obtained by silica gel chromatography of a portion, eluting with 81:51:1 dichloromethane-ethyl acetate-acetic acid followed by lyopholization of a benzene solution to give a foam which collapsed to an oil on standing: $[\alpha]^{25}_D$ +22.39° (c = 1.0, EtOH); EI MS m/z (relative intensity) 337 (M^+) (2), 220 (35), 163 (100); ^{1}H NMR ($CDCl_3$) δ 1.30 (s, 3 H, $C(CH_3)_3$ (minor rotamer)), 1.42 (s, 6 H, $C(CH_3)_3$ (major rotamer)), 2.90-3.2 (m, 2 H, β-CH_2), 3.60 (s, 2 H, CH_2), 3.69 (s, 3 H, OCH_3), 3.90 (m, 0.3 H, α-CH (minor rotamer)), 4.09 (m, 0.7 H, α-CH (major rotamer)), 4.99 (d, 0.7 H, J = 8 Hz, NH (major rotamer)), 6.30 (m, 0.3 H, NH (minor rotamer)), 7.15 (m, 2 H, ArH), 7.22 (m, 2 H, ArH). Anal. Calcd for $C_{17}H_{23}NO_6$: C, 60.52; H, 6.87; N, 4.15. Found: C, 60.28; H, 7.09; N, 3.97.

(*S*)-α-[[(1,1-Dimethylethoxy)carbonyl]amino]-4-[2-(1,1-dimethylethoxy)-2-oxoethyl]benzenepropanoic Acid (8c). A solution of 1.471 g of **7c** in 25 mL of methanol and 5 mL of 1 N sodium hydroxide solution was stirred at room temperature for 2 h. The mixture was acidified with a slight excess of hydrochloric acid, was diluted with 100 mL of ether and was washed with water and saturated sodium chloride solution. The residue obtained after filtration and evaporation was chromatographed over 100 g of silica gel, eluting with 40:59:0.5 ethyl acetate-hexane-acetic acid, and the product-containing fractions were combined, evaporated, diluted with toluene, and evaporated finally under high vacuum to give 1.105 g (78%) of **8c** as a white wax: $[\alpha]^{25}_D$ +21.41° (c = 1.00, EtOH); ^{1}H NMR ($CDCl_3$) δ 1.42 (s, 9 H, $C(CH_3)_3$), 1.44 (s, 9 H, $C(CH_3)_3$), 3.07 (m, 1 H, β-CH*H*), 3.15 (m, 1 H, β-C*H*H), 3.50 (s, 2 H, $ArCH_2$), 4.57 (m, α-CH), 4.93 (m, 1 H, NH), 7.14 (d, 2 H, J = 8 Hz, ArH), 7.21 (d, 2 H, J = 8 Hz, ArH). Anal. Calcd for $C_{20}H_{29}NO_6$: C, 63.31; H, 7.70; N, 3.69. Found: C, 62.94; H, 7.68; N, 3.65.

The dicyclohexylamine salt was crystallized from ether-hexane: mp 133-135 °C; $[\alpha]^{25}_D$ +35.9° (c = 1.02); FAB MS m/z 561 (M^+ + H); ^{1}H NMR ($CDCl_3$) δ 1.15-1.50 (m, 28, cyclohexyl, $C(CH_3)_3$), 1.62 (m, 2 H, cyclohexyl), 1.78 (m, 4 H, cyclohexyl), 1.95 (m, 4 H, cyclohexyl), 2.90 (m, 2 H, 2 CHN), 3.10 (m, 1 H, β-C*H*H), 3.20 (m, 1 H, β-CH*H*), 3.46 (s, 2 H, $ArCH_2$), 4.70 (m, α-CH), 5.25 (m, 1 H, NH), 7.11 (d, 2 H, J = 8 Hz, ArH), 7.16 (d, 2 H, J = 8 Hz, ArH). Anal. Calcd for $C_{32}H_{52}N_2O_6$: C, 68.54; H, 9.35; N, 5.00. Found: C, 68.39; H, 9.36; N, 4.95.

Acknowledgment. We thank members of the Physical Chemistry Department, Hoffmann-LaRoche, Inc., for determination of the spectral and microanalytical data for the compounds reported herein. We thank Joseph Michalewsky for the enantiomeric purity determinations. We also thank Drs. W. Danho and R. W. Kierstead for their support and advice during the course of these studies.

Registry No. **1a**, 86937-00-0; **1b**, 19391-35-6; **1c**, 4326-36-7; **2a**, 123993-19-1; **2b**, 123993-20-4; **2c**, 112766-18-4; **3a**, 123993-21-5; **3b**, 123993-22-6; **4a**, 123993-23-7; **4b**, 123993-24-8; **5b**, 123993-25-9; **5c**, 123993-26-0; **6b**, 123993-27-1; **6c**, 123993-28-2; **6c**·DCHA, 123993-34-0; **7b**, 123993-29-3; **7c**, 123993-30-6; **8b**, 123993-31-7; **8c**, 123993-32-8; **8c**·DCHA, 123993-35-1; **10**, 123993-33-9; H_2C=CHCOOBu-*t*, 1663-39-4; (*E*)-Bu_3SnCH=CHCOOMe, 82101-74-4; Bu_3SnCH_2CH=CH_2, 24850-33-7; H-Tyr-OH, 60-18-4.

Synthesis and 1,3-Dipolar Cycloaddition Reactions of Novel Heteropentalene Mesomeric Betaines, Pyrrolo[1,2-*c*]imidazole Mesomeric Betaines

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A series of novel heteropentalene mesomeric betaines, pyrrolo[1,2-*c*]imidazole mesomeric betaines (**10a-i**), were prepared by condensation of 2-formylpyrroles with aromatic imines. The mesomeric structures **10a-i** are proposed on the basis of spectral and microanalytical data and the results of their participation in 1,3-dipolar cycloaddition reactions. Peri-, regio-, and stereoselectivity of cycloadditions of mesomeric betaines **10a-i** with acetylenic (DMAD, ethyl propiolate, ethyl phenylpropiolate, benzyl phenylpropiolate, and phenylacetylene) and olefinic (dimethyl fumarate and dimethyl maleate) dipolarophiles have been studied. High periselectivity was observed in cycloadditions with both series of dipolarophiles, with the dipolarophile adding exclusively across the 1,3-azomethine ylide dipole (**10A**). The respective formation of 2,2'-bipyrroles and 2',3'-dihydro-2,2'-bipyrroles in the cycloaddition of acetylenic and olefinic dipolarophiles could be rationalized by considering rearrangements of the expected bicyclic cycloadducts **16** and **19**.

It has been demonstrated that there are 10 general types of neutral heteropentalenes which are isoconjugate with the pentalenyl dianion,[1] and in a more general way are considered as isoconjugate with even nonalternant hydrocarbon dianions.[1i] In Ramsden's classification of heteropentalenes,[1b,i] four of these general types are conveniently described as heteropentalene mesomeric betaines of type A (**1**), type B (**2**), type C (**3**), and type D (**4**). These compounds are intrinsically interesting, particularly from the point of view of their electronic structure and their participation in 1,3-dipolar cycloaddition reactions. Most of the known heteropentalene mesomeric betaines are of type A and type B; very few examples of types C and D have been reported. Pyrrolo[1,2-*c*]imidazole mesomeric bentaine **3a** belongs to the type C class of heteropentalene mesomeric betaines, and so far only one example of these class of compounds, **5**, has been observed.[1h,2] The betaine **5** was trapped by 2 equiv of dimethyl acetylenedicarboxylate (DMAD) to give the adduct **6**. In continuing our investigation of the reaction of 2-formylpyrroles with ammonium salts and amines,[3] we describe a general and

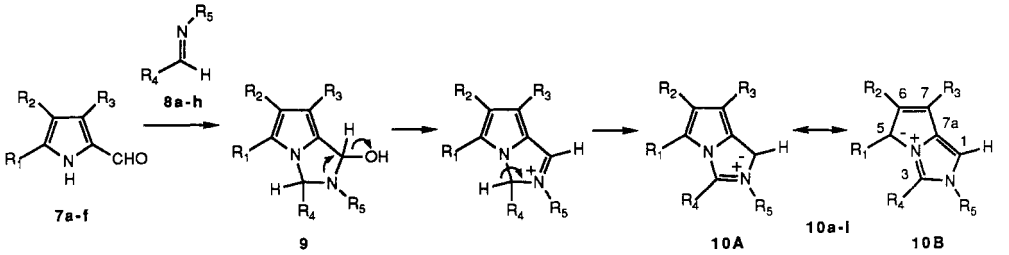
(1) For the reviews on chemical and physical properties of heteropentalene mesomeric betaines, see: (a) Cava, M. P.; Lakshmikantham, M. V. *Acc. Chem. Res.* **1975**, *8*, 139. (b) Ramsden, C. A. *Tetrahedron* **1977**, *33*, 3203. (c) Volz, H.; Kowarsch, H. *Heterocycles* **1977**, *7*, 1319. (d) Potts, K. T. In *Special Topics in Heterocyclic Chemistry*; Weissberger, A., Taylor, E. C., Eds.; Wiley: New York, 1977; Vol. XXX, pp 317-379. (e) Gleiter, R.; Bartetzko, R.; Brahler, G.; Bock, H. *J. Org. Chem.* **1978**, *43*, 3893. (f) Elguero, J.; Claramunt, R. M.; Summers, A. J. H. *Adv. Heterocycl. Chem.* **1978**, *22*, 183. (g) Potts, K. T. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; John Wiley & Sons: New York, 1984; Vol. II, pp 1-82. (h) Ramsden. C. A. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: Oxford, 1984; Vol. VI, pp 1027-1048. (i) Ollis, W. D.; Stanforth, S. P.; Ramsden, C. A. *Tetrahedron* **1985**, *41*, 2239.

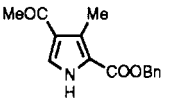
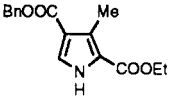
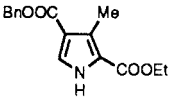
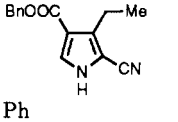
(2) No experimental details were given for these observations in ref 1h.

(3) Musicki, B.; Malley, M. F.; Gougoutas, J. Z. *Heterocycles* **1989**, *29*, 1137.

0022-3263/90/1955-0910$02.50/0

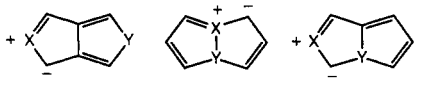
Table I. Preparation of Pyrrolo[1,2-c]imidazole Mesomeric Betaines 10a–i



compd	R_1	R_2	R_3	compd	R_4	R_5	compd[a]	yields, %
7a	COOBn	Me	COMe	**8a**		Me	**10a**	61
7b	COOEt	Me	COOBn	**8b**		Me	**10b**	86
7b	COOEt	Me	COOBn	**8c**		Bu	**10c**	38
7c	CN	Et	COOBn	**8d**		Me	**10d**	89
7d	COOEt	Me	COOEt	**8e**	Ph	Me	**10e**	58
7d	COOEt	Me	COOEt	**8f**	Ph	Pr	**10f**	59
7d	COOEt	Me	COOEt	**8g**	*o*-$MeOC_6H_4$	*c*-C_6H_{11}	**10g**	57
7e	COOEt	Me	COMe	**8h**	Ph	PhCHMe	**10h**	36
7f	COMe	Me	COOEt	**8e**	Ph	Me	**10i**	50

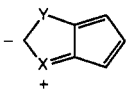
[a] The substituents R_1–R_5 on mesomeric betaines **10a–i** correspond to substituents R_1–R_3 of 2-formylpyrroles **7a–f** and R_4, R_5 of imines **8a–h**, respectively.

facile method for the synthesis of pyrrolo[1,2-*c*]imidazole mesomeric betaines and investigation of their 1,3-dipolar cycloaddition reactions.



