ₆	110	15ab	0	16 a b	85 (100)
3	4a	t-Bu	СН	14b Ph	CD ₂ Cl ₂	60	15ab	0	16ab	(6)
4	4b	Ме	СН	14a Me	C ₆ D ₆	110	15ba	0	16ba	69 (100)
5	4b	Me	СН	14b Ph	C ₆ D ₆	110	15bb	0	16bb	89 (100)
6	4b	Ме	СН	14b Ph	CD ₂ Cl ₂	60	15bb	(43)	16bb	(9)
7	4c	PhCH ₂	СН	14a Me	C ₆ D ₆	110	15ca	0	16ca	81 (100)
8	4c	PhCH ₂	СН	14a Me	CD_2Cl_2	60	15ca	84	16ca	0
9	4c	PhCH ₂	СН	14b Ph	C ₆ D ₆	110	15cb	0	16cb	68 (100)
10	4c	PhCH ₂	СН	14b Ph	CD ₂ Cl ₂	60	15cb	82	16cb	(10)
11	4d	Мө	Ν	14b Ph	C ₆ D ₆	110	15db	(1)	16db	86 (99)
12	4d	Ме	Ν	14b Ph	CD ₂ Cl ₂	60	15db	(40)	16db	(8)
13	4e	PhCH ₂	Ν	14a Me	C ₆ D ₆	110	15ea	0	16ea	71
14	4e	PhCH ₂	Ν	14b Ph	C ₆ D ₆	110	15eb	0	16eb	91 (100)
15	4e	PhCH ₂	N	14b Ph	CD ₂ Cl ₂	r.t.	15eb	89	16eb	0

Table 2. Cycloaddition of Betaines 4 with Ynamines 14^{*a.b.*}

/--X

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

tricyclic adduct **15db** (entry 12), while **16db** was obtained in high yield from a reaction at 110 $^{\circ}$ C in benzene (entry 11). It should be emphasized that the cycloaddition reaction of **4e** with **14b** in CH₂Cl₂ 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 CH₂Cl₂ 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 ¹H-NMR at 95 $^{\circ}$ 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).

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.

