Pyrrolodiazines. 2. Structure and Chemistry of Pyrrolo[1,2-*a*]pyrazine and 1,3-Dipolar Cycloaddition of Its Azomethine Ylides

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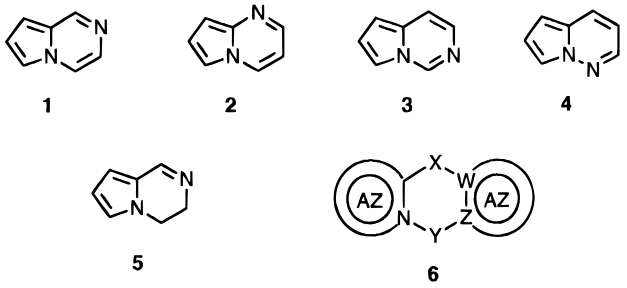
A new synthesis of the pyrrolo[1,2-*a*]pyrazine system from pyrrole is described. In light of the *ab initio* calculations carried out on this heterocyclic system some of its basic chemistry was investigated and included electrophilic substitution, addition of organolithium reagents, metalation with lithium diisopropylamide and subsequent reaction with electrophiles, and formation of salts by quaternization of the nonbridgehead nitrogen. N-ylides obtained from these salts undergo 1,3-dipolar cycloaddition with suitable dipolarophiles to give dipyrrolo[1,2-*a*]pyrazines, pyrazolo[1,5-*a*]-pyrrolo-[2,1-*c*]pyrazines, and heterobetaines. Examples of intramolecular 1,3-dipolar cycloadditions are also reported.

Introduction

Although the chemistry and applications of indolizines as drugs, dyestuffs, and light-screening agents[1] have been extensively studied, little attention has been paid to some of their aza analogues such as the pyrrolodiazines[2] (Chart 1). This is probably because of difficulties associated with their preparation, with the four possible pyrrolodiazine isomers **1**−**4** all being prepared by synthetic routes which are both lengthy and poor yielding. The syntheses of the pyrrolo[1,2-*a*]pyrimidine **2**,[3] the pyrrolo[1,2-*c*]pyrimidine **3**,[4] and the pyrrolo[1,2-*b*]pyridazine **4**[5] are reported in an overall yield of less than 5% while the pyrrolo[1,2-*a*]-pyrazine **1**[6] system was prepared in a total yield of 18%. Moreover, only one of the six possible dihydro derivatives, the 3,4-dihydropyrrolo[1,2-*a*]pyrazine **5**[7] is known, and its synthesis has also been reported in low yield.

We became interested in these types of bicyclic systems because of their potential for use as starting materials in a simple route to N-bridged heteroaromatics **6** (Chart 1) in which two azoles are joined through their respective nitrogens by a carbon link. The resulting tricyclic system possesses two bridgehead nitrogens, one of which is eventually quaternized. As demonstrated in an earlier report in this series,[8] the heterocyclic system **5** can be prepared in an acceptable yield and bridged 2,2′-biazole

Chart 1



X, Y = (CH)n; CH=CH; n = 0,1,2
W, Z = C, N
AZ = Azole, azolium

derivatives can be obtained by 1,3-dipolar cycloaddition reactions of azomethine ylides generated from 3,4-dihydropyrrolo[1,2-*a*]pyrazinium salts.

Following on from these studies we now report an improved synthesis of the pyrrolo[1,2-*a*]pyrazine system **1**, a study of its structure by *ab initio* calculations, and a description of its basic chemistry, including the 1,3-dipolar cycloaddition of pyrrolo[1,2-*a*]pyrazinium ylides of **1**.

Computational Methods

The electronic structures of the pyrrolo[1,2-*a*]pyrazine **1** and the N-protonated species **1a** were studied using *ab initio* MO techniques. All geometric optimizations were carried out at the closed shell self-consistent field (SCF) level of theory using Schlegel's algorithm.[9] The 6-31G*[10] basis set was used to optimize the geometries. The energies were recalculated by MP2/6-31G*single

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(1) Flitsch, W. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; 1994; Vol. 4, pp 443−495.
(2) For a review of azaindolizines see: (a) Amarnath, V.; Madhav, R. *Synthesis* **1974**, 837−859. (b) Kuhla, D. E.; Lombardino, J. G. *Adv. Heterocycl. Chem.* **1977**, *21*, 1−63. (c) Blewit, H. L. *Chem. Heterocycl. Compd.* **1977**, *30*, 117−178. (d) Maury, G. *Chem. Heterocycl. Compd.* **1977**, *30*, 179−24.
(3) Buchan, R.; Fraser, M.; Shand, C. *J. Org. Chem.* **1977**, *42*, 2448.
(4) Wong, J. L.; Brown, S. M.; Rapoport, H. *J. Org. Chem.* **1965**, *30*, 2398.
(5) Flitsch, W.; Krämer, U. *Liebigs Ann. Chem.* **1970**, *735*, 35.
(6) Herz, W.; Tocker, S.; *J. Am. Chem. Soc.* **1955**, *77*, 6355.
(7) Skoldinov, A.; Peresada, B.; Likhosherstov, A. *Zh. Org. Khim.* **1983**, *19*, 450.
(8) Pablo, M. S.; Gandásegui, T.; Vaquero, J. J.; Garcia Navio, J. L.; Alvarez-Builla, J. *Tetrahedron* **1992**, *48*, 8793.
(9) Schlegel, H. B.; *J. Comput. Chem.* **1982**, *3*, 214.
(10) (a) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2257. (b) Frisch, M. J.; Pople, J. A.; Binkley, J. S. *J. Chem. Phys.* **1984**, *80*, 3265. (c) Clark, T.; Chandrasekhar, J.; Spitznagel, G. W.; Schleyer, P. V. R. *J. Comput. Chem.* **1983**, *4*, 294.

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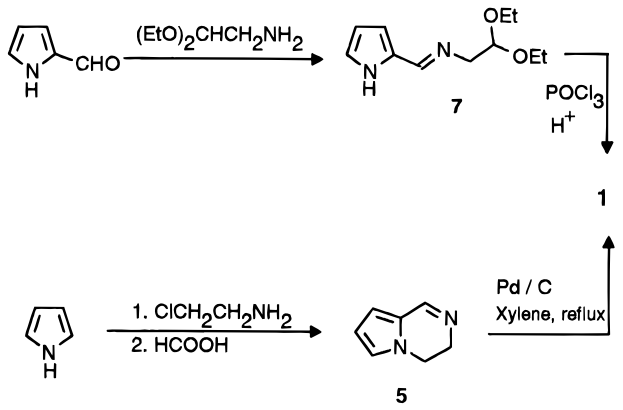
Scheme 1



point calculations on the HF/6-31G* geometries (MP2/6-31G*//HF/6-31G*level of theory). The charges were obtained from the Mulliken population analysis of the HF/6-31G* wave function. All calculations were performed using the GAUSSIAN-92[11] series of programs.

Results and Discussion

The only synthesis of **1** which appears in the literature was reported by Herz and Tocker.[6] This procedure involves the intermediacy of the pyrrolacetal **7** (Scheme 1), which was obtained by the condensation of 2-pyrrolecarboxaldehyde and aminoethylacetal in 90% yield. The cyclization (21% yield) was carried out by treatment with polyphosphoric acid and phosphorus oxychloride, and the method gave an overall yield of 18%. In our hands, attempts to improve the yield of the cyclization step by employing different acid media failed. We consequently considered synthesizing **1** by oxidizing the dihydro derivative **5** which, as we previously reported,[8] could be prepared in 59% yield (Scheme 1). The oxidation was carried out with Pd/C in refluxing xylene to give **1** in an acceptable 65% yield.

Complementary to the synthesis, the structure of the pyrrolo[1,2-*a*]pyrazine **1** and its N-protonated form **1a** (a model of either protonated or *N*-alkyl derivatives) were calculated. The geometries and charges on the heavy atoms of **1** and **1a** are presented in Figure 1 and the calculated geometrical parameters obtained are listed in Tables 1 and 2. The nitrogen atoms show negative charges, with N5 being the most negative. From frequency calculations at the RHF/6-31G* level of theory we obtained a gas phase basicity of 227.4 kcal/mol for **1**. In Figure 2, the HOMO and LUMO and their energy levels are presented. Only atomic orbitals with coefficients larger than 0.1 are depicted.

With respect to the reactivity of the system, in a very early paper concerning the chemistry of diazaindenes, Paudler and Dunham[12] reported that **1** undergoes electrophilic bromination and nitration at the 6- and 8-positions while attempts at Vilsmeier formylation failed to give the corresponding formyl derivatives, in contrast to the ready formylation of indolizines[13] and some derivatives of azaindolizines.[14] When we repeated the bromination of **1** using 1 equiv of bromine, a 1:1 mixture of the 8-bromo derivative **8** and the 6,8-dibromopyrrolo[1,2-*a*]pyrazine **9** was obtained which essentially is in accord with the earlier reported studies.[12,15] However, it is noteworthy that in our hands Vilsmeier−Haack formylation of **1** with dimethylformamide and phosphorous oxychloride gave a 60% yield of the 8-formyl substituted derivative **10**. These results are broadly in agreement with theoretical calculations which indicate C_7 and C_8 to be the carbons of greatest electron surplus.

In the reaction of **1** with 1 equiv of *n*-butyllithium in THF at −78 °C the butyl anion adds to the electron deficient C1 position to give the butylated derivative **11** in 21% yield after quenching. The metalation reaction of **1** with 1.1 equiv of the lithium diisopropylamide (LDA) at −78 °C, followed by the addition of several electrophiles (Scheme 2), afforded the 4-substituted derivatives **12a**−**d** in good yields, with none of the 1-substituted derivatives being obtained in spite of the charge density distribution obtained by theoretical calculations being quite similar for both positions.

Table 1. Optimized Geometrical Parameters for Pyrrolo[1,2-*a*]pyrazine (1)[a]

bond lengths (HF/6-31G*)		bond angles (HF/6-31G*)	
C1−N2	1.279	C1−N2−C3	117.6
N2−C3	1.379	N2−C3−C4	123.5
C3−C4	1.337	N2−C3−H3	116.1
C4−N5	1.378	C3−C4−H4	124.1
N5−C6	1.355	C1−C8a−C8	135.3
C6−C7	1.371	C6−C7−C8	108.2
C7−C8	1.407	H6−C6−C7	130.8
C8−C8a	1.374	H7−C7−C6	125.2
C8a−C1	1.430	C7−C8−C8a	106.7
N5−C8a	1.381	H7−C7−C8	126.6
		C7−C8−H8	127.3
		H7−C8−C8a	126.0
		C8a−C1−H1	118.4
		H1−C1−N2	118.0
		N5−C8a−C8	108.0

[a] Bond lengths are in angstroms and bond angles in degrees.

Table 2. Optimized Geometrical Parameters for Pyrrolo[1,2-*a*]pyrazine 1a[a]

bond lengths (HF/6-31G*)		bond angles (HF/6-31G*)	
C1−N2	1.318	C1−N2−C3	121.9
N2−C3	1.390	N2−C3−C4	120.3
C3−C4	1.328	N2−C3−H3	116.7
C4−N5	1.387	C3−C4−H4	123.2
N5−C6	1.325	C1−C8a−C8	134.4
C6−C7	1.395	C6−C7−C8	108.1
C7−C8	1.379	H6−C6−C7	129.4
C8−C8a	1.397	H7−C7−C6	125.0
C8a−C1	1.373	C7−C8−C8a	107.0
N5−C8a	1.407	H7−C7−C8	127.0
		C7−C8−H8	127.4
		H7−C8−C8a	125.7
		C8a−C1−H1	121.8
		H1−C1−N2	118.1
		C1−N2−H2	119.4

[a] Bond lengths are in angstroms and bond angles in degrees.

(11) GAUSSIAN-92, Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, G.; Andrés, J. L.; Raghavachari, K.; Binkey, J. S.; González, C.; Martin, R. L.; Fox, D. J.; DeFrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. Gaussian Inc., Pittsburgh PA, 1992.

(12) Paudler, W.; Dunham, D. *J. Heterocycl. Chem*. **1965**, *2*, 410.

(13) Mackenzie, S.; Reid, D. *J. Chem. Soc. C* **1970**, 145.

(14) (a) Fraser, M. *J. Org. Chem*. **1972**, *37*, 3027. (b) Buchan, R.; Fraser, M.; Shand, C. *J. Org. Chem*. **1976**, *41*, 351. (c) Fuentes, O.; Paudler, W. *J. Heterocycl. Chem*. **1975**, *12*, 379. (d) Buchan, R.; Fraser, M.; Shand, C. *J. Org. Chem*. **1977**, *42*, 2448.