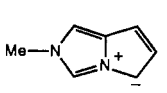
Type A (1) Type B (2) Type C (3)

1a X=Y=NH **2a** X=Y=N **3a** X=NH, Y=N

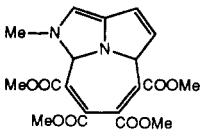


Type D (4)

4a X=Y=NH



5

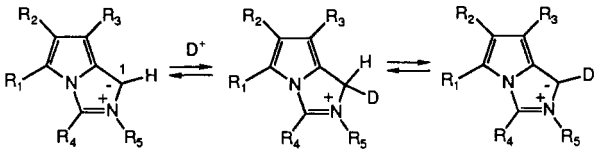


6

Results and Discussion

2-Formylpyrroles **7a–c** with R_1 and R_3 as electron-withdrawing substituents[4] (1 mol) easily undergo condensation in the presence of primary aliphatic amines (0.5 mol) to afford pyrrolo[1,2-*c*]imidazole mesomeric betaines **10a–d** (Table I). Mechanistically, the reaction might proceed by initial formation of imine **8a–d**,[5] derived from reaction of **7a–c** with the primary aliphatic amine. Condensation of **8a–d** with unreacted 2-formylpyrrole **7a–c** to give 2,3-dihydro-1*H*-pyrrolo[1,2-*c*]imidazole **9**, followed by dehydration and deprotonation, would afford the observed product **10A** ↔ **10B**. The condensations are performed simply by heating the 2-formypyrrole at reflux with a primary amine in benzene or methanol. Other aromatic imines (**8e–h**) undergo similar condensation with 2-formylpyrroles. The imines **8g,h** required for the preparation of mesomeric betaines **10g,h** were obtained by heating equimolar amounts of aromatic aldehyde and amine and were used directly in the condensation reaction without isolation and purification.

Scheme I



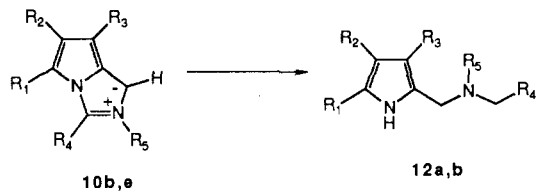
10A

(4) The presence of two electron-withdrawing substituents R_1 and R_3 seems to be necessary for a successful condensation. No reaction was observed by heating at reflux 2-formylpyrrole (**7**) (R_1 = H, R_2 = Me, R_3 = Et; R_1 = Me, R_2 = Me, R_3 = Et; R_1 = Me, R_2 = COMe, R_3 = Me; R_1 = Me, R_2 = COOBn, R_3 = Et; R_1 = COOBn, R_2 = COMe, R_3 = Me) and **8e** in benzene for 6 h. Only starting materials were recovered. Under the same reaction condtions, **7** (R_1 = H, R_2 = Me, R_3 = COMe; R_1 = COOEt, R_2 = Me, R_3 = Me) afforded a complex mixture of products.

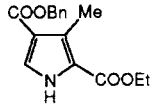
(5) It is known that simple 2-formylpyrroles react readily with primary amines to give the corresponding 2-pyrrylmethyleneimines.[6a] In the cases where it was impossible to isolate the imine, a Cu complex of the imine was prepared.[6b]

(6) (a) Jones, R. A.; Bean, G. P. *The Chemistry of Pyrroles*; Academic Press: London, 1977; pp 295–303. (b) Yeh, K.; Barker, H. R. *Inorg. Chem.* **1967**, *6*, 830.

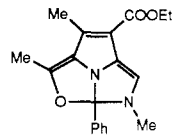
Scheme II



10b,e 12a,b

compd	compd	R_1	R_2	R_3	R_4	R_5	yields, %
10b	12a	COOEt	Me	COOBn		Me	85
10e	12b	COOEt	Me	COOEt	Ph	Me	42

The structures of pyrrolo[1,2-*c*]imidazole mesomeric betaines **10a–i** are in complete agreement with spectroscopic and microanalytical data. The ^1H NMR signal for the proton at the 1-position in mesomeric betaines **10a–i** appears as a sharp singlet at 6.50–7.00 ppm. This proton can be easily exchanged with deuterium in acidic media (CD_3OD/CD_3COOD), demonstraing considerable delocalization of the negative charge to the 1-carbon, as described by mesomeric dipolar structure **10A** (Scheme I). The ^{13}C signal for the corresponding carbon atom appears in the range of 98–105 ppm. Use of $Ph^{13}CHNMe$[7] in the condensation with 2-formylpyrrole **7d** allowed isolation of ^{13}C-enriched **10e** and the chemical shift for the 3-carbon was assigned as 126.1 (s) ppm. The ^{13}C chemical shift for the carbonyl carbon of the acetyl group in **10i** (181.2 ppm) is comparable to the chemical shift of the acetyl carbonyl in **7f** (189.1 ppm). Since the ^{13}C chemical shifts of the α-carbons in enol ethers are in the range of 130–160 ppm,[8] this excludes the alternative enol ether oxaaza[2.2.2]-cyclazine structure (**11**) which could originate from **10i** by



11

10π-electron cyclization. Molecular models of mesomeric betaines **10a–i** show that the steric interactions between the phenyl or pyrrole ring at the 3-position and substituents at the 2- and 5-positions are relieved through rotations from a planar structure about the phenyl- or pyrrole–pyrrolo[1,2-*c*]imidazole bond. This is reflected in a shielding effect (~0.5 ppm) observed for the CH_3 and CH_2 protons of the COOEt, COMe, and COOBn groups at the 5-position in **10a–c,e–i**. A very low streching vibration of the CN group (2189 cm^{-1}) at the 5-position in **10d** [compared to the streching vibration of another CN group in **10d** (2220 cm^{-1}) or the CN group of 2-formylpyrrole **7c** (2228 cm^{-1})] illustrates the contribution of mesomeric dipolar structure **10B**.

As further proof for the proposed structures of the mesomeric betaines, **10b,e** were reduced with sodium cyanoborohydride in acetonitrile in the presence of acetic acid at room temperature to afford 2-(aminomethyl)-pyrroles **12a,b**, respectively (Scheme II). Their structures were confirmed by independent synthesis (see the Experimental Section).

(7) $Ph^{13}CHNMe$ (**8e**), 99% ^{13}C-enriched, was prepared from $Ph^{13}CHO$ and methylamine as described in ref 20.

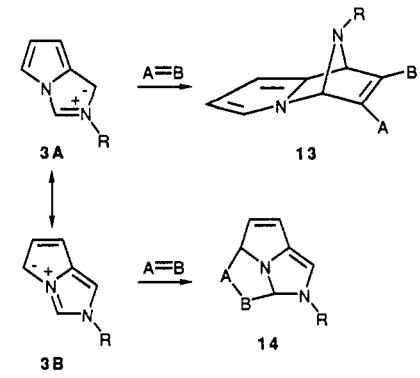
(8) Breitmaier, E.; Voelter, W. In *Carbon-13 NMR Spectroscopy*; VCH: New York, 1987; pp 213–215, 278–279.

Table II. UV–Visible and Fluorescence Properties of Pyrrolo[1,2-*c*]imidazole Mesomeric Betaines 10a–i

compd	absorbance λ_{max} (log ϵ), nm[a]	emission λ_{max}, nm[b]
10a	373 (4.48), 238 (4.49) 205 (4.45)	502[c]
10b	358 (4.58), 225 (4.61) 210 (460)	500[d]
10c	359 (4.45), 225 (4.55) 2.10 (4.54)	500[d]
10d	358 (4.45), 270 sh (4.15) 233 (4.58), 210 (4.66)	493[d]
10e	360 (4.43), 270 sh (3.93) 238 (4.24), 205 (4.27)	463[d]
10f	360 (4.41), 270 sh (3.95) 238 (4.24), 205 (4.30)	450[d]
10g	362 (4.44), 270 sh (3.94) 236 (4.23), 205 (4.37)	459[d]
10h	379 (4.44), 280 (3.83) 240 (4.20), 205 (4.40)	458[d]
10i	376 (4.34), 260 (4.21) 238 (4.14), 205 (4.29)	452[c]

[a] In CH_3OH. [b] Excitation wavelength 350 nm. [c] In CCl_4. [d] In CH_2Cl_2.

Scheme III



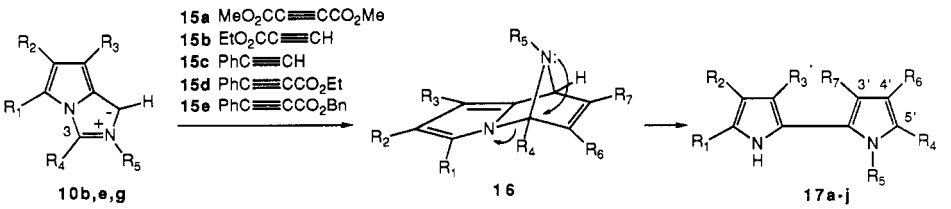
3A **13** **3B** **14**

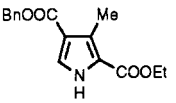
Regarding the electronic properties of interest, all mesomeric betaines **10a–i** display strong UV–visible absorption and fluorescence (Table II).

The structural features of the heteropentalene mesomeric betaines provide possibilities for diverse 1,3-dipolar cycloaddition reactions which would lead to unique monocyclic and ring-annulated heterocycles.[1g] Two dipolar azomethine ylide forms of pyrrolo[1,2-*c*]imidazole mesomeric betaines, **3A** and **3B** (Scheme III), could potentially participate in dipolar cycloaddition reactions. The cycloaddition of the dipolarophile across azomethine ylide **3A** would lead to bicyclic product **13** (Scheme III), whereas the addition across the azomethine ylide **3B** would afford cycloadduct **14**. When DMAD (**15a**) was added to a solution of mesomeric betaine **10e** in benzene at room temperature, smooth conversion of the starting material occurred in 2 h, and the isolated product was characterized as 2,2′-bipyrrole **17a** (Table III) on the basis of its spectral properties. Formation of **17a** can be rationalized by considering rearrangement of the expected bicyclic cycloadduct (**16**) formed by DMAD addition across the azomethine ylide dipole **10A**. The exclusive participation of azomethine ylide dipole **10A** in cycloaddition reactions was also observed with other acetylenic dipolarophiles (**15b–e**) (Table III).