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

			4b	5	b	14a		
reactants	мо	C1	N3	C1 ^b	C2	C1 ^b	C2	
4b	НОМО	0.36	-0.54					
	LUMO	-0.53	0.33					
5b	LUMO			-0.44	0.34			
14a	номо					-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. ¹H and ¹³C-NMR spectra were recorded on a JEOL FT-NMR JNM EX 270 spectrometer (¹H-NMR, 270 MHz; ¹³C-NMR, 68 MHz) and a JEOL FT-NMR JNM EX 90 spectrometer (¹H-NMR, 90 MHz; ¹³C-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-CH₂Cl₂); IR (KBr) 1700 (C=O) cm⁻¹; ¹H-NMR (d₆-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); ¹³C-NMR (d₆-DMSO, 68 MHz) δ 114.0, 131.4, 134.1, 140.0, 144.9; MS (EI) *m*/z 136 (M⁺); Anal. Calcd for C₅H₄N₄O: 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[1,2d][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 CH₂Cl₂ (100 mL). The organic layer was separated and the aqueous layer was extracted with CH₂Cl₂ (100 mL x 5). The combined organic extracts were dried over anhydrous MgSO₄ 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-CH₂Cl₂); IR (KBr) 1626 (C=O) cm⁻¹; ¹H-NMR (CDCl₃, 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 = 2.6Hz, J = 1.3 Hz, H-6), 8.23 (s, 1H, H-1); ¹³C-NMR (CDCl₃, 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 C₇H₇N₃O: C, 56.37; H, 4.73; N, 28.17%. Found: C, 55.99; H, 4.53; N, 28.17%. 10b: m.p. 115-119 ℃ (colorless prisms from hexane); IR (KBr) 1700 (C=O) cm^{-1} ; ¹H-NMR (CDCl₃, 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); ¹³C-NMR (CDCl₃, 68 MHz) & 38.6, 108.8, 115.4, 117.1, 125.6, 131.7, 145.0; MS (CI) m/z 150 (M⁺ + 1); Anal. Calcd for C7H7N3O: 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 μ L, 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-CH₂Cl₂); IR (KBr) 1638 (C=O) cm⁻¹; ¹H-NMR (CDCl₃, 270 MHz) δ 5.30 (s, 2H, PhCH₂), 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); ¹³C-NMR (CDCl₃, 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 C₁₃H₁₁N₃O: 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; ¹H-NMR (CDCl₃, 270 MHz) δ 5.29 (s, 2H, PhCH₂), 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); ¹³C-NMR (CDCl₃, 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 C₁₃H₁₁N₃O: 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-CH₂Cl₂); IR (KBr) 1650 (C=O) cm⁻¹; ¹H-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); ¹³C-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 C₆H₆N₄O: 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-CH₂Cl₂); IR (KBr) 1656 (C=O) cm⁻¹; ¹H-NMR (CDCl₃, 270 MHz) δ 5.43 (s, 2H, PhCH₂), 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); ¹³C-NMR (CDCl₃, 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 C₁₂H₁₀N₄O: 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 CH₂Cl₂); IR (KBr) 1638 (C=O) cm⁻¹; ¹H-NMR (CDCl₃, 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); ¹³C-NMR (CDCl₃, 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 C₁₂H₉N₃O: 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-6one (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% (¹H-NMR) of **4a**. **6aa**: m.p. 111-112 °C (yellow prisms from Et₂O-hexane); IR (KBr) 1740 (COOMe), 1704 (C=O) cm⁻¹; ¹H-NMR (CDCl₃, 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-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); ¹³C-NMR (CDCl₃, 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 C₁₆H₁₉N₃O₅: 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 Et₂O); IR (KBr) 1758 (COOMe), 1712 (COOMe), 1704 (C=O) cm⁻¹; ¹H-NMR (CDCl₃, 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=); ¹³C-NMR (CDCl₃, 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 C₁₆H₁₉N₃O₅: 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-2pyrazolin-5-one (13ba). To a xylene solution (5 mL) of 4b (114.9 mg, 0.998 mmol) was added 184.1 μ L (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% ('H-NMR) of 4b. 6ba: m.p. 120-121 °C (yellow prisms from hexane-Et₂O); IR (KBr) 1768 (COOMe), 1718 (COOMe), 1682 (C=O) cm⁻¹; ¹H-NMR (CDCl₃, 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); ¹³C-NMR (CDCl₃, 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 C13H13N3O5: 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 Et₂O); IR (KBr) 1758 (COOMe), 1716 (COOMe), 1668 (C=O) cm⁻¹; ¹H-NMR $(CDCl_{3}, 90 \text{ MHz}) \delta 3.53 \text{ (s, 3H, N-Me)}, 3.95 \text{ (s, 3H, Me)}, 4.05 \text{ (s, 3H, Me)}, 6.48 \text{ (dd, 1H, } J = 4.0 \text{ Hz}, J = 4.0 \text{ H$ 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=); ¹³C-NMR (CDCl₃, 23 MHz) & 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 C₁₃H₁₃N₃O₅: 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-2pyrazolin-5-one (13ca). A mixture of 227.3 mg (1.01 mmol) of 4c and 185 μ L (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-CH₂Cl₂); IR (KBr) 1740 (COOMe), 1730 (COOMe), 1688 (C=O) cm⁻¹; ¹H-NMR (CDCl₃, 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); ¹³C-NMR (CDCl₃, 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 C₁₉H₁₇N₃O₃: 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 CH₂Cl₂); IR (KBr) 1758 (COOMe), 1712 (COOMe) 1704 (C=O) cm⁻¹; ¹H-NMR (CDCl₃, 270 MHz) δ 3.96 (s, 3H, Me), 4.07 (s, 3H, Me), 5.11 (s, 2H, PhCH₂), 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=); ¹³C-NMR (CDCl₃, 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 C₁₉H₁₇N₃O₅: 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 Et₂O); IR (KBr) 1768 (COOMe), 1732 (COOMe) 1684 (C=O) cm⁻¹; ¹H-NMR (CDCl₃, 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=); ¹³C-NMR (CDCl₃, 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 C₁₈H₁₅N₃O₅: 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-6one (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-CH₂Cl₂); IR (KBr) 1711 (COOEt), 1674 (C=O) cm⁻¹; ¹H-NMR (CDCl₃, 270 MHz) δ 3.25 (t, 3H, CH₃), 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); ¹³C-NMR (CDCl₃, 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 C₁₇H₁₅N₃O₃: 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 N₂ 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; ¹H-NMR (CDCl₃, 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); ¹³C-NMR (CDCl₃, 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 C₁₁H₁₁N₃O₃: 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 N₂ atmosphere. The tube was heated at 110 °C for 20 h and monitored by ¹H-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-CH₂Cl₂); IR (KBr) 1680 (C=O), 1558 (C=N) cm⁻¹; ¹H-NMR (C₆D₆, 270 MHz) δ 0.74 (t, 6H, J = 7.3 Hz, (CH₂CH₃)x₂), 1.58 (s, 9H, *t*-Bu), 1.60 (s, 3H, Me) 2.62 (q, 2H, J = 7.3 Hz, -CH₂-), 3.01 (brs, 2H, -CH₂-), 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); ¹³C-NMR (CDCl₃, 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 (C1) *m/z* 303 (M⁺ + 1); Anal. Calcd for C₁₇H₂₆N₄O: 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-CH₂Cl₂); IR (KBr) 1670 (C=O), 1556 (C=N) cm⁻¹; ¹H-NMR (C₆D₆, 270 MHz, 80 °C) δ 0.82 (t, 6H, J = 7.3 Hz, (CH₂CH₃)x2), 1.49 (s, 9H, *t*-Bu), 2.76 (q, 2H, J = 7.3 Hz, -CH₂-), 3.23 (brs, 2H, -CH₂-), 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); ¹³C-NMR (CDCl₃, 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 C₂₂H₂₈N₄O: 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-CH₂Cl₂); IR (KBr) 1672 (C=O), 1552 (C=N) cm⁻¹; ¹H-NMR (CDCl₃, 270 MHz) δ 1.03 (t, 6H, J = 7.3 Hz, (CH₂CH₃)x2), 2.00 (s, 3H, Me), 3.07 (q, 2H, J = 7.3 Hz, -CH₂-), 3.1-3.3 (brs, 2H, -CH₂-), 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); ¹³C-NMR (CDCl₃, 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 (Cl) *m*/z 261 (M⁺ + 1); Anal. Calcd for C₁₄H₂₀N₄O: 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*₆benzene (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-CH₂Cl₂); IR (KBr) 1676 (C=O), 1564 (C=N) cm⁻¹; ¹H-NMR (C₆D₆, 270 MHz, 80 °C) δ 0.82 (t, 6H, *J* = 7.3 Hz, (CH₂CH₃)x2), 2.77 (q, 2H, *J* = 7.3 Hz, -CH₂-), 3.06-3.10 (brs, 2H, -CH₂-), 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); ¹³C-NMR (CDCl₃, 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 C₁₉H₂₂N₄O: 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-CH₂Cl₂); IR (KBr) 1662 (C=O), 1556 (C=N) cm⁻¹; ¹H-NMR (CDCl₃, 270 MHz) δ 0.97 (t, 6H, J = 7.3 Hz, (CH₂CH₃)x2), 1.14 (s, 3H, Me), 2.93 (q, 2H, J = 7.3 Hz, -CH₂-), 3.26 (brs, 2H, -CH₂-), 4.19 (d, 1H, J = 13.9 Hz, PhCHH), 5.49 (d, 1H, J = 13.9 Hz, PhCHH), 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); ¹³C-NMR (CDCl₃, 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 C₂₀H₂₄N₄O: 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-CH₂Cl₂); IR (KBr) 1660 (C=O), 1560 (C=N) cm⁻¹; ¹H-NMR (C₆D₆, 270 MHz, 80 °C) δ 0.70 (t, 6H, J = 7.3 Hz, (CH₂CH₃)x2), 2.66 (q, 2H, J = 7.3 Hz, -CH₂-), 3.08 (brs, 2H, -CH₂-), 4.62 (d, 1H, J = 14 Hz, PhC<u>H</u>H), 5.32 (d, 1H, J = 14 Hz, PhCH<u>H</u>), 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); ¹³C-NMR (CDCl₃, 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 C₂₅H₂₆N₄O: 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-C₆H₆); IR (KBr) 1692 (C=O) cm⁻¹; ¹H-NMR (C₆D₆, 270 MHz) δ 0.99 (t, 6H, J = 6.9 Hz, (CH₂CH₃)x2), 1.19 (q, 2H, J = 6.9 Hz, -CH₂-), 3.25 (brs, 2H, -CH₂-), 3.5 (s, 3H, N-Me), 7.07 (s, 1H, H-1), 7.2-7.3 (m, 7H, Ph and imidazole protons); ¹³C-NMR (CDCl₃, 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 C₁₈H₂₁N₅O: 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-C₆H₆); IR (KBr) 1686 (C=O) cm⁻¹; ¹H-NMR (C₆D₆, 270 MHz) δ 0.99 (t, 6H, J = 6.9 Hz, (CH₂CH₃)x2), 1.18 (q, 2H, J = 6.9 Hz, -CH₂-), 3.25 (brs, 2H, -CH₂-), 3.7 (s, 3H, N-Me), 4.2 (d, 1H, J = 14 Hz, PhCHH), 5.48 (d, 1H, J = 14 Hz, PhCHH), 7.07 (s, 1H, H-1), 7.27-7.32 (m, 7H, Ph and imidazole protons); ¹³C-NMR (CDCl₃, 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 C₁9H₂₃N₅O: 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; ¹H-NMR (C₆D₆, 270 MHz) δ 0.8-1.0 (brs, 6H, (CH₂C<u>H</u>₃)x2), 2.8-3.4 (brs, 4H, (CH₂)x2), 4.48 (d, 1H, J = 14 Hz, PhC<u>H</u>H), 5.22 (d, 1H, J = 14Hz, PhCH<u>H</u>), 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); ¹³C-NMR (CDCl₃, 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 C₂₄H₂₅N₅O: 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-5one (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 d2-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 N₂ atmosphere. The tube was heated at 60 °C for 20 h and monitored by ¹H-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; ¹H-NMR (C₆D₆, 270 MHz) δ 0.88 (t, 6H, J = 6.9 Hz, (CH₂CH₃)x2), 1.52 (s, 3H, Me), 2.74 (q, 2H, J = 6.9 Hz, -CH₂-), 3.76 (d, 1H, J = 12.9 Hz, PhCHH), 3.85 (s, 1H, H-9), 4.09 (d, 1H, J = 12.9 Hz, PhCHH), 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); ¹³C-NMR (CDCl₃, 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 C₂₀H₂₄N₄O: 336.1950 Found: 336.1950. **6,9-Benzylimino-7-diethylamino-8-phenyl-5,6-dihydropyrrolo**[1,2-c][1,3]diazepin-5one (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 °C 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; ¹H-NMR (C₆D₆, 270 MHz) δ 0.76 (t, 6H, *J* = 7.3 Hz, (CH₂CH₃)x2), 2.69 (q, 2H, *J* = 7.3 Hz, -CH₂-), 3.43 (q, 2H, *J* = 7.3 Hz, -CH₂-), 3.88 (d, 1H, *J* = 12.9 Hz, PhCHH), 4.14 (d, 1H, *J* = 12.9 Hz, PhCHH), 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); ¹³C-NMR (CDCl₃, 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 C₂₅H₂₆N₄O: 398.2107 Found: 398.2082.