(15) For the most recent studies on the chemistry of pyrrolo[1,2-*a*]-pyrazine derivatives see: (a) Buchan, R.; Fraser, M. Kong, P. V. S.; Kong Thoo Lin, K. T. *J. Org. Chem*. **1989**, *54*, 1074. (b) Buchan, R.; Fraser, M.; Kong Thoo Lin, P. V. S. *Heterocycles* **1989**, *28*, 857. (c) Kong Thoo Lin, P. V. S.; Buchan, R.; Fraser, M.; McHattie, D. *Heterocycles* **1990**, *31*, 1459.

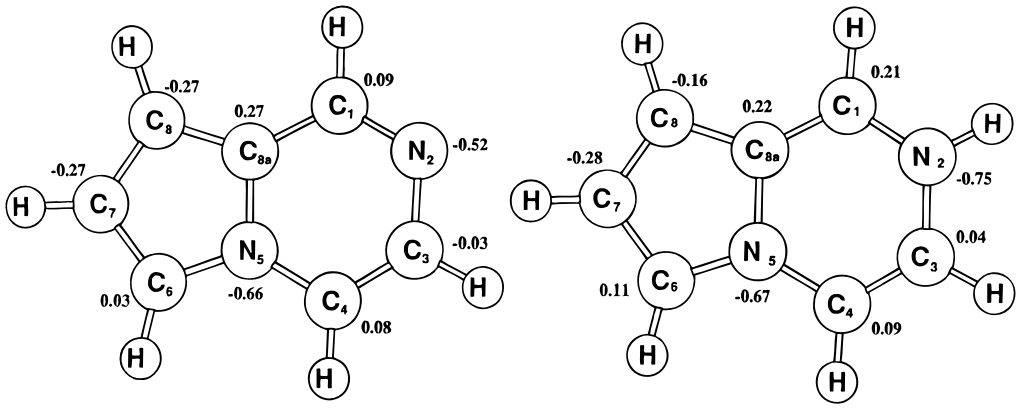


Figure 1. Optimized geometries and atomic charges for pyrrolo[1,2-*a*]pyrazine **1** (left) and the N-protonated form **1a** (right) obtained at the HF/6-31G** level.

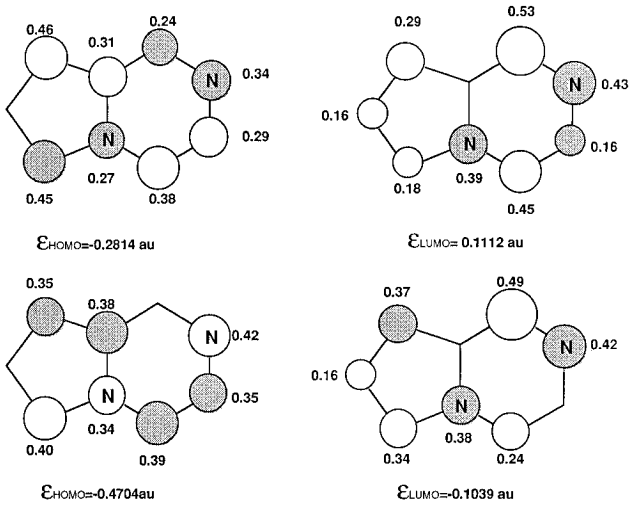
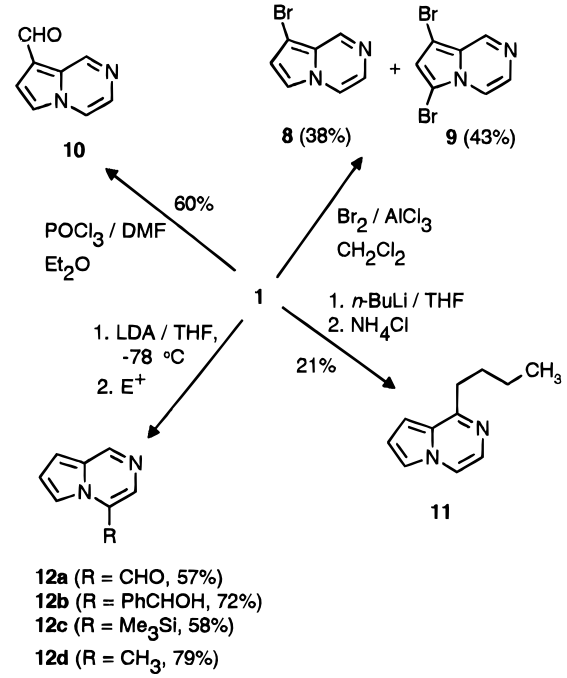


Figure 2. HOMO and LUMO of the pyrrolo[1,2-*a*]pyrazine **1** (above) and the N-protonated form **1a** (below) with the orbital energies and the renormalized HF/6-31G* MO coefficients.

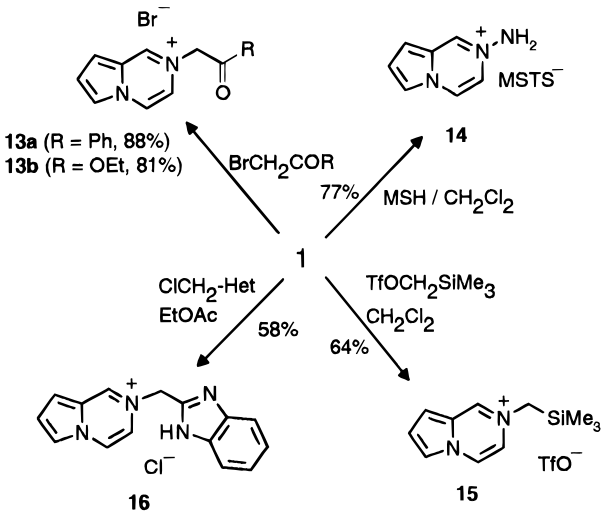
When **1** was treated with alkylating agents the corresponding salts **13**, **15**, and **16** were obtained in good yields (Scheme 3). N-Amination also occurred easily on treatment of **1** with *O*-(mesitylenesulfonyl)hydroxylamine (MSH) in dichloromethane at 0 °C to give the salt **14** in 77% yield. From these salts the corresponding ylides were generated which were then subjected to 1,3-dipolar cycloaddition under various conditions.

The stabilized N-ylides generated from **13a** (R = Ph) and **13b** (R = OEt) in a two-phase liquid−liquid dichloromethane−potassium carbonate system reacted with dimethylacetylenedicarboxylate (DMAD) to afford in each case a mixture of two compounds in combined yield of 56% and 47%, respectively. Although complete separation of both components was difficult, ^{1}H NMR showed that the major product corresponded to the dihydrodipyrrolo[1,2-*a*:2′,1′-*c*]pyrazine **18** while the minor component was the dipyrrolo[1,2-*a*:2′,1′-*c*]pyrazine **19** (Scheme 4). The formation of **18** probably involves a 1,3-hydrogen shift of the initial cycloadduct **17** to give **18** which is then oxidized in part to **19**. The stereochemistry of **18a** and **18b** was established on the basis of their ^{1}H NMR spectra which show coupling constants between the H2 and H3 protons of 11.7 Hz for **18a** and 11.9 Hz for **18b**, consistent with a *trans* disposition for these hydrogens. To simplify product isolation the mixtures of **18** and **19** were readily aromatized with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in dichloromethane, giving overall yields from **13a** and **13b** of 52% and 43% for **19a** and **19b**, respectively.

Scheme 2

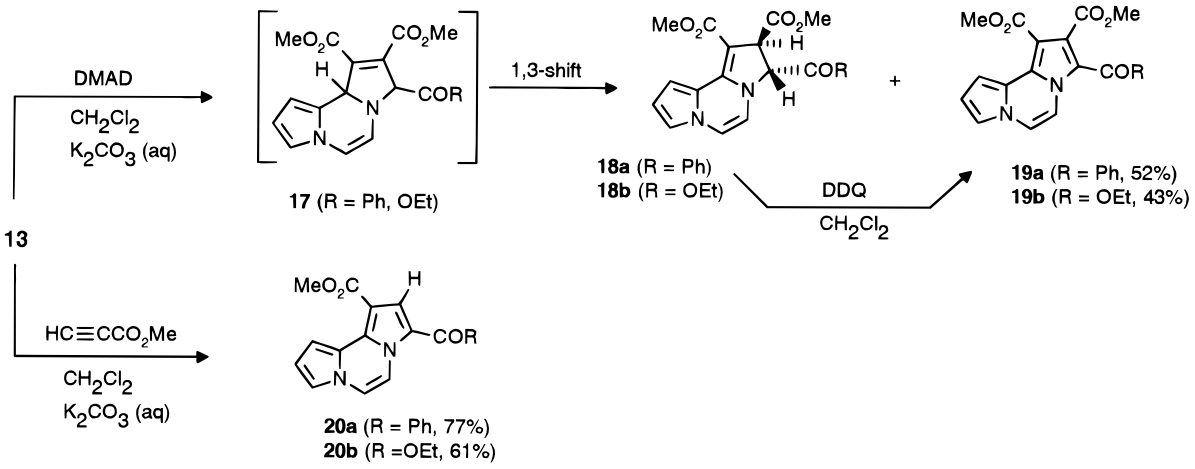


Scheme 3

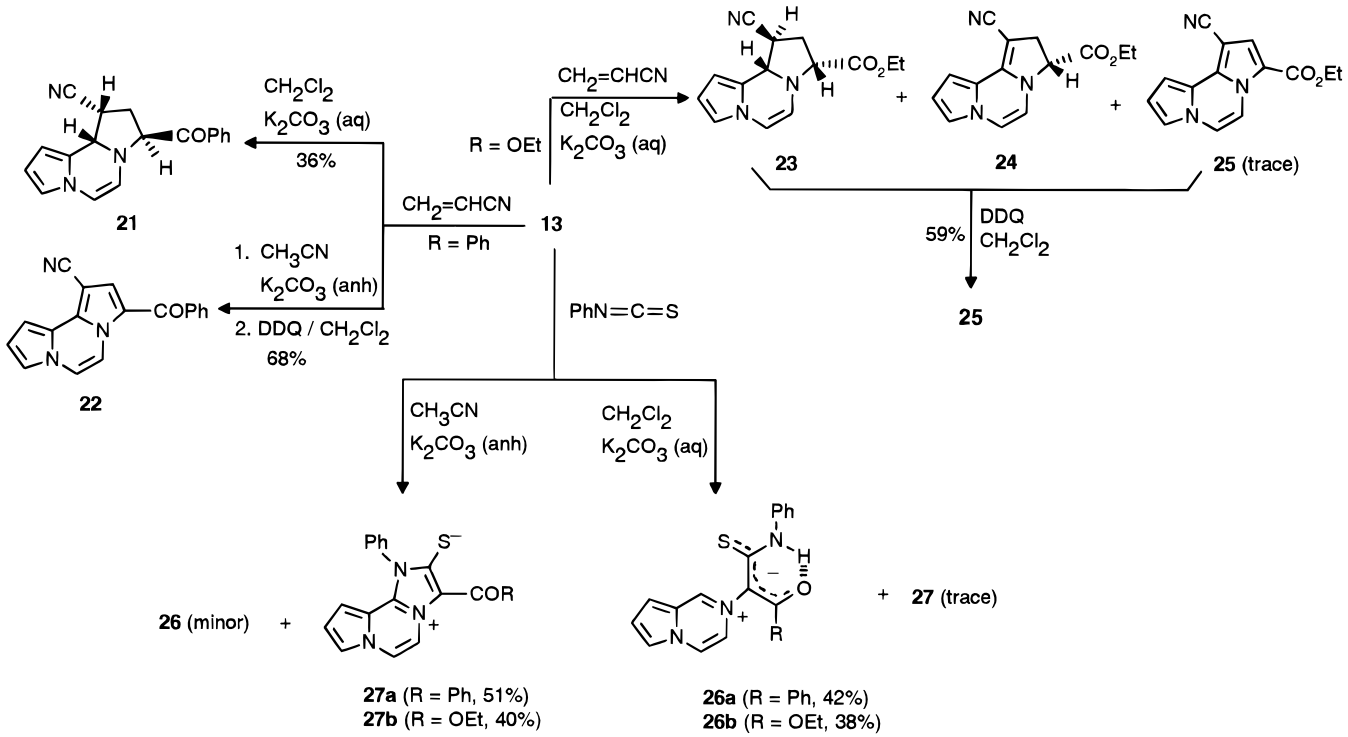


As expected, dipolar cycloaddition with unsymetrically

Scheme 4



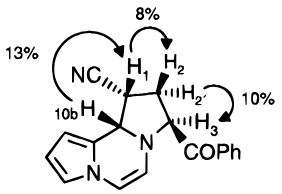
Scheme 5



substituted acetylenic or olefinic dipolarophiles was highly regioselective affording in all cases a single cycloadduct. Thus, the cycloadditions of **13a**,**b** with methyl propiolate, following the same procedure as before for DMAD, gave the dipyrrolo[1,2-*a*:2′,1′-*c*]pyrazine **20** directly.