The unsymmetrical dipolarophiles **15b,c** underwent cycloaddition with high regioselectivity. Ethyl propiolate afforded **17b** and **17c** in the ratio 14:1, whereas phenylacetylene gave single regioisomer **17d**. The regiochemistry of H and COOEt in **17b** and H and Ph in **17d** was determined by reaction of mesomeric betaine **10e**, ^{13}C-labeled

Table III. Cycloaddition of Acetylenic Dipolarophiles to Pyrrolo[1,2-*c*]imidazole Mesomeric Betaines



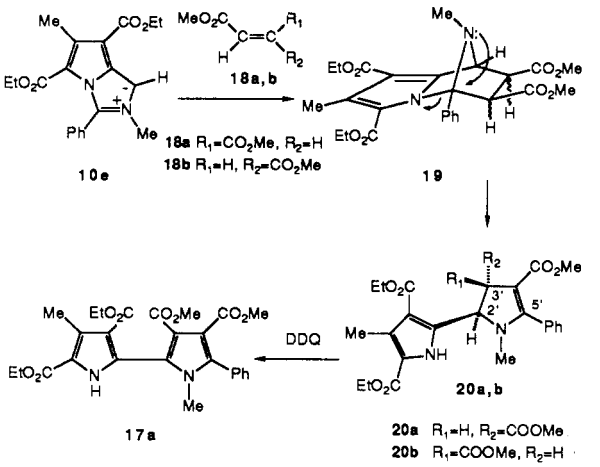
compd	compd	compd	R_1	R_2	R_3	R_4	R_5	R_6	R_7	yields, %
10e	**15a**	**17a**	COOEt	Me	COOEt	Ph	Me	COOMe	COOMe	83
10e	**15b**	**17b**	COOEt	Me	COOEt	Ph	Me	H	COOEt	31
		17c	COOEt	Me	COOEt	Ph	Me	COOEt	H	2
10e	**15c**	**17d**	COOEt	Me	COOEt	Ph	Me	H	Ph	59
10e	**15d**	**17e**	COOEt	Me	COOEt	Ph	Me	COOEt	Ph	62
		17f	COOEt	Me	COOEt	Ph	Me	Ph	COOEt	14
10e	**15e**	**17g**	COOEt	Me	COOEt	Ph	Me	COOBn	Ph	65
		17h	COOEt	Me	COOEt	Ph	Me	Ph	COOBn	15
10g	**15a**	**17i**	COOEt	Me	COOEt	*o*-$MeOC_6H_4$	*c*-C_6H_{11}	COOMe	COOMe	28
10b	**15a**	**17j**	COOEt	Me	COOBn		Me	COOMe	COOMe	53

at the 3-position, with ethyl propiolate and phenylacetylene, respectively. According to Table III, the isolated **17b** and **17d** were labeled at the 5′-position. The ^{13}C NMR measurements of ^{13}C-enriched samples of **17b** and **17d** provided the carbon–carbon coupling constants between C-5′ and the pyrrole carbon bearing the hydrogen[9] as $^1J_{CC}$ = 67.8 and 68.1 Hz, respectively. Since these are typical values for one-bond C–C coupling constants of aromatic carbon atoms,[10] they indicate that the carbon bearing the hydrogen is in the 4′-position. The cycloaddition of ethyl and benzyl phenylpropiolate (**15d,e**) to **10e** afforded both regioisomers in the respective ratios **17e**:**17f** = 4.4:1 and **17g**:**17h** = 4.3:1. The location of substituents in 3′- and 4′-position in **17e–h** was established as follows: hydrogenolysis of the benzyl ester **17g** (1 atm of H_2, 10% Pd–C, MeOH) afforded carboxylic acid **17k** (R_6 = COOH, R_7 = Ph). Decarboxylation of **17k** was effected in 3% HCl–EtOH at room temperature and afforded a product identical with 2,2′-bipyrrole **17d**. Treatment of **17k** with diazoethane in ether–THF at 0 °C provided **17e**. The opposite regioselectivity in cycloaddition of **15b** and **15d** could be associated more with the steric influence of the phenyl group in mesomeric betaine **10e** then with charge distribution in azomethine ylide.

Interestingly, the sterically hindered mesomeric betaine **10g** reacts readily with DMAD to afford two rotational isomers of **17i** in the ratio 58:42 based on the ^1H NMR spectrum (benzene-d_6). The ^1H and ^{13}C NMR spectra of **17i** showed two sets of signals with very close chemical shift values. However, a single molecular ion peak was observed in the mass spectrum. Furthermore, ^1H NMR variable-temperature studies of **17i** indicated the presence of a single rotational isomer at 130 °C.

We next investigated the 1,3-dipolar cycloaddition reaction of mesomeric betaine **10e** with two olefinic dipolarophiles, dimethyl maleate (**18a**) and dimethyl fumarate (**18b**) (Scheme IV). On reaction in refluxing benzene, both **18a** and **18b** afforded mixtures of 2′,3′-dihydro-2,2′-bipyrroles **20a,b** in the ratio **20a**:**20b** = 8.4:1 (78% and 8%)

Scheme IV



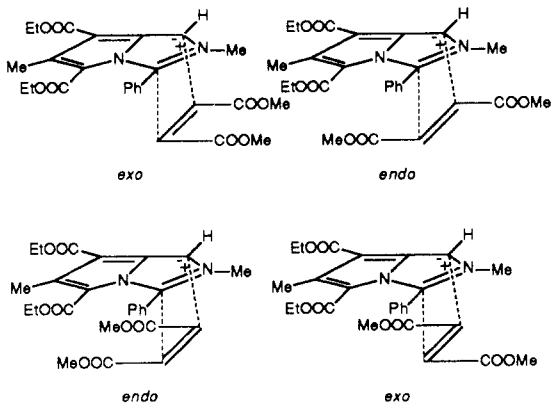
and 5.3:1 (77% and 15%), respectively. The structures **20a,b** are in agreement with spectroscopic data, and both isomers gave 2,2′-bipyrrole **17a** on treatment with DDQ in CH_2Cl_2 at room temperature. The position of the double bond in dihydropyrrole ring of **20a,b** was unambiguously assigned, again through ^{13}C-isotopic labeling. The observed ^{13}C chemical shifts of ^{13}C-enriched 5′-carbons in **20a,b**[11] are 163.7 (s) and 165.1 (s) ppm, respectively. The stereochemistry of the hydrogens at the 2′- and 3′-position in **20a,b** was determined on the basis of NOE experiments and equilibration studies. In the case of cis isomer **20b**, NOE enhancement was observed between H-2′ and H-3′ and between H-2′ and the *N*-methyl group. Trans isomer **20a** displayed significant NOE enhancement only between H-2′ and the *N*-methyl group. Isomers **20a,b** were respectively equilibrated in 0.2 M CH_3ONa/CH_3OH. After 5 days at room temperature, each isomer afforded the same ratio **20a**:**20b** = 9:1. Formation of **20a,b** can be explained by a mechanism (Scheme IV) similar to that proposed in Table III for the cycloaddition of acetylenic dipolarophiles. Here again, **10e** behaves as a 1,3-azomethine ylide dipole (**10A**), affording the bicyclic intermediate **19**, which then rearranges to **20a,b**. In order to establish that the observed

(9) The chemical shift of the pyrrole carbon bearing a hydrogen in **17b,d** can be easily identified by proton selective decoupling experiments.

(10) (a) Wray, V. In *Progress in Nuclear Magnetic Resonance Spectroscopy*; Emsley, J. W., Feeney, J., Sutcliffe, L. H., Eds.; Pergamon Press: Oxford, 1980; Vol. XIII, pp 177–256. (b) Levy, G. C.; Lichter, R. L.; Nelson, G. L. In *Carbon-13 Nuclear Magnetic Resonance Spectroscopy*; John Wiley & Sons: New York, 1980; p 125.

(11) 2′,3′-Dihydro-2,2′-bipyrroles (**20a,b**) 99% ^{13}C-enriched at 5′-position were prepared by reaction of **10e** (^{13}C-labeled at 3-position) with dimethylfumarate.

Scheme V



ratios **20a**:**20b** are the result of endo or exo cycloaddition of **18a**,**b** across the 1,3-azomethine ylide dipole (**10A**) and not to equilibration at the 3′-position of **20a** or **20b** under the reaction conditions, experiments were performed with **20a**,**b** deuterium labeled at the 2′-position (eq 1–4).[12] In

10e+18a+20a-D → **20a+20b+20a-D** (**20b-D** not formed) (1)

10e+18a+20b-D → **20a+20b+20b-D** (**20a-D** not formed) (2)

10e+18b+20a-D → **20a+20b+20a-D** (**20b-D** not formed) (3)

10e+18b+20b-D → **20a+20b+20b-D** (**20a-D** not formed) (4)

each experimental run the amount of deuterated product (**20a**-D and **20b**-D) used was approximately equal the amount of protiated product (**20a**) expected to be formed in cycloaddition reaction. After completion of the reaction, the isomers were separated and analyzed by ^{1}H NMR for the presence of **20a**,**b**-D. The results clearly indicate that there is no **20a** ⇌ **20b** equilibration under the reaction conditions. The course of the cycloadditions was also followed by ^{1}H NMR spectroscopy (benzene-d_6) and no **18a** ⇌ **18b** isomerization was observed. Assuming that the stereochemistry of the starting olefins is retained in cycloadduct **19**, **20a** is the result of exo and endo cycloaddition of **18a** and **18b**, respectively, whereas **20b** is the result of endo and exo cycloaddition of **18a** and **18b**, respectively (Scheme V). However, since the isolation of the intermediate **19** was not achieved, no decisive arguments can be advanced regarding the observed **20a**:**20b** ratio. One plausible explanation, though, may be that preferential formation of **20a** in each case could be due to the involvement of reversible cycloadditions which under equilibrating conditions yield predominantly the thermodynamically favored trans isomer **20a** (eq 5, 6).

20a ← *exo*-**19** ⇌ (**18a**) **10e** ⇌ (**18a**) *endo*-**19** → **20b** (5)

20b ← *exo*-**19** ⇌ (**18b**) **10e** ⇌ (**18b**) *endo*-**19** → **20a** (6)

Concluding Remarks

Quantitative theoretical studies of heteropentalene mesomeric betaines **1a**–**4a** have been made using Hückel[1h,13] and CNDO/2[1b] methods. According to these calculations, the energy levels of the type C system (**3a**) are intermediate between those of type A (**1a**) and B (**2a**) systems, and as a result, mesomeric betaine **3** should display the characteristics of both systems A (**1**) and B (**2**). From the results of the cycloaddition reactions of substituted pyrrolo[1,2-*c*]imidazole mesomeric betaine derivatives **10a**–**i** with acetylenic and olefinic dipolarophiles, it is clear that the addition of these dipolarophiles is highly periselective and occurs exclusively across the 1,3-azomethine ylide dipole (**10A**). Therefore, the chemistry of the cycloaddition reactions of **10a**–**i** resembles that of the type A (**1**) mesomeric betaine systems. This result is complementary to the observation of Ramsden,[1h] who was able to trap the species **5** by DMAD in a reaction which is characteristic of type B heteropentalene mesomeric betaines. At this point, it is not clear whether the site selectivity in cycloadditions of **10a**–**i** is determined exclusively by the relative size of HOMO coefficients at the alternative site of addition or is also affected to some extent by steric factors due to the presence of a substituent in the 5-position in **10a**–**i**.[14] The cycloaddition reactions of pyrrolo[1,2-*c*]imidazole mesomeric betaines with other dipolarophiles are currently under investigation in our laboratory.