6,9-Benzylimino-7-diethylamino-8-phenyl-5,6-dihydroimidazo[1,2-*c***]**[1,3]diazepin-5one (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; ¹H-NMR (CDCl₃, 270 MHz) δ 0.94 (t, 6H, *J* = 6.9 Hz, (CH₂C<u>H</u>₃)x2), 3.0 (q, 2H, *J* = 6.9 Hz, -CH₂-), 3.43 (q, 2H, *J* = 6.9 Hz, -CH₂-), 3.96 (d, 1H, *J* = 12.6 Hz, PhC<u>H</u>H), 4.16 (d, 1H, *J* = 12.6 Hz, PhCH<u>H</u>), 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); ¹³C-NMR (CDCl₃, 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 C₂₄H₂₅N₅O: 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 P2₁/a (#14), a = 16.643 (7) Å, b = 10.655 (3) Å, c = 20.680 (6) Å, $\beta = 110.05$ (3)°, V = 3445 (2) Å³, Z = 8, Dc = 1.285 g/cm⁻¹, F(000) = 1408, $\mu(Mo K\alpha) = 0.91$ cm⁻¹, graphite monochromated MoK α ($\lambda = 0.71069$ Å), T = 25 °C. Final discrepancy factor: R = 0.060 and Rw = 0.050.