When acrylonitrile was reacted for 2 h with the ylide of **13a** in dichloromethane−aqueous potassium carbonate the endo cycloadduct **21** was the major isolated compound. However, when the reaction was carried out for 35 h at room temperature in dry acetonitrile using anhydrous potassium carbonate as base the aromatized derivative **22** was obtained (Scheme 5). A more complex mixture containing the tetrahydro derivative **23** as the major product, the dihydro derivative **24** as a minor component and a trace of the fully aromatized **25** was obtained when **13b** was reacted with acrylonitrile under two-phase liquid−liquid conditions. ^{1}H NMR analysis of the crude mixture lent support to the structures of the components. Although chromatography failed to fully separate these three derivatives we were able to isolate and purify a small amount of **24** and obtain ^{1}H NMR evidence that showed the double bond on the dihydropyrrole ring to be located between the C1−C10b carbons and the H3 proton to be coupled to the H2 protons with coupling constants of J_{cis} = 6.5 Hz and J_{trans} = 12.1 Hz. The derivative **25** was obtained in 59% yield after DDQ oxidation of the reaction mixture.

A regioisomeric structure for **21** (and hence for **22**−**25**) was discarded on the basis of chemical shifts and coupling between H10b (d), H1 (m), H2 (two hydrogens, td), and H3 (dd) which clearly shows that the cyano and



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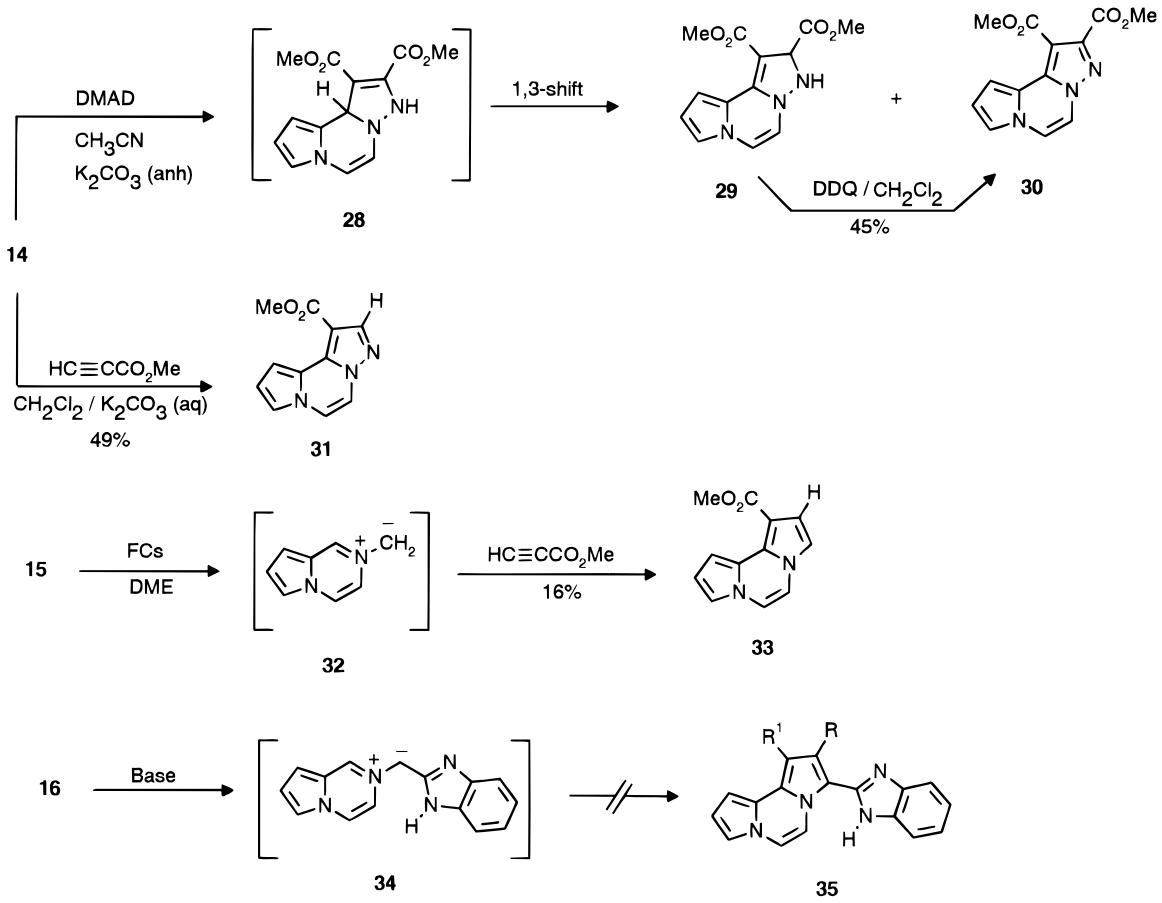
carbonyl groups are not adjacent to each other. The coupling constant between H1 and H10b (J = 6 Hz) and

Scheme 6



NOE difference ^{1}H NMR spectra led to the establishment of the *cis* arrangement for these hydrogens. The assigned stereochemistry was supported by the NOE observed between the H1 and the H2 protons (*cis* arrangement) and the NOE observed between the H2′ proton *(trans* arrangement with respect to H1) and the H3 proton.

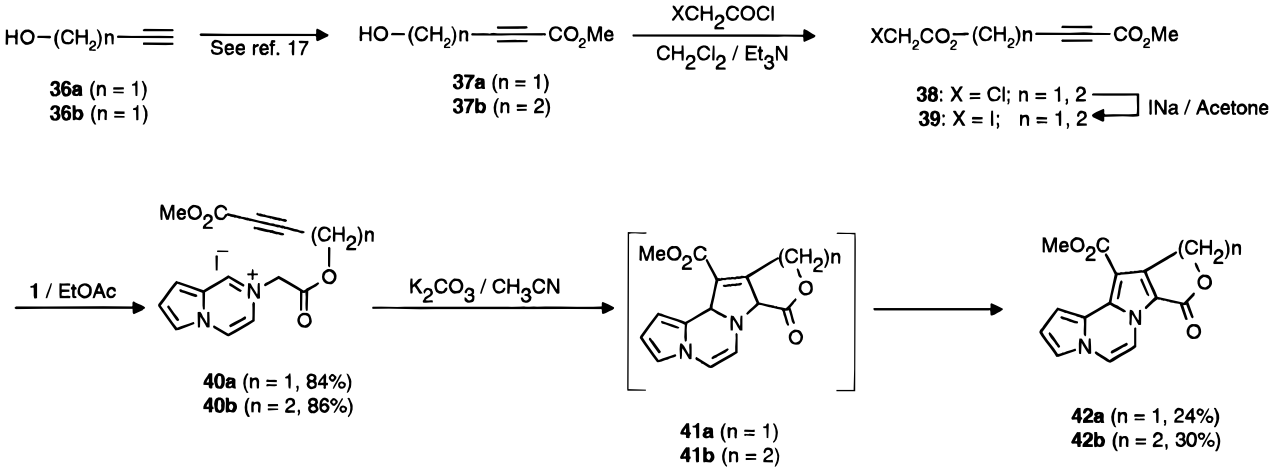
The cycloaddition reaction of **13a**,**b** with heterocumulenes was also tested under the standard two-phase liquid−liquid conditions using phenyl isothiocyanate as a dipolarophile (Scheme 5). The reaction led however to the N-ylides **26** in moderate yield after 4 h at room temperature. This result was not unexpected since these ylides seem to be particularly stabilized, not only by charge delocalization but also by an intramolecular hydrogen bond. A similar observation has been reported for some heteroaryl-stabilized cycloimmonium ylides and isothiocyanate derivatives.[16] ^{1}H NMR evidence consistent with the proposed structure **26** was obtained and confirmed the presence of the characteristic H1 pyrrolo-[1,2-*a*]pyrazinium proton at 8.8 ppm and the NH proton at δ 12−14 ppm. After some effort, we were able to obtain the desired mesomeric conjugate betaines **27** in 40−51% yield using the solid−liquid dry acetonitrile−potassium carbonate system and stirring at room temperature for 20−40 h. Under these conditions a small amount of the ylide is still present as a minor product (12−20% yield). The formation of **27** probably proceeds via initial formation of **26**, and this supposition was easily proved by conversion of the ylide **26** into the heterobetaine **27** using the same conditions described for the synthesis of **27**.

We also studied the cycloaddition reaction of the *N*-amino salt **14** with DMAD and methyl propiolate and found that a mixture of the dihydro derivative **29** and the fully aromatized pyrazolo[1,5-*a*]pyrrolo[2,1-*c*]pyrazine **30** was formed in the first case while the cycloadduct **31** was the only isolated compound in the latter (Scheme 6). In the reaction with DMAD a likely initial transient cycloadduct **28** undergoes a 1,3-sigmatropic hydrogen shift to give **29** which is in part oxidized to **30**. The mixture can be separated by chromatography on silica gel. The ^{1}H NMR of the dihydro derivative confirms the presence of the double bond of the dihydropyrazolo moiety between the C1 and C10b carbons since the value of the coupling constant between H2 and NH (J = 12.5 Hz) seems to be too high to be assigned to homoallylic H10b and NH protons which would support an isomeric 3,10b-dihydropyrazolo[1,5-*a*]pyrrolo[2,1-*c*]pyrazine derivative. DDQ oxidation of the mixture yielded **30** in 45% yield.

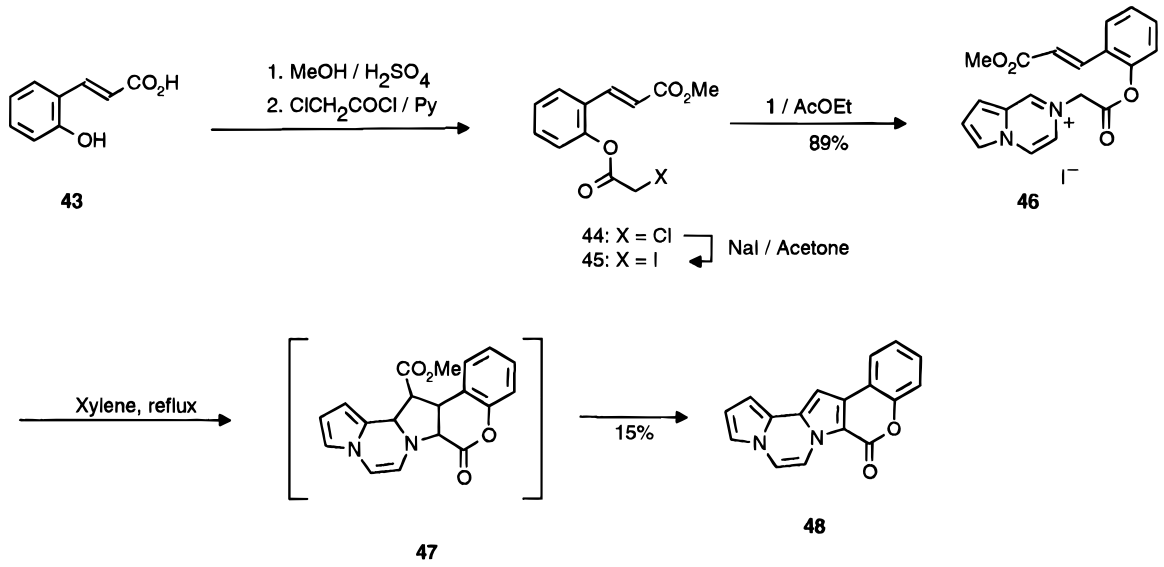
Fluoride-induced desilylation of the salt **15** gave the nonstabilized ylide **32** which underwent cycloaddition with methyl propiolate to yield the cycloadduct **33** in 16% yield. Attempts to trap this ylide with other dipolarophiles such as DMAD and acrylonitrile failed under various conditions. The use of a tributylammonium salt as an alternative source of fluoride also proved unsuccessful. Finally, all our attempts to access benzimidazole-substituted pyrrolopyrazines **35** by trapping the heteroaryl-stabilized N-ylide **34** were fruitless either with

(16) (a) Cuadro, A. M.; Novella, J. L.; Molina, A.; Alvarez-Builla, J.; Vaquero, J. J. *Tetrahedron* **1990**, *46*, 6033. (b) Molina, A.; Cuadro, A. M.; Alvarez-Builla, J.; Vaquero, J. J.; Garcia Navio, J. L. *Heterocycles* **1990**, *31*, 1451. (c) Minguez, J. M.; Gandasegui, T.; Vaquero, J. J.; Alvarez-Builla, J. L.; Garcia Navio, J. L.; Gago, F.; Ortiz, A. R.; Gomez-Sal, P.; Torres, R.; Rodrigo, M. M. *J. Org. Chem*. **1993**, *58*, 6030.