Experimental Section

General. The ^{1}H NMR spectra were recorded at 300 and 500 MHz on Brucker AM-300 and AM-500 spectrometers, respectively. When $CDCl_3$ was used as the solvent, chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane as an internal standard. When benzene-d_6 was used as the solvent, chemical shifts are reported in reference to benzene (7.15 ppm). The ^{13}C NMR spectra were recorded at 62, 75, and 125 MHz on Brucker AM-250, AM-300, and AM-500 spectrometers, respectively. Chemical shifts are reported in parts per million in reference to $CDCl_3$ (77.00 ppm), benzene-d_6 (128.00 ppm), or acetone-d_6 (29.80 ppm). $CDCl_3$ used for NMR spectroscopy was passed through basic alumina before use. The IR spectra were recorded on a Nicolet 7199 FT-IR spectrometer. The electron impact (EI) mass spectra were recorded on a Kratos MS-50L double-focusing mass spectrometer at 70 eV using direct insertion techniques. Chemical ionization (CI) mass spectra were recorded on the Kratos MS-50L using isobutane as the reagent gas. The fast atom bombardment (FAB) spectra were recorded on the Kratos MS-50L (gas, xenon; high voltage, 6 keV; matrix, *m*-nitrobenzyl alcohol). The UV–visible spectra were measured on a Perkin-Elmer Model 124 double-beam spectrophotometer. Fluorescence spectra were measured on a Perkin-Elmer 4A fluorescence spectrometer. All melting points are uncorrected. Chromatographic separations were performed on open gravity columns with E. Merck Kieselgel 60 (70–230 mesh). Preparative TLC (PTLC) separations were carried out on E. Merck precoated TLC plates (silica gel 60 F-254, layer thickness 0.5 mm). Commercial grade reagents were distilled before use.

Pyrrolo[1,2-*c*]imidazole Mesomeric Betaine (10a). A solution of 2-formylpyrrole **7a**[15] (1.00 g, 3.51 mmol), methylamine hydrochloride (128.6 mg, 1.905 mmol), and anhydrous sodium acetate (156.2 mg, 1.905 mmol) in methanol (20 mL) was heated at reflux for 1 h. The solvent was evaporated, and the residue was dissolved in CH_2Cl_2. The organic phase was washed with water and dried over $MgSO_4$, then the solvent was evaporated. The residue was purified by column chromatography (hexanes–EtOAc, 1:1, 1:2) to afford **10a** (600 mg, 61%) as a brown oil: ^{1}H NMR (300 MHz, benzene-d_6) δ 1.81 (s, 3 H), 2.09 (s, 3 H), 2.62 (s, 3 H), 2.79 (s, 3 H), 2.90 (s, 3 H), 4.60 (d, 1 H, J = 12.4 Hz), 5.14 (d, 1 H, J = 12.4 Hz), 5.22 (d, 1 H, J = 12.5 Hz), 5.37 (d, 1 H, J = 12.5 Hz), 6.09 (br s, 1 H), 6.95–7.13 (m, 8 H), 7.40 (d, 2 H, J = 7.9 Hz), 13.18 (br s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.27 (q), 13.71 (q), 28.82 (q), 29.75 (q), 35.54 (q), 64.97 (t), 66.26 (t), 104.71 (d), 108.28 (s), 119.14 (s), 121.84 (s), 123.20 (s), 127.58 (s), 127.83 (d), 127.83 (d), 127.88 (s), 128.18 (s), 128.25 (d), 128.25 (d), 128.46 (d), 128.46 (d), 128.92 (s), 135.73 (s), 135.84 (s), 136.48 (s), 160.12 (s), 160.75 (s), 189.80 (s), 194.15 (s); IR (neat) 3175–2894, 1714, 1682, 1664, 1613, 1563, 1488, 1455, 1444, 1396, 1284, 1263,

(12) Deuterated **20a**,**b** were prepared by the reaction of **10e** deuterated at the 1-position with dimethyl fumarate. The ^{1}H NMR spectra of **20a**,**b**-D indicated ~95% deuterium enrichment.

(13) Matsumoto, A.; Hee Lee, J.; Yoshida, M.; Simamura, O. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 1490.

(14) Mok, K.-L.; Nye, M. J. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1810.

(15) Clesy, P. S.; Liepa, A. J. *Aust. J. Chem.* **1971**, *24*, 1933.

1200, 1106, 1087 cm^{-1}; MS (FAB) m/e (relative intensity) 566 [(M + H)$^+$, 78], 565 (M$^+$, 81), 458 (24), 308 (8), 154 (39), 136 (37), 91 (100); HRMS (FAB) m/e (M$^+$) calcd 565.2212, obsd 565.2198.

Pyrrolo[1,2-c]imidazole Mesomeric Betaine (10b). A solution of 2-formylpyrrole **7b**[16] (3.150 g, 10.0 mmol), methylamine hydrochloride (709 mg, 10.5 mmol), and anhydrous sodium acetate (861 mg, 10.5 mmol) in methanol (15 mL) was heated at reflux for 30 min. The solvent was evaporated, and the residue was dissolved in CH_2Cl_2. The organic phase was washed with water and dried over $MgSO_4$, and then the solvent was evaporated. The residue was triturated with methanol at 0 °C. Recrystallization from methanol afforded **10b** (2.670 g, 86%) as a pale green solid: mp 193–194 °C; ^{1}H NMR (300 MHz, benzene-d_6) δ 0.86 (t, 3 H, J = 7.0 Hz), 1.00 (t, 3 H, J = 7.0 Hz), 2.47 (s, 3 H), 2.94 (s, 3 H), 3.09 (s, 3 H), 3.73–3.79 (m, 1 H), 3.90–3.96 (m, 1 H), 4.11 (q, 2 H, J = 7.0 Hz), 4.64 (d, 1 H, J = 12.1 Hz), 4.82 (d, 1 H, J = 12.1 Hz), 5.36 (d, 1 H, J = 12.4 Hz), 5.75 (d, 1 H, J = 12.4 Hz), 6.41 (s, 1 H), 6.69–6.72 (m, 2 H), 6.91–6.97 (m, 3 H), 7.12–7.26 (m, 3 H), 7.56 (d, 2 H, J = 7.2 Hz), 11.25 (br s, 1 H); ^{13}C NMR (125 MHz, acetone-d_6) δ 11.73 (q), 13.38 (q), 14.63 (q), 14.83 (q), 35.87 (q), 59.33 (t), 60.99 (t), 64.66 (t), 66.18 (t), 92.74 (s), 105.13 (d), 108.34 (s), 118.65 (s), 119.53 (s), 122.33 (s), 125.26 (s), 128.40 (d), 128.61 (d), 128.61 (d), 128.61 (d), 129.04 (d), 129.24 (d), 130.37 (s), 136.59 (s), 136.85 (s), 139.20 (s), 143.47 (s), 160.92 (s), 161.36 (s), 163.79 (s), 164.30 (s); IR (KBr) 3186, 3160, 2978, 2949, 1717, 1700, 1677, 1653, 1580, 1496, 1478, 1455, 1431, 1402, 1379, 1293, 1261, 1209, 1173, 1120, 1089, 1058, 702 cm^{-1}; MS (FAB) m/e (relative intensity) 626 [(M + H)$^+$, 37], 625 (M$^+$, 50), 580 (10), 534 (6), 472 (10), 154 (11), 91 (100). Anal. Calcd for $C_{35}H_{35}N_3O_8$: C, 67.19; H, 5.64; N, 6.72. Found: C, 67.40; H, 5.54; N, 6.69.

Pyrrolo[1,2-c]imidazole Mesomeric Betaine (10c). A solution of 2-formylpyrrole **7b** (630 mg, 2.00 mmol) and butylamine (87.6 mg, 1.20 mmol) in benzene (20 mL) was heated at reflux (Dean–Stark apparatus) for 2 h. The solvent was evaporated, and the residue was triturated with [(hexanes–EtOAc, 4:1)–methanol 1:1] at 0 °C. Recrystallization from methanol afforded **10c** (252 mg, 38%) as a pale green solid: mp 140.5–141.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.73 (t, 3 H, J = 7.2 Hz), 0.99–1.22 (m, 2 H), 1.06 (t, 3 H, J = 7.0 Hz), 1.31 (t, 3 H, J = 7.1 Hz), 1.42 (quintet, 2 H, J = 7.4 Hz), 2.63 (s, 3 H), 2.69 (s, 3 H), 3.46–3.65 (m, 2 H), 3.78–3.98 (m, 2 H), 4.16–4.27 (m, 2 H), 4.80 (d, 1 H, J = 11.9 Hz), 4.92 (d, 1 H, J = 11.9 Hz), 5.19 (d, 1 H, J = 12.6 Hz), 5.43 (d, 1 H, J = 12.6 Hz), 6.57 (s, 1 H), 6.76–6.79 (m, 2 H), 7.01–7.06 (m, 3 H), 7.32–7.49 (m, 5 H), 10.68 (br s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.52 (q), 13.19 (q), 13.30 (q), 14.21 (q), 14.46 (q), 19.40 (t), 31.71 (t), 48.17 (t), 59.18 (t), 60.79 (t), 64.80 (t), 65.95 (t), 92.42 (s), 102.67 (d), 107.62 (s), 116.60 (s), 119.21 (s), 121.55 (s), 123.94 (s), 127.73 (d), 127.93 (d), 127.98 (d), 128.18 (d), 128.23 (d), 128.42 (d), 130.35 (s), 135.00 (s), 135.86 (s), 137.59 (s), 143.55 (s), 160.82 (s), 161.30 (s), 163.15 (s), 164.49 (s); IR (KBr) 3194, 2960, 2934, 1715, 1701, 1679, 1645, 1578, 1456, 1402, 1382, 1258, 1196, 1172, 1127, 1091, 1056 cm^{-1}; MS (FAB) m/e (relative intensity) 668 [(M + H)$^+$, 25], 667 (M$^+$, 33), 622 (7), 577 (5), 514 (6), 91 (100). Anal. Calcd for $C_{38}H_{41}N_3O_8$: C, 68.35; H, 6.19; N, 6.29. Found: C, 68.18; H, 6.10; N, 6.28.