X-Ray crystallographic analysis of 13ba: $C_{13}H_{13}N_{3}O_5$, M = 291.16, red prismatic, monoclinic, space group P2₁/c (#14), a = 7.825 (2) Å, b = 18.319 (2) Å, c = 9.769 (2) Å, $\beta = 111.56$ (2)°, V = 1302.4 (4) Å³, Z = 4, Dc = 1.485 g/cm⁻¹, F(000) = 608, μ (Cu K α) = 9.42 cm⁻¹, graphite monochromated CuK α ($\lambda = 1.54178$ Å), T = 23 °C. Final discrepancy factor: R = 0.072 and $R_w = 0.102$.

X-Ray crystallographic analysis of 16ca: C₂₀H₂₄N₄O, M = 336.44, colorless prismatic, triclinic, space group P1 (#2), a = 9.654 (1) Å, b = 12.316 (2) Å, c = 7.971 (2) Å, $\alpha = 96.21$ (2)°, $\beta = 94.49$ (2)°, $\gamma = 82.58$ (1)°, V = 923.7 (3) Å³, Z = 2, Dc 1.210 g/cm⁻¹, F(000) = 360.00, $\mu(Mo K\alpha) = 0.77$ cm⁻¹, graphite monochromated MoK α ($\lambda = 0.71069$ 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 μ L) 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: lnk = -11.2 (353 K), lnk = -10.5 (358 K), lnk = -10.0 (363 K), lnk = -9.61 (368 K), lnk = -9.26 (373 K).

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