Scheme 7



Scheme 8



acetylenic or olefinic dipolarophiles (hererocumulenes included) (Scheme 6).

Intramolecular cyclization was also examined with acetylenic and olefinic salts **40** and **46**. Both salts were prepared by N-alkylation of **1** with appropriate chains **39** and **44** which incorporated an acetylenic or olefinic moiety respectively (Schemes 7 and 8). The methyl 4-(iodoacetoxy)-2-butynoate (**39a**) and pentynoate **39b** were obtained by acylation and subsequent halogen exchange of the (hydroxyalkyl)propiolates **37**, themselves prepared from the commercially available propynyl and butynyl alcohols **36** following the method described by Thomas and Munt.[17] Furthermore, the alkylating methyl 3-[2-(iodoacetoxy)phenyl]acrylate (**44**) was easily prepared from commercial 3-(2-hydroxyphenyl)acrylic acid (**43**) which after esterification was transformed into **44** using conditions analogous to those described above for the transformation of **37** into **39**.

The treatment of salts **40** with potassium carbonate in dry acetonitrile afforded the corresponding tetracyclic cycloadducts **42** in moderate yields. Attempts to improve the yields of these intramolecular cycloadditions using the aforementioned two-phase liquid−liquid conditions were not successful, since extensive decomposition of the salt **40** via hydrolysis of the internal ester functionality occurred. Other attempts to obtain **42** in better yields by refluxing in toluene or xylene under basic or neutral conditions also failed. Refluxing salt **46** in xylene for 24 h was found, on the other hand, to be the only way of generating the chromon-7-one derivative **48**, albeit in only 15% yield. In this case the salt **46** seems to be much more sensitive to the two-phase system and is extensively decomposed under such conditions. Under the thermal conditions the fully aromatized pentacyclic system **48** forms, we believe, via the initial cycloadduct **47**. The intramolecular cycloaddition process was accompanied by substantial decomposition of the salt **46**. Thus after 24 h in boiling xylene the ^{1}H NMR of the crude mixture suggested it contained a mixture of **48**, **1**, and methyl 3-(2-hydroxyphenyl)acrylate together with uncharacterized resinous material.

In conclusion, an alternative synthesis of the pyrrolo[1,2-*a*]pyrazine is reported together with *ab initio* studies of its structure and of the derivative protonated at the nonbridgehead nitrogen. The study of the basic chemistry of this heterocyclic system and cycloaddition of some of its azomethine ylides led to several novel tri- and tetracyclic systems with two bridgehead nitrogens. We are continuing to explore alternative syntheses for the other isomeric pyrrolodiazines and we will report our additional findings at a later date.

(17) Munt, P. S.; Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1989**, *8*, 480.

Experimental Section

All melting points were measured in open capillary tubes and are uncorrected. Infrared spectra spectral bands are reported in cm^{-1} units. NMR spectra were recorded at 300 and 500 MHz, and the chemical shifts are expressed in parts per million downfield from tetramethylsilane, with multiplicity, coupling constants in hertz, and number of protons. Elemental analyses were performed in the microanalytical laboratory of the University. Mass spectra were determined at an ionizing voltage of 70 eV. Column chromatography was carried out using silica gel (Merck 60, 230−400 mesh). The calculations were performed on the Supercomputer FUJITSU VP 2400. All chemicals were of reagent grade and used without further purification. *O*-(Mesitylenesulfonyl)hydroxylamine (MSH) was prepared following the literature procedure.[18]

Pyrrolo[1,2-*a*]pyrazine (1). To 2.0 g (16.6 mmol) of 3,4-dihydropyrrolo[1,2-*a*]pyrazine (**5**)[7,8] in xylene (35 mL) was added 2.24 g of palladium on activated carbon 10%. The mixture was refluxed for 20 h and then cooled and filtered through Celite. The solution was concentrated under reduced pressure to leave an oily residue. Chromatography of this material using a 1:1 hexane−EtOAc mixture gave 1.20 g (62%) of **1**: bp 72 °C, 2 mmHg (lit.[6] bp 71 °C, 2 mmHg). IR (neat) 3097, 1614, 1458, 1306, 1076 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.78 (d, 1H, J = 4.2 Hz), 6.87 (dd, 1H, J = 2.5 Hz, J = 4.2 Hz), 7.41 (d, 1H, J = 2.5 Hz), 7.47 (d, 1H, J = 4.9 Hz), 7.79 (d, 1H, J = 4.9 Hz), 8.78 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 145.0, 128.1, 126.7, 117.8, 114.5, 114.2, 103.0; MS *m*/*z* (rel int) 119 (71), 118 (100, M^+), 105 (97), 91 (90), 57 (37).

Bromination of 1. To 0.30 g (2.24 mmol) of aluminum chloride was added a solution of **1** (0.12 g, 1.01 mmol) in CH_2Cl_2 (2 mL). After stirring for 15 min, bromine (0.16 g, 1 mmol) was slowly added and stirring was continued overnight. The reaction mixture was then poured into cold water and extracted with CH_2Cl_2. The organic phase was washed successively with water (2 × 5 mL) and saturated NaCl solution (2 × 5 mL) and dried over $MgSO_4$. The solvent was evaporated under reduced pressure and the residue chromatographed. Elution with CH_2Cl_2−acetone (9:1) gave 75 mg (38%) of the 8-bromopyrrolo[1,2-*a*]pyrazine (**8**) and 120 mg (43%) of the 6,8-dibromopyrrolo[1,2-*a*]pyrazine (**9**).

8-Bromopyrrolo[1,2-*a*]pyrazine (8): brown powder from EtOH; mp 73−75 °C; IR (KBr) 1651, 1610, 1355, 1303 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.87 (d, 1H, J = 2.8 Hz), 7.36 (d, 1H, J = 2.8 Hz), 7.52 (d, J = 4.9 Hz), 7.73 (d, 1H, J = 4.9 Hz), 8.78 (s, 1H). Anal. Calcd for $C_7H_5BrN_2$: C, 42.67; H, 2.56; N, 14.22. Found: C, 42.94; H, 2.73; N, 14.07.

6,8-Dibromopyrrolo[1,2-*a*]pyrazine (9): brown powder from EtOH; mp 122−123 °C (lit.[12] mp 122 °C, sublimation at 55 °C/0.03 mmHg); IR (KBr) 1632, 1606, 1419, 1297, 1233 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.92 (s, 1H), 7.68 (d, 1H, J = 5.1 Hz), 7.80 (d, 1H, J = 5.1 Hz), 8.73 (s, 1H). Anal. Calcd for $C_7H_4Br_2N_2$: C, 30.47; H, 1.46; N, 10.15. Found: C, 30.52; H, 1.57; N, 9.86.

8-Pyrrolo[1,2-*a*]pyrazinecarboxaldehyde (10). To a suspension of $POCl_3$ (143 mg, 0.93 mmol) in dry Et_2O (2 mL) cooled to 0 °C was added DMF (68 mg, 0.93 mmol). The mixture was stirred until an insoluble oil formed (about 10 min). The oil was then dissolved in CH_2Cl_2, and a CH_2Cl_2 solution (4 mL) containing **1** (100 mg, 0.85 mmol) was added. The reaction mixture was then stirred for 3 h at room temperature followed by 1 h at reflux. The solvent was evaporated under reduced pressure, and the residue was treated with cold water (10 mL), neutralized with NaOAc, and extracted with EtOAc (3 × 5 mL). The organic phase was dried over Na_2SO_4, the solvent evaporated under reduced pressure, and the residue chromatographed. Elution with CH_2Cl_2−acetone (9:1) gave the formyl derivative **10** which was recrystallized from EtOH to give yellow prisms (75 mg, 60%): mp 115−117 °C; IR (KBr) 1646, 1603, 1465, 1364, 1103, 1018 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.85 (d, 1H, J = 4.8 Hz), 7.50 (d, 1H, J = 4.4 Hz), 7.95 (d, 1H, J = 4.8 Hz), 9.06 (s, 1H), 9.38 (d, 1H, J = 4.4 Hz), 9.91 (s, 1H). Anal. Calcd for $C_8H_6N_2O$: C, 65.75; H, 4.14; N, 19.17. Found: C, 65.88; H, 4.43; N, 19.04.

1-Butylpyrrolo[1,2-*a*]pyrazine (11). To a solution of **1** (100 mg, 0.85 mmol) in 5 mL of dry THF was added 0.53 mL (0.85 mmol) of a 1.6 M solution of *n*-butyllithium in hexane at −78 °C under argon. After 90 min, the mixture was hydrolyzed with NH_4Cl and extracted with EtOAc (2 × 10 mL). The combined organic extracts were washed with water (3 × 5 mL) and dried over Na_2SO_4, and the solvent was removed under reduced pressure. Chromatography of the residue using hexane−EtOAc (7:3) as eluent gave the title compound as a brown oil (30 mg, 21%): IR (neat) 2957, 1611, 1461, 1077 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (t, 3H, J = 7.2 Hz), 1.41−1.48 (m, 2H), 1.79−1.84 (m, 2H), 2.95 (t, 2H, J = 7.6 H), 6.76−6.78 (m, 1H), 6.82 (dd, 1H, J = 2.5 Hz, J = 4.0 Hz), 7.37 (dd, 1H, J = 1.5 Hz, J = 2.5 Hz), 7.41 (d, 1H, J = 5.0 Hz), 7.68 (d, 1H, J = 5.0 Hz); MS *m*/*z* (rel int) 174 (20, M^+), 145 (25), 132 (100), 118 (94). Anal. Calcd for $C_{11}H_{14}N_2$: C, 75.82; H, 8.10; N, 16.08. Found: C, 76.12; H, 8.14; N, 15.71.

4-Pyrrolo[1,2-*a*]pyrazinecarboxaldehyde (12a). To a solution of **1** (0.20 g, 1.70 mmol) in 8 mL of dry THF at −78 °C under argon was added 0.95 mL (1.90 mmol) of LDA (2 M) in THF. After stirring for 40 min at −78 °C, DMF (140 mg, 1.90 mmol) was added dropwise and stirring was continued for 4 h at that temperature. The reaction mixture was then quenched with a solution of NH_4Cl and extracted with Et_2O. The organic phase was washed with water and brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was chromatographed using a mixture of hexane−EtOAc (7:3) as eluent, to give 140 mg of **12a** (57%): mp 116−117 °C (yellow prisms from EtOH); IR (KBr) 1668, 1606, 1419, 1298, 1088, 1043 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.08−7.15 (m, 2H), 8.19 (s, 1H), 8.94−8.99 (m, 2H), 9.92 (s, 1H); MS *m*/*z* (rel int) 146 (100, M^+), 118 (41), 91 (87), 63 (50). Anal. Calcd for $C_8H_6N_2O$: C, 65.75; H, 4.14; N, 19.17. Found: C, 65.31; H, 4.31; N, 18.82.

Phenylpyrrolo[1,2-*a*]pyrazin-4-ylmethanol (12b). To a stirred solution of **1** (100 mg, 0.85 mmol) in anhydrous THF (5 mL) maintained at −78 °C under an argon atmosphere was added LDA (2 M) in THF (0.46 mL, 0.93 mmol), and stirring was continued for 30 min. Then, benzaldehyde (98 mg, 0.93 mmol) was added. After 2 h, the mixture was hydrolyzed with NH_4Cl and extracted with EtOAc (3 × 5 mL). The organic extracts were dried over Na_2SO_4 and evaporated to give an oil that was triturated with a mixture of petroleum ether−EtOAc (2 mL). Crystallization from EtOH afforded **12b** as a pale brown powder (136 mg, 72%): mp 152−153 °C; IR (KBr) 3167, 2829, 1616, 1450, 1311, 1046 cm^{-1}; ^1H NMR (DMSO-d_6) δ 6.03 (d, 1H, J = 4.7 Hz), 6.41 (d, 1H, J = 4.7 Hz), 6.84 (bs, 2H), 7.26−7.36 (m, 3H), 7.48 (d, 2H, J = 7.3 Hz), 7.52 (s, 1H), 7.60 (s, 1H), 8.78 (s, 1H). Anal. Calcd for $C_{14}H_{12}N_2O$: C, 74.98; H, 5.39; N, 12.49. Found: C, 75.15; H, 5.74; N, 12.55.