Pyrrolo[1,2-c]imidazole Mesomeric Betaine (10d). A solution of 2-formylpyrrole **7c**[17] (600 mg, 2.13 mmol), methylamine hydrochloride (158.7 mg, 2.35 mmol), and anhydrous sodium acetate (192.8 mg, 2.35 mmol) in methanol (4 mL) was heated at reflux for 30 min. The solvent was evaported, and the residue was dissolved in CH_2Cl_2. The organic phase was washed with water and dried over $MgSO_4$, and then the solvent was evaported. The residue was purified by column chromatography (hexanes–EtOAc, 4:1). Trituration with methanol at 0 °C and then recrystallization from methanol afforded **10d** (531.8 mg, 89%) as a pale green crystals: mp 179.5–180.5 °C dec; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.05 (t, 3 H, J = 7.3 Hz), 1.28 (t, 3 H, J = 7.3 Hz), 2.17–2.31 (m, 2 H), 2.94–3.03 (m, 2 H), 3.47 (s, 3 H), 5.00 (d, 1 H, J = 11.9 Hz), 5.13 (d, 1 H, J = 11.9 Hz), 5.35 (d, 1 H, J = 12.1 Hz), 5.58 (d, 1 H, J = 12.1 Hz), 6.48 (s, 1 H), 7.00–7.03 (m, 2 H), 7.15–7.17 (m, 3 H), 7.35–7.45 (m, 3 H), 7.53 (d, 2 H, J = 7.3 Hz), 12.05 (br s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.93 (q), 15.17 (q), 19.11 (t), 19.62 (t), 35.38 (q), 66.29 (t), 66.67 (t), 86.22 (s), 89.59 (s), 104.77 (s), 105.48 (d), 112.18 (s), 113.74 (s), 115.31 (s), 117.86 (s), 119.85 (s), 128.10 (d), 128.28 (d), 128.43 (d), 128.48 (d), 128.48 (d), 128.52 (d), 134.56 (s), 134.70 (s), 136.37 (s), 140.98 (s), 150.52 (s), 161.86 (s), 165.04 (s); IR (KBr) 3142–2733, 2220, 2189, 1710, 1650, 1579, 1498, 1470, 1451, 1292, 1280, 1270, 1227, 1158, 1142, 1107 cm^{-1}; MS (FAB) m/e (relative intensity) 560 [(M + H)$^+$, 40], 559 (M$^+$, 49), 452 (8), 307 (18), 154 (100), 91 (76). Anal. Calcd for $C_{33}H_{29}N_5O_4$: C, 70.82; H, 5.22; N, 12.52. Found: C, 70.50; H, 5.18; N, 12.45.

Pyrrolo[1,2-c]imidazole Mesomeric Betaine (10e). A solution of 2-formylpyrrole **7d**[19] (2.53 g, 10.0 mmol) and imine **8e**[20] (1.31 g, 11.0 mmol) in benzene (50 mL) was heated at reflux for 1 h. The solvent was evaporated, and the residue was separated by column chromatography (hexanes–EtOAc, 10:1, 6:1, 4:1) to afford **10e** (2.04 g, 58%) as a pale green oil. Trituration and recrystallization from ether provided a pale green solid: mp 122–123 °C; ^{1}H NMR (300 MHz, benzene-d_6) δ 0.77 (t, 3 H, J = 7.1 Hz), 1.23 (t, 3 H, J = 7.1 Hz), 2.51 (s, 3 H), 3.38 (s, 3 H), 3.81 (q, 2 H, J = 7.1 Hz), 4.41 (q, 2 H, J = 7.1 Hz), 6.72 (s, 1 H), 6.78–6.82 (m, 2 H), 6.99–7.04 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.98 (q), 14.13 (q), 14.71 (q), 35.86 (q), 58.51 (t), 58.51 (t), 92.03 (s), 103.44 (d), 106.85 (s), 126.11 (s), 127.63 (s), 127.96 (d), 129.24 (d), 129.42 (d), 136.10 (s), 144.47 (s), 160.45 (s), 164.67 (s); IR (KBr) 2978, 2946, 2933, 1687, 1651, 1619, 1520, 1481, 1263, 1248, 1191, 1176, 1133, 1097, 1059, 1015, 772 cm^{-1}; MS (EI) m/e (relative intensity) 354 (M$^+$, 100), 326 (7), 309 (19), 282 (23), 254 (17), 210 (9), 105 (14), 77 (12). Anal. Calcd for $C_{20}H_{22}N_2O_4$: C, 67.78; H, 6.26; N, 7.91. Found: C, 67.50; H, 6.13; N, 7.85. **10e** ^{13}C-enriched; ^{13}C NMR (75 MHz, $CDCl_3$) δ 126.11 (s), $^3J_{C\text{-}3,H\text{-}1}$ = 4.6 Hz.

Pyrrolo[1,2-c]imidazole Mesomeric Betaine (10f). A solution of 2-formylpyrrole **7d** (1.012 g, 4.00 mmol) and imine **8f**[21] (647 mg, 4.40 mmol) in benzene (10 mL) was heated at reflux for 1 h. The solvent was evaporated, and the residue was separated by column chromatography (hexanes–EtOAc, 20:1, 10:1, 6:1) to afford **10f** (895 mg, 59%) as a pale green oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, 3 H, J = 7.5 Hz), 0.93 (t, 3 H, J = 7.1 Hz), 1.40 (t, 3 H, J = 7.1 Hz), 1.80 (sextet, 2 H, J = 7.4 Hz), 2.80 (s, 3 H), 3.76 (q, 2 H, J = 7.1 Hz), 3.92 (t, 2 H, J = 7.5 Hz), 4.33 (q, 2 H, J = 7.1 Hz), 6.98 (s, 1 H), 7.33–7.37 (m, 2 H), 7.45–7.50 (m, 3 H); ^{13}C NMR (125 MHz, benzene-d_6) δ 10.65 (q), 14.01 (q), 14.58 (q), 15.11 (q), 23.83 (t), 49.58 (t), 58.51 (t), 58.80 (t), 93.07 (s), 102.16 (d), 107.42 (s), 125.55 (s), 127.91 (d), 128.69 (s), 129.23 (d), 130.01 (d), 137.07 (s), 144.07 (s), 160.56 (s), 164.82 (s); IR (neat) 2975, 2934, 1692, 1666, 1619, 1483, 1420, 1403, 1382, 1271, 1187, 1128, 1094 cm^{-1}; MS (EI) m/e (relative intensity) 382 (M$^+$, 100), 354 (5), 337 (11), 310 (22), 282 (6), 105 (11); HRMS (EI) m/e (M$^+$) calcd 382.1893, obsd 382.1887.

Pyrrolo[1,2-c]imidazole Mesomeric Betaine (10g). A solution of *o*-methoxybenzaldehyde (749 mg, 5.51 mmol) and cyclohexylamine (521 mg, 5.25 mmol) in benzene (60 mL) was heated at reflux (Dean–Stark apparatus) for 30 min. The solution was cooled, and 2-formylpyrrole **7d** (1.265 g, 5.00 mmol) was added. Heating at reflux was resumed for 3 h, and then the solvent was evaporated. The residue was separated by column chromatography (hexanes–EtOAc, 20:1, 10:1, 6:1) to afford **10g** (1.29 g, 57%) as a pale green oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.96 (t, 3 H, J = 7.1 Hz), 1.17–1.26 (m, 2 H), 1.40 (t, 3 H, J = 7.1 Hz), 1.69–2.04 (m, 8 H), 2.79 (s, 3 H), 3.70–3.89 (m, 3 H), 3.73 (s, 3 H), 4.33 (q,

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(17) 2-Formylpyrrole **7c** was prepared by the following transformations: formylation of benzyl 4-ethyl-2-methylpyrrole-3-carboxylate[18] with $HC(OEt)_3$ in CF_3COOH at room temperature afforded benzyl 5-formyl-4-ethyl-2-methylpyrrole-3-carboxylate. The 5-formylpyrrole was then converted to the oxime, which was dehydrated in refluxing Ac_2O to benzyl 5-cyano-4-ethyl-2-methylpyrrole-3-carboxylate. Treatment of 5-cyanopyrrole with SO_2Cl_2 (2 equiv) in AcOH at 50 °C followed by hydrolysis afforded 2-formylpyrrole (**7c**): mp 112.5–113.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.21 (t, 3 H, J = 7.5 Hz), 2.90 (q, 2 H, J = 7.5 Hz), 5.38 (s, 2 H), 7.35–7.44 (m, 5 H), 9.94 (br s, 1 H), 10.20 (s, 1 H); IR (KBr) 3220–2933, 2228, 1722, 1662, 1647, 1442, 1373, 1280, 1240, 1143, 1092 cm^{-1}. Anal. Calcd for $C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.92. Found: C, 68.15; H, 5.02; N, 9.84.

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2 H, J = 7.1 Hz), 7.00 (d, 1 H, J = 8.7 Hz), 7.01 (s, 1 H), 7.06 (t, 1 H, J = 7.3 Hz), 7.22 (dd, 1 H, J = 1.3, 7.4 Hz), 7.50 (dt, 1 H, J = 1.4, 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.16 (q), 14.44 (q), 14.89 (q), 24.94 (t), 25.48 (t), 25.53 (t), 33.90 (t), 34.21 (t), 55.36 (q), 57.41 (d), 58.45 (t), 58.57 (t), 91.78 (s), 98.19 (d), 107.36 (s), 110.67 (d), 116.99 (s), 119.96 (d), 122.51 (s), 130.91 (d), 131.41 (d), 136.45 (s), 143.94 (s), 158.26 (s), 160.77 (s), 165.00 (s); IR (neat) 2934, 1690, 1665, 1620, 1518, 1483, 1417, 1273, 1180, 1133, 1115, 1093 cm^{-1}; MS (EI) m/e (relative intensity) 452 (M^+, 100), 407 (5), 379 (6), 318 (7), 251 (11); HRMS (FAB) m/e (M^+) calcd 452.2311, obsd 452.2318.

Pyrrolo[1,2-*c*]imidazole Mesomeric Betaine (10h). A solution of benzaldehyde (570 mg, 5.37 mmol) and α-methylbenzylamine (651 mg, 5.37 mmol) in benzene (20 mL) was heated at reflux (Dean–Stark apparatus) for 30 min. The solution was cooled, and 2-formylpyrrole **7e**[22] (1.090 g, 4.89 mmol) was added. Heating at reflux was resumed for 5 h, and then the solvent was evaporated. The residue was separated by column chromatography (hexanes–EtOAc, 10:1, 4:1, 2:1) to afford **10h** (739 mg, 36%) as a brown semisolid: ^{1}H NMR (300 MHz, benzene-d_6) δ 0.75 (t, 3 H, J = 7.1 Hz), 1.10 (d, 3 H, J = 7.1 Hz), 2.45 (s, 3 H), 3.07 (s, 3 H), 3.61–3.78 (m, 2 H), 4.90 (q, 1 H, J = 7.1 Hz), 6.58–6.61 (m, 2 H), 6.87–7.02 (m, 8 H), 7.43 (br s, 1 H); ^{13}C NMR (62 MHz, benzene-d_6) δ 14.45 (q), 14.75 (q), 21.52 (q), 30.01 (q), 57.19 (d), 58.66 (t), 100.63 (d), 106.10 (s), 107.52 (s), 125.90 (s), 126.03 (d), 128.06 (d), 128.11 (d), 128.76 (s), 128.96 (d), 129.55 (d), 130.25 (d), 137.24 (s), 140.70 (s), 142.24 (s), 160.59 (s), 188.04 (s); IR (neat) 2981, 1676, 1619, 1516, 1471, 1416, 1403, 1380, 1202, 1136 cm^{-1}; MS (EI) m/e (relative intensity) 414 (M^+, 37), 310 (98), 238 (6), 160 (10), 105 (100); HRMS (EI) m/e (M^+) calcd 414.1943, obsd 414.1936.