4-(Trimethylsilyl)pyrrolo[1,2-*a*]pyrazine (12c). To a solution of **1** (100 mg, 0.85 mmol) in anhydrous THF (5 mL) was added, at −78 °C under argon, 0.46 mL (0.93 mmol) of LDA (2 M) in THF. After 45 min chlorotrimethylsilane (106 mg, 0.93 mmol) was added dropwise. Stirring was continued for 90 min. After hydrolysis, the mixture was extracted with Et_2O (3 × 5 mL). The ethereal phase was washed with water and brine (3 × 10 mL) and dried over Na_2SO_4. The solvent was removed to give a brown oil that was chromatographed using hexane−EtOAc (7:3) as eluent to afford **12c** (93 mg, 58%). White powder from petroleum ether: mp 67−69 °C; IR (KBr) 1590, 1414, 1336, 1302, 1251, 1040, 950 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.45 (s, 9H), 6.80 (dd, 1H, J = 1.5 Hz, J = 4.2 Hz), 6.88 (dd, 1H, J = 2.5 Hz, J = 4.2 Hz), 7.48 (dd, 1H, J = 1.5 Hz, J = 2.5 Hz), 7.52 (s, 1H), 8.80 (s, 1H); MS *m*/*z* (rel int) 190 (91, M^+), 175 (100), 145 (18), 105 (30). Anal. Calcd for $C_{10}H_{14}N_2Si$: C, 63.11; H, 7.41; N, 14.72. Found: C, 62.69; H, 7.30; N, 14.81.

4-Methylpyrrolo[1,2-*a*]pyrazine (12d). To a solution of **1** (0.20 g. 1.70 mmol) in anhydrous THF (10 mL) at −78 °C and under argon was added LDA (2 M) (0.95 mL, 1.90 mmol) in THF. After 30 min methyl iodide (240 mg, 1.7 mmol) was added and the reaction mixture was allowed to warm to room temperature and stirring was continued overnight. The

(18) Tamura, Y.; Minamikawa, J.; Ikeda, M. *Synthesis* **1977**, 1.

mixture was hydrolyzed with NH_4Cl and extracted with Et_2O (3 × 10 mL). The organic phase was washed with water and brine and dried over Na_2SO_4. After evaporating the solvent, **12d** was obtained as a dark oil (176 mg, 79%): IR (neat) 1612, 1425, 1256, 1045 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.49 (s, 3H), 6.85 (dd, 1H, J = 1.1 Hz; J = 4.0 Hz), 6.94 (dd, 1H, J = 2.8 Hz, J = 4.0 Hz), 7.31 (d, 1H, J = 2.8 Hz), 7.38 (s, 1H), 8.75 (s, 1H). Anal. Calcd for $C_8H_8N_2$: C, 72.70; H, 6.10; N, 21.20. Found: C, 72.98; H, 5.99; N, 21.61.

2-Phenacylpyrrolo[1,2-*a*]pyrazinium Bromide (13a). A mixture of **1** (1.06 g, 9.0 mmol) and phenacyl bromide (1.77 g, 9.0 mmol) was refluxed in acetone (20 mL) for 4 h. The yellow precipitate that appeared was filtered off to afford a solid which was recrystallized from EtOH to give 2.5 g (88%) of the title compound as pale yellow crystals: mp 179−181 °C; IR (KBr) 1696, 1652, 1348, 1231, 759 cm^{-1}; ^1H NMR (DMSO-d_6) δ 6.22 (s, 2H), 7.49 (dd, 1H, J = 2.4 Hz, J = 4.4 Hz), 7.65 (t, 2H, J = 7.8 Hz), 7.73 (d, 1H, J = 5.9 Hz), 7.74−7.76 (m, 1H), 7.82 (d, 1H, J = 4.2 Hz), 8.06 (d, 2H, J = 8.4 Hz), 8.51−8.52 (m, 1H), 8.84 (d, 1H, J = 5.8 Hz), 9.45 (s, 1H). Anal. Calcd for $C_{15}H_{13}BrN_2O$: C, 56.80; H, 4.13; N, 8.83. Found: C, 56.48; H, 4.46; N, 8.69.

2-[(Ethoxycarbonyl)methyl]pyrrolo[1,2-*a*]pyrazinium Bromide (13b). To a solution of **1** (1.0 g, 8.50 mmol) in EtOAc (20 mL) was added 1.50 g (9.0 mmol) of ethyl bromoacetate, and the mixture was refluxed for 4 h. The resulting precipitate was filtered off, washed with EtOAc, and recrystallized from acetonitrile to give 1.95 g (81%) of the title salt as a pale yellow powder: mp 182−183 °C; IR (KBr) 1751, 1648, 1207, 1149 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.24 (t, 3H, J = 7.2 Hz), 4.22 (q, 2H, J = 7.2 Hz), 5.43 (s, 2H), 7.47 (dd, 1H, J = 2.4 Hz, J = 4.5 Hz), 7.79 (d, 1H, J = 6.0 Hz), 7.80−7.82 (m, 1H), 8.52−8.53 (m, 1H), 8.85 (d, 1H, J = 6.0 Hz), 9.55 (s, 1H); MS m/z (rel int) 206 (31, M^+), 177 (36), 133 (55), 110 (100). Anal. Calcd for $C_{11}H_{13}BrN_2O$: C, 46.34; H, 4.60; N, 9.82. Found: C, 45.90; H, 4.56; N, 9.92.

2-Aminopyrrolo[1,2-*a*]pyrazinium Mesitylenesulfonate (14). To a solution of MSH (0.45 g, 2.10 mmol) in 5 mL of dry CH_2Cl_2 was added 0.25 g (2.10 mmol) of **1**, and the mixture was stirred at room temperature for 1 h. The precipitate was filtered off and washed with Et_2O to give 0.54 g (77%) of a white solid: mp 167−169 °C (white powder from EtOH−Et_2O); IR (KBr) 3229, 3137, 1601, 1556, 1219, 1169, 1012 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.15 (s, 3H), 2.48 (s, 6H), 6.71 (s, 2H), 7.33 (dd, 1H, J = 2.2 Hz, J = 4.4 Hz), 7.51 (d, 1H, J = 4.4 Hz), 7.62 (d, 1H, J = 5.9 Hz), 7.70 (bs, 2H), 8.25−8.30 (m, 1H), 8.70 (d, 1H, J = 5.9 Hz), 9.30 (s, 1H). Anal. Calcd for $C_{16}H_{19}N_3SO_3$: C, 57.64; H, 5.74; N, 12.60. Found: C, 57.59; H, 5.93; N, 12.83.

2-[(Trimethylsilyl)methyl]pyrrolo[1,2-*a*]pyrazinium Trifluoromethanesulfonate (15). A mixture of **1** (0.20 g, 1.70 mmol) and (trimethylsilyl)methyl trifluoromethanesulfonate (0.40 g, 1.70 mmol) in 8 mL of dry CH_2Cl_2 was stirred at room temperature under argon for 3 h. The solvent was removed under reduced pressure to leave a solid which was filtered off and washed with Et_2O. Recrystallization from hexane−EtOAc gave 0.38 g (64%) of a pale brown powder: mp 104−105 °C; IR (KBr) 3106, 1653, 1342, 1278, 1256, 859 cm^{-1}; ^1H NMR (DMSO-d_6) δ 0.12 (s, 9H), 4.13 (s, 2H), 7.38 (dd, 1H, J = 2.5 Hz, J = 4.4 Hz), 7.57−7.59 (m, 2H), 8.34 (d, 1H, J = 2.5 Hz), 8.75 (d, 1H, J = 5.8 Hz), 9.34 (s, 1H). Anal. Calcd for $C_{12}H_{17}F_3N_2SO_3SSi$: C, 40.67; H, 4.83; N, 7.90. Found: C, 40.66; H, 4.69; N, 7.86.

2-(Benzimidazol-2-ylmethyl)pyrrolo[1,2-*a*]pyrazinium Chloride (16). A mixture of **1** (0.11 g, 0.93 mmol) and 2-(chloromethyl)benzimidazole (0.17 g, 1.0 mmol) was refluxed in EtOAc (4 mL) for 6 h. The solvent was then evaporated under reduced pressure and the solid residue washed with Et_2O (3 × 3 mL) and recrystallized to give 154 mg (58%) of the title compound: mp 197−198 °C (brown powder from EtOH); IR (KBr) 3208, 1625, 1535, 1193 cm^{-1}; ^1H NMR (DMSO-d_6) δ 4.20 (bs, 1H), 6.09 (s, 2H), 7.33−7.36 (m, 2H), 7.48 (dd, 1H, J = 2.5 Hz, J = 4.4 Hz), 7.64−7.68 (m, 2H), 7.82 (d, 1H, J = 4.4 Hz), 7.94 (d, 1H, J = 5.8 Hz), 8.50 (d, 1H, J = 2.5 Hz), 8.83 (d, 1H, J = 5.8 Hz), 9.80 (s, 1H). Anal. Calcd for $C_{15}H_{13}ClN_4$: C, 63.27; H, 4.60; N, 19.68. Found: C, 63.43; H, 4.46; N, 19.97.

Reaction of 13a with DMAD. To a suspension of 0.20 g (0.63 mmol) of **13a** in 15 mL of CH_2Cl_2 were added 0.22 g (1.60 mmol) of DMAD and an aqueous solution of K_2CO_3 (6 mL, 50%). The mixture was stirred for 5 h at room temperature, and then the organic phase was separated, washed with water (3 × 10 mL), and dried over Na_2SO_4. After removing the solvent under reduced pressure, the oily residue was chromatographed. Elution with hexane−EtOAc (9:1) allowed the separation of the dihydro derivative **18a** as a dark oil and the fully aromatized **19a** as a yellow solid. When the crude mixture containing **18a** and **19a** was treated with 74 mg (0.32 mmol) of DDQ in 5 mL of CH_2Cl_2 and stirred at room temperature for 1 h, compound **19a** was obtained. Recrystallization from EtOH afforded 123 mg (52%) as yellow needles.

3-Benzoyl-1,2-bis(methoxycarbonyl)-2,3-dihydrodipyrrolo[1,2-*a*;2′,1′-*c*]pyrazine (18a): IR (KBr) 1773, 1678, 1598, 1316, 1155 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.43 (s, 3H), 3.87 (s, 3H), 4.55 (d, 1H, J = 11.7 Hz), 5.50 (d, 1H, J = 11.7 Hz), 5.79 (d, 1H, J = 5.8 Hz), 6.13−6.19 (m, 1H), 6.22 (dd, 1H, J = 2.9 Hz, J = 3.3 Hz), 6.27 (d, 1H, J = 5.8 Hz), 6.62−6.68 (m, 1H), 7.52 (t, 2H, J = 7.3 Hz), 7.65 (t, 1H, J = 7.3 Hz), 8.00 (d, 2H, J = 7.3 Hz). Anal. Calcd for $C_{21}H_{18}N_2O_5$: C, 66.66; H, 4.79; N, 7.40. Found: C, 66.39; H, 5.27; N, 7.79.

3-Benzoyl-1,2-bis(methoxycarbonyl)dipyrrolo[1,2-*a*;2′,1′-*c*]pyrazine (19a): mp 142−144 °C; IR (KBr) 1736, 1696, 1682, 1627, 1493, 1234, 1214 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.25 (s, 3H), 3.87 (s, 3H), 6.75 (dd, 1H, J = 3.9 Hz, J = 2.7 Hz), 7.30 (dd, 1H, J = 2.7 Hz, J = 1.5 Hz), 7.45 (t, 2H, J = 7.3 Hz), 7.46 (d, 1H, J = 6.3 Hz), 7.57 (t, 1H, J = 7.3 Hz), 7.72 (d, 2H, J = 8.7 Hz), 7.79 (d, 1H, J = 3.9 Hz), 8.33 (d, 1H, J = 6.3 Hz); MS m/z (rel int) 376 (100, M^+), 345 (18), 313 (25), 258 (10), 105 (45). Anal. Calcd for $C_{21}H_{16}N_2O_5$: C, 67.02; H, 4.28; N, 7.44. Found: C, 66.82; H, 4.05; N, 7.27.

Reaction of 13b with DMAD. To 0.20 g (0.70 mmol) of the salt **13b** in 17 mL of CH_2Cl_2 were added 0.25 g (1.75 mmol) of DMAD and 7 mL of an aqueous solution (50%) of K_2CO_3. The mixture was stirred at room temperature for 6 h. The organic phase was separated and washed with water (3 × 10 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was chromatographed. Elution with hexane−EtOAc (9:1) allowed the separation of **18b** (green oil) and **19b**. Treatment of the mixture with DDQ (65 mg, 0.30 mmol) in CH_2Cl_2 (5 mL) for 1 h afforded the fully aromatized derivative **19b** (105 mg, 43%).

3-(Ethoxycarbonyl)-1,2-bis(methoxycarbonyl)-2,3-dihydropyrrolo[1,2-*a*]pyrazine (18b): IR (KBr) 1742, 1691, 1596, 1434, 1023 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.38 (t, 3H, J = 7.1 Hz), 3.67 (s, 3H), 3.82 (s, 3H), 4.39 (q, 2H, J = 7.2 Hz), 4.44 (d, 1H, J = 11.9 Hz), 5.36 (d, 1H, J = 11.9 Hz), 6.01 (d, 1H, J = 5.7 Hz), 6.08−6.13 (m, 1H), 6.17−6.21 (m, 1H), 6.33 (d, 1H, J = 5.7 Hz), 6.65 (dd, 1H, J = 2.5 Hz, J = 1.3 Hz); MS m/z (rel int) 346 (100, M^+), 315 (40), 287 (65). Anal. Calcd for $C_{17}H_{18}N_2O_6$: C, 58.96; H, 5.24; N, 8.09. Found: C, 58.74; H, 5.29; N, 8.24.

3-(Ethoxycarbonyl)-1,2-bis(methoxycarbonyl)dipyrrolo-[1,2-*a*]pyrazine (19b): mp 129−130 °C (white needless, EtOH); IR (KBr) 1746, 1707, 1502, 1221, 1172 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.37 (t, 3H, J = 7.2 Hz), 3.90 (s, 3H), 3.95 (s, 3H), 4.34 (q, 2H, J = 7.2 Hz), 6.74 (dd, 1H, J = 2.7 Hz, J = 4.0 Hz), 7.28 (dd, 1H, J = 2.7 Hz, J = 1.7 Hz), 7.44 (d, 1H, J = 6.2 Hz), 7.86 (dd, 1H, J = 1.3 Hz, J = 4.0 Hz), 8.60 (d, 1H, J = 6.2 Hz); MS m/z (rel int) 344 (100, M^+), 313 (16), 272 (30), 241 (77). Anal. Calcd for $C_{17}H_{16}N_2O_6$: C, 59.30; H, 4.68; N, 8.14. Found: C, 59.48; H, 4.83; N, 8.08.

3-Benzoyl-1-(methoxycarbonyl)dipyrrolo[1,2-*a*:2′,1′-*c*]-pyrazine (20a). To a solution containing 0.20 g (0.63 mmol) of the salt **13a** in CH_2Cl_2 (15 mL) were added methyl propiolate (0.13 g, 1.58 mmol) and an aqueous solution of K_2CO_3 (50%, 6 mL), and the reaction mixture was stirred at room temperature for 3 h. The organic phase was then separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phases were washed with water and saturated NaCl solution. The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure to give **20a**. Recrystallization from EtOH gave 150 mg (77%) of yellow needles: mp 174−175 °C; IR (KBr) 1722, 1612, 1472, 1223

cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.89 (s, 3H), 6.79 (dd, 1H, J = 2.6 Hz, J = 4.1 Hz), 7.35 (dd, 1H, J = 2.6 Hz, J = 1.4 Hz), 7.48−7.51 (m, 2H), 7.53 (d, 1H, J = 6.1 Hz), 7.56 (s, 1H), 7.57−7.60 (m, 1H), 7.82 (d, 1H, J = 6.9 Hz), 8.00 (d, 1H, J = 4.1 Hz), 8.87 (d, 1H, J = 6.1 Hz); MS *m*/*z* (rel int) 318 (100, M^+), 287 (32), 241 (7), 213 (13). Anal. Calcd for $C_{19}H_{14}N_2O_3$: C, 71.69; H, 4.43; N, 8.80. Found: C, 71.56; H, 4.38; N, 8.86.

3-(Ethoxycarbonyl)-1-(methoxycarbonyl)dipyrrolo[1,2-*a*;2′,1′-*c*]pyrazine (20b). To 0.15 g (0.52 mmol) of **13b** in 12 mL of CH_2Cl_2 were added 0.11 g (1.30 mmol) of methyl propiolate and an aqueous solution of K_2CO_3 (50%, 5 mL). The mixture was stirred at room temperature for 3 h. The organic phase was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic extracts were washed with water and brine (3 × 10 mL) and dried over Na_2SO_4. After removing the solvent, the residue was chromatographed using a mixture of hexane−EtOAc (9:1) as eluent to give **20b.** Recrystallization from EtOH afforded 90 mg (61%) of white prisms: mp 158−160 °C; IR (KBr) 1698, 1488, 1228, 1182 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40 (t, 3H, J = 7.2 Hz), 3.92 (s, 3H), 4.36 (q, 2H, J = 7.2 Hz), 6.73 (dd, 1H, J = 2.7 Hz, J = 4.2 Hz), 7.25 (d, 1H, J = 2.7 Hz), 7.40 (d, 1H, J = 6.0 Hz), 7.75 (s, 1H), 7.91 (d, 1H, J = 4.1 Hz), 8.60 (d, 1H, J = 6.0 Hz). Anal. Calcd for $C_{15}H_{14}N_2O_4$: C, 62.93; H, 4.93; N, 9.79. Found: C, 63.04; H, 4.82; N, 9.55.

3-Benzoyl-1-cyano-1,2,3,10b-tetrahydrodipyrrolo[1,2-*a*;2′,1′-*c*]pyrazine (21). To a suspension of 200 mg (0.63 mmol) of **13a** in 15 mL of CH_2Cl_2 were added 85 mg (1.60 mmol) of acrylonitrile and 6 mL of an aqueous solution of K_2CO_3 (50%). The yellow orange-mixture was stirred at room temperature for 2 h. The organic phase was separated, washed with water and brine (3 × 10 mL), and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was chromatographed using hexane−EtOAc (8:2) as eluent to give 65 mg (36%) of the tetrahydro derivative **21** as a yellow oil. Traces of the dihydro derivative and the fully aromatized compound were also separated: IR (neat) 2236, 1678, 1481, 1223, 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.54 (td, 1H, J = 13.5 Hz, J = 5.7 Hz, J = 2.5 Hz), 2.67 (td, 1H, J = 13.5 Hz, J = 8.5 Hz, J = 2.5 Hz), 3.43−3.47 (m, 1H,), 4.84 (d, 1H, J = 6.0 Hz), 5.21 (dd, 1H, J = 5.7 Hz, J = 8.5 Hz), 5.83 (d, 1H, J = 5.9 Hz), 6.07 (d, 1H, J = 2.4 Hz), 6.14 (d, 1H, J = 5.9 Hz), 6.20−6.21 (m, 1H), 6.66 (dd, 1H, J = 3.3 Hz, J = 1.5 Hz), 7.51 (t, 2H, J = 7.7 Hz), 7.61 (d, 1H, J = 7.3 Hz), 7.98 (d, 2H, J = 7.9 Hz); MS *m*/*z* (rel int) 289 (16, M^+), 235 (72), 184 (100), 157 (53), 105 (65). Anal. Calcd for $C_{18}H_{15}N_3O$: C, 74.72; H, 5.23; N, 14.52. Found: C, 74.60; H, 5.43; N, 14.39.

3-Benzoyl-1-cyanodipyrrolo[1,2-*a*:2′,1′-*c*]pyrazine (22). To 0.20 g (0.63 mmol) of **13a** in 12 mL of dry acetonitrile were added 85 mg (1.60 mmol) of acrylonitrile and 0.34 g (2.50 mmol) of anhydrous K_2CO_3. The orange mixture was stirred at room temperature for 35 h. The potassium carbonate was filtered off and washed with CH_2Cl_2. The combined organic extracts were washed with water and brine (3 × 10 mL). After drying with Na_2SO_4, the solvent was removed and the residue was chromatographed using hexane−EtOAc (7:3) as eluent to give **22** as the main compound together with minor amounts of dihydro and tetrahydro compounds. Treatment of the mixture with DDQ (45 mg, 0.2 mmol) in CH_2Cl_2 (4 mL) afforded the title compound which after recrystallization from EtOH−Et_2O gave 0.32 g (68%) of yellow prisms: mp 167−168 °C; IR (KBr) 2224, 1732, 1612, 1472, 1336, 1242 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.83 (t, 1H, J = 3.5 Hz), 7.33−7.36 (m, 3H), 7.49−7.54 (m, 3H), 7.59−7.61 (m, 1H), 7.79 (d, 2H, J = 7.0 Hz), 8.80 (d, 1H, J = 6.2 Hz). Anal. Calcd for $C_{18}H_{11}N_3O$: C, 75.78; H, 3.89; N, 14.73. Found: C, 76.01; H, 3.81; N, 14.82.

Reaction of 13b with Acrylonitrile. To 0.25 g (0.87 mmol) of **13b** in 20 mL of CH_2Cl_2 were added 115 mg (2.30 mmol) of acrylonitrile and an aqueous solution of K_2CO_3 (8 mL, 50%). The mixture was stirred at room temperature for 2 h. The organic phase was separated, washed with water and brine (3 × 10 mL), and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was chromatographed using hexane−EtOAc (8:2) as eluent to give an oily mixture containing the tetrahydro derivative **23**, the dihydro compound **24**, and traces of the fully aromatized compound **25**. When this mixture was treated with DDQ (115 mg, 0.5 mmol) in 10 mL of CH_2Cl_2, 129 mg (59%) of **25** were obtained.

1-Cyano-3-(ethoxycarbonyl)-2,3-dihydrodipyrrolo[1,2-*a*:2′,1′-*c*]pyrazine (24): IR (neat) 2177, 1723, 1592, 1118 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (t, 3H, J = 7.0 Hz), 3.12 (dd, 1H, J = 6.5 Hz, J' = 14.5 Hz), 3.32 (dd, 1H, J = 14.5 Hz, J = 12.5 Hz), 4.23−4.26 (m, 2H), 4.69 (dd, 1H, J = 6.5 Hz, J = 12.5 Hz), 6.24 (d, 1H, J = 6.0 Hz), 6.49 (dd, 1H, J = 2.5 Hz, J = 4.0 Hz), 6.61 (d, 1H, J = 6.0 Hz), 6.95 (dd, 1H, J = 1.0 Hz, J = 2.5 Hz), 7.14 (d, 1H, J = 4.0 Hz).

1-Cyano-3-(ethoxycarbonyl)dipyrrolo[1,2-*a*:2′,1′-*c*]pyrazine (25): white prisms (from hexane−EtOAc); mp 152−154 °C; IR (KBr) 2219, 1702, 1488, 1403, 1235, 1105 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40 (t, 3H, J = 7.1 Hz), 4.37 (q, 2H, J = 7.1 Hz), 6.77 (t, 1H, J = 3.3 Hz), 7.25−7.28 (m, 2H), 7.42 (d, 1H, J = 6.2 Hz), 7.49 (s, 1H), 8.54 (d, 1H, J = 6.2 Hz). Anal. Calcd for $C_{14}H_{11}N_3O_2$: C, 66.40; H, 4.38; N, 16.59. Found: C, 66.08; H, 4.44; N, 16.36.

2-(1-Benzoyl-2-(phenylamino)-2-sulfidovinyl)pyrrolo-[1,2-*a*]pyrazin-2-ium (26a). To a mixture of 0.20 g (0.63 mmol) of **13a** in 15 mL of CH_2Cl_2 and 6 mL of an aqueous solution of K_2CO_3 (50%) was added 100 mg (0.75 mmol) of phenyl isothiocyanate. The yellow solution was stirred at room temperature for 2 h, and the organic phase was separated, washed with water and brine (3 × 10 mL), and dried over Na_2SO_4. The solvent was evaporated and the residue chromatographed using hexane−EtOAc (7:3) as eluent to give the title compound as an orange powder after recrystallization from hexane (98 mg, 42%): mp 169−171 °C; IR (KBr) 3061, 1646, 1564, 1499, 1395, 1188 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.12−7.17 (m, 6H), 7.29−7.38 (m, 5H), 7.72 (d, 1H, J = 2.2 Hz), 7.78 (d, 1H, J = 5.5 Hz), 7.82 (d, 2H, J = 8.0 Hz), 8.76 (s, 1H), 14.32 (bs, 1H). Anal. Calcd for $C_{22}H_{17}N_3OS$: C, 71.14; H, 4.61; N, 11.31. Found: C, 71.45; H, 4.68; N, 11.08.