Pyrrolo[1,2-*c*]imidazole Mesomeric Betaine (10i). A solution of 2-formylpyrrole **7f**[3] (100.4 mg, 0.45 mmol), imine **8e** (107.1 mg, 0.90 mmol), and acetic acid (54 mg, 0.90 mmol) in methanol (6 mL) was heated at reflux for 4 h. The solvent was evaported, and the residue was separated by PTLC (hexanes–EtOAc, 1:2) to afford **10i** (73 mg, 50%) as a plae brown solid. Recrystallization from ether–EtOAc provided a sample for microanalysis: mp 159–160 °C; ^{1}H NMR (300 MHz, benzene-d_6) δ 1.25 (t, 3 H, J = 7.1 Hz), 2.15 (s, 3 H), 2.55 (s, 3 H), 2.96 (s, 3 H), 4.41 (q, 2 H, J = 7.1 Hz), 6.66 (s, 1 H), 6.86–6.90 (m, 2 H), 7.08–7.13 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.78 (q), 14.64 (q), 28.42 (q), 36.09 (q), 58.78 (t), 93.78 (s), 103.78 (d), 119.78 (s), 127.27 (d), 127.92 (s), 128.55 (s), 129.04 (d), 129.26 (d), 135.42 (s), 142.35 (s), 164.73 (s), 181.16 (s); IR (KBr) 3148, 3047, 2986, 1680, 1607, 1518, 1495, 1479, 1419, 1389, 1238, 1195, 1133, 1092, 771 cm^{-1}; MS (EI) m/e (relative intensity) 324 (M^+, 100), 309 (6), 296 (9), 281 (21), 279 (19), 252 (12), 208 (7). Anal. Calcd for $C_{19}H_{20}N_2O_3$: C, 70.35; H, 6.22; N, 8.64. Found: C, 70.22; H, 6.08; N, 8.70.

Deuterium Exchange Experiments on 10b and 10e. The experiments were performed in the NMR tube. A solution of mesomeric betaine **10b** (4 mg) and CD_3COOD (1 μL) in CD_3OD (600 μL) was heated at 80 °C (oil bath temperature) for 3 h. During this time complete hydrogen–deuterium exchange at the 1-position occurred. In a similar experiment, complete hydrogen–deuterium exchange was observed when a solution of mesomeric betaine **10e** (4 mg) and CD_3COOD (1 μL) in CD_3OD (600 μL) was kept at room temperature for 10 h.[23]

Ethyl 2-[[*N*-[[3-(Benzyloxycarbonyl)-5-(ethoxycarbonyl)-4-methylpyrrol-2-yl]methyl]-*N*-methylamino]methyl]-3-(benzyloxycarbonyl)-4-methylpyrrole-5-carboxylate (12a). To a solution of mesomeric betaine **10b** (100 mg, 0.16 mmol) and acetic acid (300 μL) in acetonitrile (25 mL), stirring at room temperature, was added in portions $NaBH_3CN$ (300 mg, 4.77 mmol) over 3 h. The stirring was continued for 9 h, and then the solvent was evaporated. The residue was treated with CH_2Cl_2, and the organic phase was washed with water and then saturated $NaHCO_3$ and was dried over $MgSO_4$. PTLC separation (6% CH_3OH–CH_2Cl_2) and recrystallization from methanol afforded **12a** (85.7 mg, 85%) as white crystals: mp 120–121 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (t, 6 H, J = 7.1 Hz), 2.26 (s, 3 H), 2.55 (s, 6 H), 3.95 (s, 4 H), 4.29 (q, 4 H, J = 7.1 Hz), 5.29 (s, 4 H), 7.26–7.42 (m, 10 H), 9.95 (br s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.97 (q), 14.43 (q), 43.80 (q), 54.30 (t), 60.34 (t), 65.73 (t), 113.60 (s), 119.03 (s), 128.07 (d), 128.19 (d), 128.54 (d), 130.78 (s), 136.49 (s), 139.29 (s), 161.31 (s), 164.88 (s); IR (KBr) 3307, 3271, 2976, 2938, 1711, 1701, 1687, 1664, 1567, 1481, 1446, 1372, 1298, 1276, 1254, 1123, 1089, 776, 732 cm^{-1}; MS (FAB) m/e (relative intensity) 630 [$(M + H)^+$, 30], 329 (13), 300 (21), 91 (100). Anal. Calcd for $C_{35}H_{39}N_3O_8$: C, 66.76; H, 6.24; N, 6.67. Found: C, 66.68; H, 6.15; N, 6.68.

Independent Synthesis of 12a. To an ice-cold solution of methylamine (33% aqueous solution, 0.75 mL) in ethanol (5 mL) was added ethyl 2-(chloromethyl)-3-(benzyloxycarbonyl)-4-methylpyrrole-5-carboxylate[24] (1.00 g, 2.98 mmol). The mixture was stirred at room temperature for 1 h and then was heated at 60 °C for 30 min. The solution was cooled and then was poured into cold water (50 mL). The precipitate was filtered and dried. Purification by column chromatography (hexanes–EtOAc, 20:1, 10:1, 2:1) afforded **12a** (621 mg, 66%) as a white solid.

Ethyl 2-[(*N*-Benzyl-*N*-methylamino)methyl]-3-(ethoxycarbonyl)-4-methylpyrrole-5-carboxylate (12b). In a manner similar to the preparation of **12a**, **12b** was obtained from mesomeric betaine **10e** as colorless oil in 42% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (t, 3 H, J = 7.1 Hz), 1.39 (t, 3 H, J = 7.1 Hz), 2.29 (s, 3 H), 2.57 (s, 3 H), 3.60 (s, 2 H), 3.90 (s, 2 H), 4.27 (q, 2 H, J = 7.1 Hz), 4.34 (q, 2 H, J = 7.1 Hz), 7.23–7.34 (m, 5 H), 9.66 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.64 (q), 14.28 (q), 14.28 (q), 42.91 (q), 53.86 (t), 59.33 (t), 59.94 (t), 62.26 (t), 112.97 (s), 118.25 (s), 127.14 (d), 128.26 (d), 128.66 (d), 130.78 (s), 138.26 (s), 140.25 (s), 161.17 (s), 165.05 (s); IR (neat) 3434, 2980, 1718, 1696, 1568, 1485, 1445, 1432, 1371, 1257, 1232, 1071, 785, 744, 700 cm^{-1}; MS (CI) m/e (relative intensity) 359 [$(M + H)^+$, 18], 313 (8), 267 (100), 238 (15), 221 (58), 175 (13), 120 (16), 91 (27); HRMS (FAB) m/e (M^+) calcd 358.1893, obsd 358.1899

Independent Synthesis of 12b. In a manner similar to the preparation of **12a**, **12b** was obtained from ethyl 2-(chloromethyl)-3-(ethoxycarbonyl)-4-methylpyrrole-5-carboxylate[25] (273.5 mg, 1.00 mmol) and *N*-methylbenzylamine (242.1 mg, 2.00 mmol) in ethanol (2 mL). The reaction was stirred at room temperature for 1 h and at 60 °C for 45 min, and then the solvent was evaporated, and the residue was partitioned between CH_2Cl_2 and water. The organic layer was washed with water and dried over $MgSO_4$. Purification by column chromatography (hexanes–EtOAc, 20:1, 10:1, 4:1) afforded **12b** (327 mg, 91%) as a colorless oil.

2,2′-Bipyrrole 17a. A solution of mesomeric betaine **10e** (35.4 mg, 0.10 mmol) and DMAD (15.6 mg, 0.11 mmol) in benzene (3 mL) was stirred at room temperature for 2 h. The solvent was evaporated, and the residue was purified by PTLC [(2% CH_3OH–CH_2Cl_2)–(hexanes–EtOAc, 2:1), 1:1] to afford **17a** (41.2 mg, 83%) as a pink, viscous oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.18 (t, 3 H, J = 7.2 Hz), 1.37 (t, 3 H, J = 7.2 Hz), 2.66 (s, 3 H), 3.24 (s, 3 H), 3.66 (s, 3 H), 3.68 (s, 3 H), 4.16 (q, 2 H, J = 7.2 Hz), 4.30 (q, 2 H, J = 7.2 Hz), 7.35–7.38 (m, 2 H), 7.43–7.46 (m, 3 H), 9.95 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.55 (q), 14.13 (q), 14.34 (q), 32.97 (q), 51.35 (q), 51.52 (q), 59.72 (t), 60.59 (t), 115.18 (s), 116.20 (s), 117.69 (s), 121.26 (s), 127.59 (s), 127.71 (s), 128.37 (d), 128.90 (d), 130.43 (d), 130.43 (s), 130.66 (s), 137.56 (s), 161.09 (s), 163.94 (s), 164.49 (s), 165.11 (s); IR (neat) 3260, 2984, 2951, 1716, 1670, 1483, 1467, 1256, 1203, 1172, 1066 cm^{-1}; MS (EI) m/e (relative intensity) 496 (M^+, 100), 464 (36), 450 (19), 419 (11), 118 (10); HRMS (EI) m/e (M^+) calcd 496.1845, obsd 496.1840.

2,2′-Bipyrroles 17b and 17c. A solution of mesomeric betaine **10e** (106.2 mg, 0.30 mmol) and ethyl propiolate (97.1 mg, 0.99 mmol) in benzene (9 mL) was stirred at room temperature for 8 h. The solvent was evaporated, and the residue was purified by column chromatography (hexanes–EtOAc, 10:1) to afford **17b** and **17c**. Recrystallization of this mixture from hexanes–EtOAc, 2:1, afforded pure **17b** (38.5 mg) as white crystals: mp 145.5–146.5 °C. Regioisomer **17c** was isolated by PTLC (hexanes–*tert*-butyl

(22) Fischer, H.; Adler, E. *Hoppe-Seyler's Z. Physiol. Chem.* **1932**, *210*, 139.

(23) Prolonged exposure of mesomeric betaines (**10a–i**) to acidic conditions leads to their slow decomposition.

(24) Ethyl 2-(chloromethyl)-3-(benzyloxycarbonyl)-4-methylpyrrole-5-carboxylate was prepared by treatment of ethyl 4-(benzyloxycarbonyl)-3,5-dimethylpyrrole-2-carboxylate with SO_2Cl_2 (1 equiv) in CH_2Cl_2 at 0 °C.