3-Benzoyl-1-phenylimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazin-4-ium-2-thiolate (27a). To 100 mg (0.31 mmol) of **13a** in 6 mL of dry acetonitrile were added 51 mg (0.37 mmol) of phenyl isothiocyanate and 174 mg (1.23 mmol) of anhydrous K_2CO_3. The mixture was stirred at room temperature for 40 h. The potassium carbonate was filtered off, the solvent removed under reduced pressure, and the residue dissolved in CH_2Cl_2. The organic layer was washed with water (3 × 5 mL) and dried over Na_2SO_4. After removing the solvent, chromatography of the residue using hexane−EtOAc (8:2) as eluent gave 23 mg (20%) of the ylide **26a** and 60 mg (51%) of **27a** as orange prisms: mp 281−283 °C (from EtOH); IR (KBr) 1664, 1576, 1511, 1339, 1123 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.70 (d, 1H, J = 4.4 Hz), 6.63−6.67 (m, 1H), 7.43−7.52 (m, 6H), 7.63−7.67 (m, 3H), 7.70 (d, 1H, J = 6.1 Hz), 7.97 (d, 2H, J = 7.1 Hz), 8.78 (d, 1H, J = 6.1 Hz). Anal. Calcd for $C_{22}H_{15}N_3OS$: C, 71.52; H, 4.09; N, 11.37. Found: C, 71.26; H, 3.87; N, 11.45.

2-(1-(Ethoxycarbonyl)-2-(phenylamino)-2-sulfidovinyl)-pyrrolo[1,2-*a*]pyrazin-2-ium (26b). To 200 mg (0.70 mmol) of **13b** in 17 mL of CH_2Cl_2 were added 7 mL of an aqueous solution of K_2CO_3 (50%) and 115 mg (0.84 mmol) of phenylisothiocyanate. The mixture was stirred at room temperature for 4 h. The organic phase was separated, washed with water and brine (3 × 10 mL), and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue chromatographed using CH_2Cl_2−acetone (19.5:0.5) as eluent to give the title compound (91 mg, 38%): mp 142−144 °C (orange powder from hexane−EtOAc); IR (KBr) 3166, 1735, 1632, 1587, 1549, 1370, 1263, 1034 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 (t, 3H, J = 7.1 Hz), 4.12 (q, 2H, J = 7.1 Hz), 7.08−7.11 (m, 1H), 7.20−7.33 (m, 4H), 7.42 (d, 1H, J = 4.1 Hz), 7.71 (d, 2H, J = 7.7 Hz), 7.83 (dd, 1H, J = 2.2 Hz, J = 1.1 Hz), 8.00 (d, 1H, J = 5.9 Hz), 8.81 (s, 1H), 11.8 (bs, 1H). Anal. Calcd for $C_{18}H_{17}N_3O_2S$: C, 63.70; H, 5.05; N, 12.38. Found: C, 63.97; H, 5.07; N, 12.47.

3-(Ethoxycarbonyl)-1-phenylimidazo[1,2-*a*]pyrrolo-[2,1-*c*]pyrazin-4-ium-2-thiolate (27b). To a mixture of 0.15 g (0.52 mmol) of **13b**, 10 mL of dry acetonitrile and 0.29 g (2.1 mmol) of anhydrous K_2CO_3 was added 85 mg (0.63 mmol) of phenylisothiocyanate. The dark red mixture was stirred for 48 h. The K_2CO_3 was filtered off, the acetonitrile removed

under reduced pressure, and the oily residue dissolved in CH_2Cl_2. The organic solution was washed with water (3 × 10 mL), dried over Na_2SO_4, and evaporated. The dark oily residue was chromatographed using hexane−EtOAc (3:7) as eluent to give 22 mg (12%) of the ylide **27a** and 71 mg (40%) of **27b** which after crystallization from EtOH afforded yellow prisms: mp 241−242 °C; IR (KBr) 3087, 1733, 1666, 1513, 1336, 1236 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.49 (t, 3H, J = 7.0 Hz), 4.49 (q, 2H, J = 7.0 Hz), 5.65 (dd, 1H, J = 4.4 Hz, J = 0.8 Hz), 6.63 (dd, 1H, J = 2.6 Hz, J = 4.4 Hz), 7.42−7.45 (m, 3H), 7.64−7.68 (m, 4H), 8.88 (d, 1H, J = 6.2 Hz). Anal. Calcd for $C_{18}H_{15}N_3O_2S$: C, 64.08; H, 4.48; N, 12.45. Found: C, 63.81; H, 4.77; N, 12.61.

Reaction of 14 with DMAD. To a suspension of 0.16 g (0.48 mmol) of **14** in 10 mL of dry acetonitrile were added 0.26 g (1.92 mmol) of anhydrous K_2CO_3 and 0.17 g (1.20 mmol) of DMAD. The yellow mixture was stirred at room temperature for 24 h, and the potassium carbonate was filtered off and washed with CH_2Cl_2. The organic extracts were washed with water and brine (3 × 10 mL) and dried over Na_2SO_4. The solvent was removed and chromatography of the residue using hexane−EtOAc (9:1) as eluent gave 13 mg (10%) of the dihydro derivative **29** as a yellow solid and 47 mg (36%) of **30** as a brown solid. Treatment of the mixture with DDQ (65 mg, 0.30 mmol) in CH_2Cl_2 (5 mL) afforded **30** in 45% yield.

1,2-Bis(methoxycarbonyl)-2,3-dihydropyrazolo[1,5-*a*]pyrrolo[2,1-*c*]pyrazine (29): mp 123−124 °C (hexane−EtOAc); IR (KBr) 1742, 1682, 1431, 1177 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.84 (s, 3H), 3.86 (s, 3H), 4.57 (d, 1H, J = 12.5 Hz), 5.48 (d, 1H, J = 12.5 Hz), 6.08 (dd, 1H, J = 1.5 Hz, J = 3.3 Hz), 6.21 (t, 1H, J = 3.3 Hz), 6.36 (d, 1H, J = 5.8 Hz), 6.56 (d, 1H, J = 5.8 Hz), 6.68 (dd, 1H, J = 1.5 Hz, J = 2.2 Hz). Anal. Calcd for $C_{13}H_{13}N_3O_4$: C, 56.72; H, 4.76; N, 15.27. Found: C, 56.38; H, 4.69; N, 14.93.

1,2-Bis(methoxycarbonyl)pyrazolo[1,5-*a*]pyrrolo[2,1-*c*]pyrazine (30): mp 126−128 °C (hexane−EtOAc); IR (KBr) 1739, 1706, 1248, 1217 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.95 (s, 3H, CH), 4.00 (s, 3H), 6.75 (dd, 1H, J = 2.9 Hz, J = 4.0 Hz), 7.31 (dd, 1H, J_{8-9} = 2.9 Hz, J = 1.4 Hz), 7.46 (d, 1H, J = 6.2 Hz), 7.52 (d, 1H, J = 6.2 Hz), 7.56 (dd, 1H, J = 4.0 Hz, J = 1.4 Hz). Anal. Calcd for $C_{13}H_{11}N_3O_4$: C, 57.14; H, 4.06; N, 15.38. Found: C, 56.89; H, 4.25; N, 15.57.

1-(Methoxycarbonyl)pyrazolo[1,5-*a*]pyrrolo[2,1-*c*]pyrazine (31). To 0.20 g (0.60 mmol) of the salt **14** in 12 mL of dry acetonitrile were added 0.33 g (2.40 mmol) of anhydrous K_2CO_3 and 0.12 g (1.50 mmol) of methyl propiolate. The mixture was stirred at room temperature for 35 h. The potassium carbonate was filtered off and washed with CH_2Cl_2 (3 × 5 mL). The combined organic extracts were washed with water and brine (3 × 10 mL) and dried over Na_2SO_4. After removing the solvent, the residue was chromatographed using CH_2Cl_2 as eluent to give the title compound as white needles after recrystallization from ethanol (63 mg, 49%): mp 160−162 °C; IR (KBr) 1702, 1570, 1536, 1401, 1272, 1237, 1157 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.93 (s, 3H), 6.76 (dd, 1H, J = 2.6 Hz, J = 3.8 Hz), 7.29 (dd, 1H, J = 1.5 Hz, J = 2.6 Hz), 7.41 (d, 1H, J = 6.0 Hz), 7.53 (d, 1H, J = 6.0 Hz), 7.74 (d, 1H, J = 3.8 Hz), 8.18 (s, 1H). Anal. Calcd for $C_{11}H_9N_3O_2$: C, 61.39; H, 4.22; N, 19.53. Found: C, 61.21; H, 4.49; N, 19.05.

1-(Methoxycarbonyl)dipyrrolo[1,2-*a*;2′,1′-*c*]pyrazine (33). To 0.16 g (0.45 mmol) of the salt **15** in 8 mL of DME were added 68 mg (0.45 mmol) of cesium fluoride and 40 mg (0.49 mmol) of methyl propiolate under an argon atmosphere. The mixture was refluxed for 20 h and then cooled and poured into cold water and extracted with CH_2Cl_2 (3 × 10 mL). The organic phase was dried over Na_2SO_4, the solvent removed, and the brown oily residue chromatographed using hexane−EtOAc (8:2) as eluent to give 15 mg (16%) of **33** as a yellow oil: IR ($CDCl_3$) 1697, 1444, 1228, 1127, 1041 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.90 (s, 3H), 6.65 (dd, 1H, J = 2.8 Hz, J = 4.0 Hz), 6.90 (d, 1H, J = 3.3 Hz), 6.95 (d, 1H, J = 3.3 Hz), 7.04 (d, 1H, J = 5.9 Hz), 7.13 (dd, 1H, J = 1.4 Hz, J = 2.8 Hz), 7.24 (d, 1H, J = 5.9 Hz), 7.72 (d, 1H, J = 4.0 Hz); MS m/z (rel int) 214 (100, M^+), 204 (17), 183 (28). Anal. Calcd for $C_{12}H_{10}N_2O_2$: C, 67.28; H, 4.71; N, 13.08. Found: C, 66.91; H, 4.35; N, 12.95.

4-(Chloroacetoxy)-2-butynoic Acid Methyl Ester (38a). To a solution of chloroacetyl chloride (1.4 mL, 17.54 mmol) in CH_2Cl_2 (50 mL) at 0 °C were added 4-hydroxy-2-butynoic acid methyl ester[17] (2.0 g, 17.54 mmol) and Et_3N (4.9 mL, 35.08 mmol) in CH_2Cl_2 (12 mL). The solution was stirred at room temperature for 3 h. The solvent was removed under reduced pressure and the residue purified by column chromatography using hexane−EtOAc (8:2) as eluent to yield **38a** (3.01 g, 90%) as an orange oil: IR (neat) 2957, 2250, 1760, 1724, 1654, 1435, 1264, 1160, 1022 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.79 (s, 3H), 4.12 (s, 2H), 4.90 (s, 2H). Anal. Calcd for $C_7H_7ClO_4$: C, 44.12; H, 3.70. Found: C, 44.15; H, 3.90.

5-(Chloroacetoxy)-2-pentynoic Acid Methyl Ester (38b). Starting from **37b**[17] (2.0 g, 15.61 mmol) and following the same procedure described for the preparation of **38a**, column chromatography (hexane:EtOAc, 9:1) gave **38b** (2.39 g, 75%) as a yellow oil: IR (neat) 2959, 2242,1751, 1714, 1435, 1261, 1166, 1080, 1017 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.73 (t, 2H, J= 6.6 H), 3.75 (s, 3H), 4.09 (s, 2H), 4.32 (t, 2H, J= 6.6 Hz). Anal. Calcd for $C_8H_9ClO_4$: C, 46.96; H, 4.43. Found: C, 47.10; H, 4.26.

4-(Iodoacetoxy)-2-butynoic Acid Methyl Ester (39a). To a solution of NaI (0.79 g, 5.27 mmol) in dry acetone (10 mL) was added **38a** (1.0 g, 5.27 mmol). The mixture was stirred at room temperature for 2 h. The precipitated NaCl was filtered off, and the solvent was removed under reduced pressure. The residue was dissolved in EtOAc, and a saturated $Na_2S_2O_3$ solution was added. The organic layer was separated, washed with a saturated $Na_2S_2O_3$ solution, and dried ($MgSO_4$). The solvent was evaporated under reduced pressure, and the residue was purified by chromatography (hexane:EtOAc, 9:1) to give **39a** (1.32 g, 89%) as a yellow oil: IR (neat) 2957, 2250, 1756, 1722, 1654, 1436, 1263, 1161, 1023, 993, 792, 751 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.73 (s, 2H), 3.77 (s, 3H), 4.84 (s, 2H). Anal. Calcd for $C_7H_7IO_4$: C, 29.81; H, 2.50. Found: C, 30.08; H, 2.69.