(25) Corwin, A. H.; Bailey, W. A., Jr.; Viohl, P. *J. Am. Chem. Soc.* **1942**, *64*, 1267.

methyl ether, 2:1, eluting two times) of the mother liquor as a colorless, viscous oil (3 mg, 2%). Additional amount of **17b** (3 mg, 31% total) was also isolated during PTLC separation of the mother liquor. **17b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.11 (t, 6 H, J = 7.1 Hz), 1.35 (t, 3 H, J = 7.1 Hz), 2.67 (s, 3 H), 3.41 (s, 3 H), 4.07 (q, 2 H, J = 7.1 Hz), 4.13 (q, 2 H, J = 7.1 Hz), 4.31 (q, 2 H, J = 7.1 Hz), 6.75 (s, 1 H), 7.35–7.45 (m, 5 H), 9.74 (br s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.71 (q), 14.03 (q), 14.03 (q), 14.36 (q), 33.22 (q), 59.55 (t), 59.58 (t), 60.52 (t), 110.11 (d), 115.73 (s), 116.85 (s), 120.59 (s), 127.77 (d), 128.56 (d), 128.94 (d), 129.38 (s), 129.44 (s), 130.47 (s), 132.12 (s), 135.94 (s), 161.32 (s), 164.21 (s), 164.27 (s); IR (neat) 3275, 2980, 2926, 1714, 1685, 1476, 1254, 1204, 1066, 764 cm^{-1}; MS (EI) m/e (relative intensity) 452 (M^+, 100), 406 (54), 361 (10), 305 (5). Anal. Calcd for $C_{25}H_{28}N_2O_6$: C, 66.36; H, 6.24; N, 6.19. Found: C, 66.12; H, 6.40; N, 5.76. **17b**, ^{13}C-enriched: ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.94 (s), $^2J_{C\text{-}5',H\text{-}4'}$ = 7.1 Hz, $^1J_{C\text{-}5',C\text{-}4'}$ = 67.8 Hz. **17c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.13 (t, 3 H, J = 7.1 Hz), 1.23 (t, 3 H, J = 7.1 Hz), 1.39 (t, 3 H, J = 7.1 Hz), 2.65 (s, 3 H), 3.25 (s, 3 H), 4.12 (q, 2 H, J = 7.1 Hz), 4.21 (q, 2 H, J = 7.1 Hz), 4.36 (q, 2 H, J = 7.1 Hz), 6.81 (s, 3 H), 7.37–7.39 (m, 2 H), 7.41–7.47 (m, 3 H), 9.05 (br s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.80 (q), 14.14 (q), 14.25 (q), 14.46 (q), 32.96 (q), 59.46 (t), 59.86 (t), 60.63 (t), 112.17 (d), 113.17 (s), 116.49 (s), 120.23 (s), 124.58 (s), 128.05 (d), 128.55 (d), 129.98 (s), 130.58 (d), 130.87 (s), 131.69 (s), 140.28 (s), 160.95 (s), 164.24 (s), 164.36 (s); IR (neat) 3267, 2981, 2934, 1703, 1651, 1553, 1468, 1373, 1254, 1197, 1100, 1061, 1037, 776 cm^{-1}; MS (EI) m/e (relative intensity) 452 (M^+, 100), 406 (74), 361 (10), 305 (15), 277 (12), 118 (14), 105 (21); HRMS (EI) m/e (M^+) calcd 452.1947, obsd 452.1944. **17c**, ^{13}C-enriched: ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.28 (s), $^3J_{C\text{-}5',H\text{-}3'}$ = 6.1 Hz.

2,2′-Bipyrrole 17d. A solution of mesomeric betaine **10e** (70.8 mg, 0.20 mmol) and phenylacetylene (372 mg, 3.64 mmol) in benzene (3 mL) was heated at reflux for 24 h. The solvent and excess phenylacetylene were evaporated, and the residue was purified by column chromatography (hexanes–EtOAc, 10:1) to afford **17d** (54.2 mg, 59%) as a pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.12 (t, 3 H, J = 7.1 Hz), 1.33 (t, 3 H, J = 7.1 Hz), 2.70 (s, 3 H), 3.42 (s, 3 H), 4.16 (q, 2 H, J = 7.1 Hz), 4.29 (q, 2 H, J = 7.1 Hz), 6.51 (s, 1 H), 7.12–7.50 (m, 10 H), 8.95 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.70 (q), 14.06 (q), 14.28 (q), 32.77 (q), 59.54 (t), 60.47 (t), 107.98 (d), 117.72 (s), 120.62 (s), 121.65 (s), 125.16 (s), 125.59 (d), 126.61 (d), 127.28 (d), 128.40 (d), 128.48 (d), 128.87 (d), 130.83 (s), 130.88 (s), 133.11 (s), 135.46 (s), 136.37 (s), 161.22 (s), 164.28 (s); IR (neat) 3269, 2981, 2930, 1702, 1670, 1556, 1509, 1481, 1467, 1382, 1265, 1250, 1068, 758, 734, 699; MS (EI) m/e (relative intensity) 456 (M^+, 86), 410 (100), 309 (6), 105 (28); HRMS (EI) m/e (M^+) calcd 456.2049, obsd 456.2042. **17d**, ^{13}C-enriched: ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.37 (s), $^2J_{C\text{-}5',H\text{-}4'}$ = 6.9 Hz, $^1J_{C\text{-}5',C\text{-}4'}$ = 68.1 Hz.

2,2′-Bipyrroles 17e and 17f. A solution of mesomeric betaine **10e** (106.2 mg, 0.30 mmol) and ethyl phenylpropiolate (697 mg, 4.0 mmol) in benzene (9 mL) was heated at reflux for 20 h. The solvent was evaporated, and the residue was purified by column chromatography (hexanes–EtOAc, 10:1, 8:1) to afford **17e** (98.1 mg, 62%) and **17f** (22.3 mg, 14%) as a colorless, viscous oils. **17e**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.79 (t, 3 H, J = 7.1 Hz), 1.21 (t, 3 H, J = 7.1 Hz), 1.28 (t, 3 H, J = 7.1 Hz), 2.60 (s, 3 H), 3.16 (s, 3 H), 3.89 (q, 2 H, J = 7.1 Hz), 4.20 (q, 4 H, J = 7.1 Hz), 7.11–7.25 (m, 5 H), 7.38–7.49 (m, 5 H), 9.57 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.60 (q), 13.44 (q), 14.20 (q), 14.20 (q), 32.59 (q), 59.12 (t), 59.58 (t), 60.55 (t), 112.40 (s), 117.97 (s), 120.49 (s), 122.84 (s), 126.28 (d), 126.83 (s), 127.31 (d), 127.95 (d), 128.32 (d), 129.55 (s), 129.81 (d), 130.27 (s), 130.51 (d), 132.16 (s), 134.53 (s), 139.30 (s), 161.36 (s), 164.10 (s), 164.58 (s); IR (neat) 3264, 2981, 2937, 1706, 1670, 1508, 1469, 1384, 1292, 1255, 1155, 1130, 760 cm^{-1}; MS (EI) m/e (relative intensity) 528 (M^+, 100), 482 (52), 129 (7), 118 (9); HRMS (EI) m/e (M^+) calcd 528.2260, obsd 528.2254. **17f**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, 3 H, J = 7.1 Hz), 1.21 (t, 3 H, J = 7.1 Hz), 1.39 (t, 3 H, J = 7.1 Hz), 2.69 (s, 3 H), 3.32 (s, 3 H), 3.94 (q, 2 H, J = 7.1 Hz), 4.19 (q, 2 H, J = 7.1 Hz), 4.36 (q, 2 H, J = 7.1 Hz), 7.13–7.21 (m, 6 H), 7.26–7.31 (m, 4 H), 9.47 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.69 (q), 13.60 (q), 14.19 (q), 14.44 (q), 33.18 (q), 59.49 (t), 59.65 (t), 60.52 (t), 114.68 (s), 117.17 (s), 120.57 (s), 124.58 (s), 126.11 (d), 127.25 (d), 127.87 (d), 128.09 (s), 128.29 (d), 129.54 (s), 130.62 (s), 130.82 (d), 131.05 (d), 131.35 (s), 133.89 (s), 135.02 (s), 161.14 (s), 164.26 (s), 164.44 (s); IR (neat) 3268, 2982, 2936, 1706, 1700, 1697, 1670, 1507, 1473, 1258, 1203, 1136, 1069, 732 cm^{-1}; MS (EI) m/e (relative intensity) 528 (M^+, 100), 482 (43), 452 (10), 118 (7); HRMS (EI) m/e (M^+) calcd 528.2260, obsd 528.2250.

2,2′-Bipyrroles 17g and 17h. A solution of mesomeric betaine **10e** (106.2 mg, 0.30 mmol) and benzyl phenylpropiolate (944 mg, 4.0 mmol) in benzene (9 mL) was heated at reflux for 14 h. The solvent was evaporated, and the residue was purified by column chromatography (hexanes–EtOAc, 10:1, 8:1) to afford **17g** (115.9 mg, 65%) and **17h** (26.0 mg, 15%) as colorless, viscous oils. **17g**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22 (t, 3 H, J = 7.1 Hz), 1.26 (t, 3 H, J = 7.1 Hz), 2.58 (s, 3 H), 3.17 (s, 3 H), 4.20 (q, 2 H, J = 7.1 Hz), 4.21 (q, 2 H, J = 7.1 Hz), 4.93 (s, 2 H), 6.70–6.73 (m, 2 H), 7.09–7.20 (m, 8 H), 7.37–7.45 (m, 5 H), 9.18 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.66 (q), 14.20 (q), 14.25 (q), 32.68 (q), 59.64 (t), 60.58 (t), 65.23 (t), 111.91 (s), 117.94 (s), 120.51 (s), 123.04 (s), 126.42 (d), 126.97 (s), 127.30 (d), 127.52 (d), 127.61 (d), 127.92 (d), 128.14 (d), 128.44 (d), 129.38 (s), 129.85 (d), 130.29 (s), 130.51 (d), 132.05 (s), 134.45 (s), 135.98 (s), 139.57 (s), 161.32 (s), 164.10 (s), 164.34 (s); IR (neat) 3263, 2981, 2938, 1708, 1668, 1469, 1444, 1378, 1255, 1151, 1062, 1009, 759 cm^{-1}; MS (EI) m/e (relative intensity) 590 (M^+, 100), 544 (23), 528 (9), 437 (7), 91 (43); HRMS (EI) m/e (M^+) calcd 590.2417, obsd 590.2426. **17h**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.19 (t, 3 H, J = 7.1 Hz), 1.37 (t, 3 H, J = 7.1 Hz), 2.62 (s, 3 H) 3.29 (s, 3 H), 4.17 (q, 2 H, J = 7.1 Hz), 4.30 (br q, 2 H), 4.94 (s, 2 H), 6.85 (d, 2 H, J = 6.6 Hz), 7.14–7.22 (m, 8 H), 7.26–7.30 (m, 5 H), 9.25 (br s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.67 (q), 14.19 (q), 14.42 (q), 33.15 (q), 59.63 (q), 60.42 (q), 65.70 (q), 114.12 (s), 117.04 (s), 120.62 (s), 124.72 (s), 126.20 (d), 127.40 (d), 127.60 (d), 127.87 (d), 128.01 (d), 128.04 (d), 128.27 (d), 129.33 (s), 130.47 (s), 130.81 (d), 130.99 (d), 131.15 (s), 133.99 (s), 134.83 (s), 135.73 (s), 160.85 (s), 164.04 (s), 164.15 (s); IR (neat) 3266, 2981, 2935, 1707, 1700, 1697, 1685, 1457, 1379, 1256, 1203, 1130, 1069 cm^{-1}; MS (EI) m/e (relative intensity) 590 (M^+, 100), 544 (13), 482 (13), 118 (10), 91 (47); HRMS (EI) m/e (M^+) calcd 590.2417, obsd 590.2410.