5-(Iodoacetoxy)-2-pentynoic Acid Methyl Ester (39b). This was prepared from NaI (0.73 g, 4.89 mmol) and **38b** (1.0 g, 4.89 mmol), using the procedure described above for **39a**, to give **39b** (1.30 g, 90%) as a colorless oil: IR (neat) 2958, 2244, 1738, 1716, 1434, 1335, 1258, 1082, 1016 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.71 (t, 2H, J= 6.6 Hz); 3.71 (s, 2H); 3.76 (s, 3H); 4.27 (t, 2H, J= 6.6 Hz). Anal. Calcd for $C_8H_9IO_4$: C, 32.46; H, 3.06. Found: C, 32.05; H, 3.16.

2-[[[[3-(Methoxycarbonyl)-2-propynyl]oxy]carbonyl]methyl]pyrrolo[1,2-*a*]pyrazinium Iodide (40a). A solution of **1** (200 mg, 1.69 mmol) and 4-(iodoacetoxy)-2-butynoic acid methyl ester (470 mg, 1.69 mmol) in EtOAc (10 mL) was stirred under reflux for 24 h. The reaction mixture was cooled, and the resulting precipitate was filtered off to give the title compound. Recrystallization from EtOH−Et_2O afforded yellow crystals (567 mg, 84%): mp 205−207 °C; IR (KBr) 3066, 2249, 1753, 1714, 1653, 1340, 1261, 1193, 1148 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.69 (s, 3H), 5.11 (s, 2H), 5.47 (s, 2H), 7.49 (dd, 1H, J = 4.4 Hz, J = 2.2 Hz), 7.74 (d, 1H, J = 6.1 Hz,), 7.84 (d, 1H, J = 4.4 Hz), 8.48−8.52 (m, 1H), 8.79 (d, 1H, J = 5.9 Hz), 9.47 (s, 1H). Anal. Calcd for $C_{14}H_{13}IN_2O_4$: C, 42.02; H, 3.27; N, 7.00. Found: C, 42.21; H, 3.56; N, 7.11.

2-[[[[4-(Methoxycarbonyl)-3-butynyl]oxy]carbonyl]methyl]pyrrolo[1,2-*a*]pyrazinium Iodide (40b). A mixture of **1** (200 mg, 1.69 mmol) and 5-(iodoacetoxy)-2-pentynoic acid methyl ester (500 mg, 1.69 mmol) in EtOAc (10 mL) was stirred at room temperature for 5 h. The precipitate was filtered off to give a brown solid which was recrystallized from EtOH−Et_2O to give the title compound (601 mg, 86%): mp 212−214 °C; IR (neat) 2951, 2242, 1751, 1708, 1655, 1565, 1339, 1264, 1201, 1152 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.84 (t, 2H, J = 6.0 Hz), 3.69 (s, 3H), 4.30 (t, 2H, J = 6.2 Hz), 5.41 (s, 2H), 7.48 (dd, 1H, J = 2.4 Hz, J = 4.6 Hz), 7.74 (dd, 1H, J = 1.5 Hz, J = 5.9 Hz), 7.82 (d, 1H, J = 4.7 Hz), 8.46−8.51 (m, 1H), 8.78 (d, 1H, J = 5.9 Hz), 9.45 (s, 1H). Anal. Calcd for $C_{15}H_{15}IN_2O_4$: C, 43.50; H, 3.65; N, 6.76. Found: C, 43.17; H, 4.01; N, 6.82.

1-(Methoxycarbonyl)-4-oxo-2-dihydrofuran[4′,3′:4,5]pyrrolo[1,2-*c*]pyrrolo[1,2-*a*]pyrazine (42a). A solution of the salt **40a** (0.50 g, 1.25 mmol) and K_2CO_3 (0.18 g, 1.25 mmol) in dry acetonitrile (12 mL) was stirred at room temperature for 24 h. The reaction mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue

which was chromatographed (hexane:EtOAc, 8:2) to yield **42a** (80 mg, 24%): mp 212−214 °C (white prisms from EtOAc); IR (KBr) 2925, 2857, 1748, 1439, 1360, 1276, 1096, 1029 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.91 (s, 3H), 5.36 (s, 2H), 6.79 (dd, 1H, J = 2.6 Hz, J = 4.0 Hz), 7.33 (dd, 1H, J = 1.5 Hz, J = 2.60 Hz), 7.47 (d, 1H, J = 6.2 Hz), 7.58 (d, 1H, J = 5.9 Hz), 7.97 (d, 1H, J = 4.0 Hz); MS *m*/*z* (relat. int.) 272 (15), 271 (100), 270 (13), 255 (1), 239 (2). Anal. Calcd for $C_{14}H_{10}N_2O_4$: C, 62.22; H, 3.73; N, 10.37. Found: C, 61.99; H, 4.01; N, 10.06.

1-(Methoxycarbonyl)-5-oxo-2,3-dihydropyran[4′,3′:2,3]-pyrrolo[1,2-*c*]pyrrolo[1,2-*a*]pyrazine (42b). A solution of the salt **40b** (0.80 g, 1.93 mmol) and K_2CO_3 (0.28 g, 1.93 mmol) in dry acetonitrile (18 mL) was stirred at room temperature for 24 h. The reaction mixture was filtered, and the filtrate was concentrated. The residue was chromatographed (hexane: EtOAc, 9:1) to give the title compound as white needles after recrystallization from AcOEt (165 mg, 30%): mp 205−207 °C; IR (neat) 1717, 1693, 1546, 1502, 1453, 1436, 1423, 1241, 1093 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.32 (t, 2H, J= 6.2 Hz), 3.93 (s, 3H), 4.58 (t, 2H, J = 6.2 Hz), 6.76 (dd, 1H, J = 2.6 Hz, J= 4.0 Hz), 7.31 (dd, 1H, J = 1.5 Hz, J = 2.6 Hz), 7.45 (d, 1H, J = 5.9 Hz), 7.91(dd, 1H, J = 1.1 Hz, J = 4.0 Hz), 8.42 (d, 1H, J = 5.9 Hz); MS *m*/*z* (rel int) 284 (100), 253 (18), 226 (15), 225 (37), 168 (21), 167 (14). Anal. Calcd for $C_{15}H_{12}N_2O_4$: C, 63.38; H, 4.25; N, 9.85. Found: C, 63.41; H, 4.69; N, 9.62.

3-(2-(Chloroacetoxy)phenyl)acrylic Acid Methyl Ester (44). To a stirred solution of **43** (1.0 g, 6.10 mmol) in MeOH (5 mL) was added H_2SO_4 (0.1 mL). The resulting reaction mixture was refluxed for 2 h and then concentrated in vacuo, and the residue was dissolved in Et_2O and washed with water, and the organic layer was dried ($MgSO_4$). Evaporation of the solvent and column chromatography of the residue (hexane: EtOAc, 8:2) gave 3-(2-hydroxyphenyl)acrylic acid methyl ester. The product was recrystallized from Et_2O to afford white needles (0.97 g, 80%): mp 131−133 °C; IR (KBr) 3392, 1693, 1626, 1603, 1455, 1327, 1227, 1197, 1174, 988 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.70 (s, 3H), 6.61 (d, 1H, J = 16.1 Hz), 6.82 (t, 1H, J = 7.6 Hz), 6.90 (d, 1H, J = 8.3 Hz), 7.23 (t, 1H, J = 7.7 Hz), 7.60 (d, 1H, J = 7.8 Hz), 7.86 (d, 1H, J = 16.1 Hz), 10.26 (s, 1H).

A solution of chloroacetyl chloride (0.57 mL, 7.05 mmol) in toluene (10 mL) was slowly added to a cooled solution of 3-(2-hydroxyphenyl)acrylic acid methyl ester (1.0 g, 5.61 mmol) in toluene (10 mL) and pyridine (1.14 mL.) The reaction mixture was stirred at room temperature for 2 h. The solid was filtered off, and the solvent was removed from the filtrate under reduced pressure. The residue was purified by chromatography (hexane:EtOAc, 8:2) to give **44** (1.34 g, 94%) as a colorless oil: IR (neat) 2955, 1775, 1715, 1635, 1436, 1177, 1135, 1092 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.71 (s, 3H), 4.77 (s, 2H), 6.69 (d, 1H, J = 16.1 Hz), 7.27 (d, 1H, J = 8.1 Hz), 7.35 (t, 1H, J = 7.5 Hz), 7.51 (t, 1H, J = 7.7 Hz), 7.65 (d, 1H, J = 16.1 Hz), 7.93 (d, 1H, J = 7.7 Hz). Anal. Calcd for $C_{12}H_{11}ClO_4$: C, 56.60; H, 4.35. Found: C, 56.62; H, 4.77.

3-(2-(Iodoacetoxy)phenyl)acrylic Acid Methyl Ester (45). To a stirred solution **44** (1.0 g, 3.93 mmol) in dry acetone (5 mL) was added a solution of NaI (0.59 g, 3.93 mmol) in dry acetone (5 mL). The reaction mixture was stirred at room temperature for 24 h. The precipitated NaCl was filtered off, and the filtrate was concentrated. The residue was dissolved in EtOAc, and the solution was washed with saturated Na_2SO_4 solution, dried ($MgSO_4$), and concentrated. The residue was chromatographed (hexane:EtOAc, 8:2) to give the title compound which was recrystallized from petroleum ether affording white needles (1.36 g, 76%): mp 57−59 °C; IR (KBr) 2951, 1751, 1712, 1637, 1322, 1210, 1176, 1093 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.70 (s, 3H), 4.11 (s, 2H), 6.67 (d, 1H, J = 16.1Hz), 7.18 (d, 1H, J = 8.1 Hz), 7.33 (t, 1H, J = 7.5 Hz), 7.49 (t, 1H, J = 7.7 Hz), 7.74 (d, 1H, J = 16.1 Hz), 7.91 (d, 1H, J = 7.7 Hz). Anal. Calcd for $C_{12}H_{11}IO_4$: C, 41.64; H, 3.20. Found: C, 41.55; H, 3.22.

2-[[[2-[2-(Methoxycarbonyl)vinyl]phenoxy]carbonyl]-methyl]pyrrolo[1,2-*a*]pyrazinium Iodide (46). A mixture of **1** (200 mg, 2.69 mmol) and 3-[2-(iodoacetoxy)phenyl]acrylic acid methyl ester (584 mg, 1.69 mmol) in EtOAc (10 mL) was stirred at room temperature for 24 h. The precipitate formed was filtered off and recrystallized from EtOAc−CH_2Cl_2 to give **46** (0.70 g, 89%) as yellow needles: mp 127−129 °C; IR (KBr) 3054, 1763, 1712, 1634, 1334, 1281, 1238, 1145 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.74 (s, 3H), 5.77 (s, 2H), 6.67 (d, 1H, J = 16.1Hz), 7.33−7.41 (m, 2H), 7.49−7.55 (m, 2H), 7.76 (d, 1H, J = 16.1 Hz), 7.88−7.95 (m, 3H), 8.52 (m, 1H), 8.83 (d, 1H, J = 5.9 Hz), 9.58 (s, 1H). Anal. Calcd for $C_{19}H_{17}IN_2O_4$: C, 49.16; H, 3.69; N, 6.03. Found: C, 49.07; H, 3.62; N, 6.12.

[1]Benzopyrano[3′,4′:2,3]pyrrolo[1,2-*c*]pyrrolo[1,2-*a*]-pyrazin-6-one (48). A solution of the salt **46** (0.66 g, 1.42 mmol) in xylene (3 mL) was heated at reflux for 24 h, and then the reaction mixture was filtered. Removal of the solvent in vacuo and purification of the residue by chromatography (hexane:EtOAc, 9:1) afforded a solid which after recrystallization from EtOAc yielded **48** (60 mg, 15%) as white crystals: mp 293−295 °C; IR (KBr) 3104, 1712, 1487, 1452, 1411, 1085, 1066, 1042 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.72 (dd, 1H, J = 3.9, 2.7 Hz); 6.90 (d, 1H, J = 3.7 Hz); 6.99 (s, 1H); 7.32−7.37 (m, 2H); 7.39 (d, 1 H, J = 5.9 Hz); 7.45−7.43 (m, 2H); 7.91(d, 1H, J = 7.7 Hz); 8.46 (d, 1H, J = 5.9 Hz); MS *m*/*z* (rel int) 275 (19), 274 (100), 245 (8), 218 (8), 217 (14), 216 (6), 164 (6), 163 (5), 137 (7). Anal. Calcd for $C_{17}H_{10}N_2O_2$: C, 74.45; H, 3.67; N, 10.21. Found: C, 74.39; H, 3.80; N, 10.08.

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