2,2′-Bipyrrole 17i. A solution of mesomeric betaine **10g** (45.2 mg, 0.10 mmol) and DMAD (17.0 mg, 0.12 mmol) in benzene (3 mL) was stirred at room temperature for 8 h. The solvent was evaporated, and the residue was purified by PTLC (hexanes–EtOAc, 2:1) to afford **17i** (16.7 mg, 28%) as a colorless oil: ^{1}H NMR (500 MHz, benzene-d_6) δ 0.53–0.56 (m), 0.64–0.78 (m), 0.89–0.93 (m), 0.97 (t, 3 H, J = 7.2 Hz), 0.99 (t, 3 H, J = 7.1), 1.01 (t, 3 H, J = 7.0 Hz), 1.06 (t, 3 H, J = 7.1 Hz) 1.28–1.40 (m), 1.52–1.58 (m), 1.75 (br d), 1.82 (br d), 1.91 (br d), 2.02 (br d), 3.00 (s, 3 H), 3.02 (s, 3 H), 3.26 (s, 3 H), 3.29 (s, 3 H), 3.39 (s, 3 H), 3.40 (s, 3 H), 3.41 (s, 3 H), 3.42 (s, 3 H), 3.72–3.81 (m), 3.92–4.12 (m), 4.22–4.26 (m), 6.55 (d, 1 H, J = 8.2 Hz), 6.58 (d, 1 H, J = 8.2 Hz), 6.88 (dt, 1 H, J = 0.9, 6.8 Hz), 6.89 (dt, 1 H, J = 0.8, 7.0 Hz), 7.13–7.18 (m, 2 H), 7.38 (dd, 1 H, J = 1.7, 7.4 Hz), 7.50 (dd, 1 H, J = 1.7, 7.5 Hz), 10.05 (br s, 1 H), 10.25 (br s, 1 H); ^{13}C NMR (125 MHz, benzene-d_6) δ 12.10 (q), 12.16 (q), 13.83 (q), 14.11 (q), 14.21 (q), 14.21 (q), 25.30 (t), 25.30 (t), 26.40 (t), 26.50 (t), 26.50 (t), 26.76 (t), 33.20 (t), 33.30 (t), 33.39 (t), 33.51 (t), 51.06 (q), 51.10 (q), 51.19 (q), 51.26 (q), 55.00 (q), 55.00 (q), 59.55 (t), 59.67 (t), 60.06 (d), 60.08 (d), 60.79 (t), 60.90 (t), 110.96 (d), 111.31 (d), 116.39 (s), 116.60 (s), 118.49 (s), 118.56 (s), 119.01 (s), 119.16 (s), 120.42 (d), 120.54 (d), 121.05 (s), 121.41 (s), 121.46 (s), 121.50 (s), 126.50 (s), 126.63 (s), 129.75 (s), 129.92 (s), 130.29 (s), 130.35 (s), 130.79 (d), 130.79 (d), 133.02 (d), 133.94 (s), 133.98 (s), 134.13 (d), 158.37 (s), 158.96 (s), 162.00 (s), 162.13 (s), 164.07 (s), 164.13 (s), 164.41 (s), 164.64 (s), 165.07 (s), 165.19 (s); IR (neat) 3254, 2940, 1717, 1669, 1551, 1465, 1321, 1256, 1169, 1066 cm^{-1}; MS (EI) m/e (relative intensity) 594 (M^+, 100), 563 (8), 562 (8), 512 (18), 466 (20), 135 (33); HRMS (EI) m/e (M^+) calcd 594.2577, obsd 594.2567.

2,2′:5′,2″-Terpyrrole 17j. A solution of mesomeric betaine **10b** (30.0 mg, 0.048 mmol) and DMAD (7.5 mg, 0.053 mmol) in benzene (3 mL) was heated at reflux for 15 min. The solvent was evaporated, and the residue was purified by PTLC [(2% MeOH–CH_2Cl_2)–(hexanes–EtOAc, 2:1), 1:1] to afford **17j** (19.6 mg, 53%) as a brown oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.41 (t, 6 H, J = 7.0 Hz), 2.63 (s, 6 H), 2.90 (s, 3 H), 3.70 (br s, 6 H), 4.39 (q, 4 H, J = 7.0 Hz), 5.03 (br s, 2 H), 5.09 (br s, 2 H), 7.14 (br d, 4 H), 7.38 (br s, 6 H), 8.89 (br s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ

11.61 (q), 14.41 (q), 32.42 (q), 51.69 (q), 60.55 (t), 65.85 (t), 116.46 (s), 116.74 (s), 121.37 (s), 126.86 (s), 128.03 (d), 128.23 (d), 128.23 (s), 128.60 (d), 130.47 (s), 135.84 (s), 160.77 (s), 163.56 (s), 164.19 (s); IR (neat) 3268, 2983, 2953, 1710, 1455, 1376, 1304, 1263, 1214, 1147, 1061, 736 cm^{-1}; MS (FAB) m/e (relative intensity) 768 [(M + H)$^+$, 9], 767 (M^+, 12), 91 (100); HRMS (FAB) m/e (M^+) calcd 767.2690, obsd 767.2670.

***trans*- and *cis*-2′,3′-Dihydro-2,2′-bipyrroles (20a,b).** A solution of mesomeric betaine **10e** (70.8 mg, 0.20 mmol) and dimethyl maleate (63.4 mg, 0.44 mmol) in benzene (4 mL) was heated at reflux for 6 h. The solvent was evaporated, and the residue was purified by PTLC [(hexanes–EtOAc, 3:1)–ether, 1:1] to afford **20a** (69.5 mg, 70%) and **20b** (8.3 mg, 8%) as a pale yellow oils. In a similar experiment, a solution of **10e** (70.8 mg, 0.20 mmol) and dimethyl fumarate (63.4 mg, 0.44 mmol) in benzene (4 mL) at reflux (3 h) afforded **20a** (77.2 mg, 77%) and **20b** (14.6 mg, 15%). **20a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (t, 3 H, J = 7.2 Hz), 1.41 (t, 3 H, J = 7.1 Hz), 2.54 (s, 3 H), 2.59 (s, 3 H), 3.47 (s, 3 H), 3.79 (s, 3 H), 3.85 (d, 1 H, J = 8.1 Hz), 4.18–4.28 (m, 1 H), 4.31–4.41 (m, 1 H), 4.38 (q, 2 H, J = 7.1 Hz), 5.47 (d, 1 H, J = 8.1 Hz), 7.44–7.48 (m, 5 H), 9.30 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.75 (q), 14.36 (q), 14.36 (q), 35.74 (q), 50.40 (q), 52.18 (q), 54.85 (d), 59.93 (t), 60.58 (t), 64.81 (d), 99.39 (s), 114.20 (s), 119.67 (s), 128.18 (d), 128.93 (d), 129.62 (d), 130.77 (s), 130.99 (s), 139.30 (s), 161.33 (s), 163.67 (s), 164.43 (s), 164.90 (s), 173.82 (s); IR (neat) 3250, 2981, 2949, 1744, 1699, 1671, 1615, 1572, 1437, 1305, 1247, 1198, 1076 cm^{-1}; MS (EI) m/e (relative intensity) 498 (M^+, 47), 466 (96), 438 (18), 393 (100), 347 (31), 315 (38), 118 (30); HRMS (EI) m/e (M^+) calcd 498.2002, obsd 498.1992. **20a**, ^{13}C-enriched: ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.7 (s), $^3J_{C\text{-}5',H\text{-}3'}$ = 3.3 Hz, $^3J_{C\text{-}5',H\text{-}2'}$ = 0 Hz. **20b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.40 (t, 3 H, J = 7.2 Hz), 1.43 (t, 3 H, J = 7.2 Hz), 2.44 (s, 3 H), 2.58 (s, 3 H), 3.37 (s, 3 H), 3.48 (s, 3 H), 4.36 (q, 4 H, J = 7.2 Hz), 4.45 (d, 1 H, J = 11.9 Hz), 5.52 (d, 1 H, J = 11.9 Hz), 7.45–7.47 (m, 5 H), 9.33 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.77 (q), 14.42 (q), 14.42 (q), 36.24 (q), 50.58 (q), 51.72 (q), 51.80 (d), 60.00 (t), 60.56 (t), 64.97 (d), 101.81 (s), 115.29 (s), 119.73 (s), 128.23 (d), 128.79 (d), 129.46 (d), 130.49 (s), 131.47 (s), 136.15 (s), 161.28 (s), 164.66 (s), 164.66 (s), 165.05 (s), 171.84 (s); IR (neat) 3256, 2983, 2947, 1742, 1699, 1620, 1590, 1436, 1371, 1245, 1191, 1072 cm^{-1}; MS (EI) m/e (relative intensity) 498 (M^+, 34), 466 (58), 438 (10), 393 (100), 347 (21), 315 (25), 118 (14); HRMS (EI) m/e (M^+) calcd 498.2002, obsd 498.1999. **20b**,^{13}C-enriched: ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1 (s), $^3J_{C\text{-}5',H\text{-}3'}$ = 3.7 Hz, $^3J_{C\text{-}5',H\text{-}2'}$ = 0 Hz.

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Supplementary Material Available: ^{1}H NMR spectra of **17i** at 25 °C, 65 °C, and 130 °C; ^{1}H NMR and ^{13}C NMR spectra of **10a,f–h**, **12b**, **17a–j**, and **20a,b**; and ^{13}C NMR spectra of ^{13}C-enriched samples of **10e**, **17b,d** and **20a,b** (42 pages). Ordering information is given on any current masthead page.

Total Synthesis of (±)-7-Epi-20-desethylgelsedine

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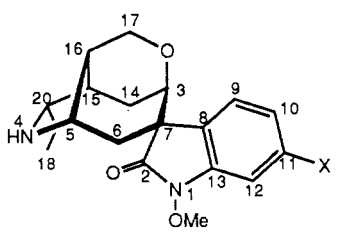
The oxindole alkaloid gelsedine contains a unique molecular architecture. The synthetic approach to this pentacyclic molecule involved the efficient preparation of the all-cis trisubstituted pyrrolidine intermediate **14**. The lactone system **18**, an excellent precursor of the pentacyclic cage framework of gelsedine, was prepared in an efficient and highly convergent manner by reaction of pyrrolidine **16** and the readily available *N*-methoxyindole system **5**. Subsequent steps led to the formation of the title compound.

Gelsedine (**1**) is an oxindole alkaloid that was isolated from *Gelsemium sempervirens* in 1953 by Schwarz and Marion.[1] Its structure was elucidated by Wenkert in 1962 through spectroscopic comparison with the related alkaloid gelsemicine (**2**).[2,3] Since that time synthetic studies toward the total synthesis of gelsedine or gelsemicine have received scant attention in the literature, and to date a successful synthesis of these alkaloids has not been reported.[4] Very recent activity toward the total synthesis of the Gelsemium alkaloids[5] prompts us to describe our progress toward the total synthesis of gelsedine.[6]



1, gelsedine (X = H)

2, gelsemicine (X = OMe)

Our retrosynthetic analysis to **1** is illustrated in Scheme I. We defined 20-desethylgelsedine (**3**) as a penultimate precursor of the target alkaloid, assuming that the C-20 ethyl (gelsedine numbering throughout the paper) could be introduced at the end of the sequence. The formation of the quaternary spirocyclic center at C-7 is the key structural problem in this pentacyclic skeleton. Recog-

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