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2-Benzotriazolylaziridines and Their Reactions with Diethyl Acetylenedicarboxylate

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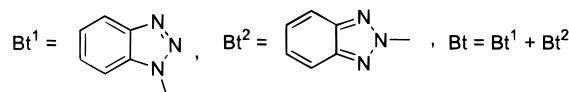
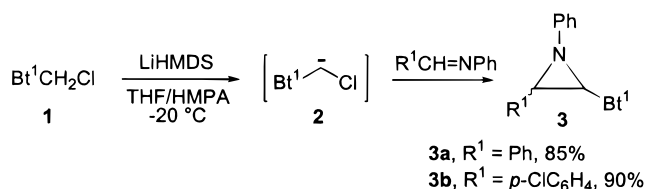
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1-Alkyl-2-benzotriazolylaziridines (**3a,b** and **8a–g**) are synthesized by two routes utilizing a novel benzotriazolyl-substituted carbenoid or 1,2-dibromoethylbenzotriazole. Lithiation of **3b** and **8e** at the position α to benzotriazole and subsequent trapping with alkyl halides leads to the 1,2-dialkyl-2-benzotriazolylaziridine analogues **12** and **20**. Compounds **3a** and **3b** react with acetylenedicarboxylic ester by C–C bond breaking to give pyrrole-3,4-dicarboxylic esters (**14a,b**). By contrast, compounds **8a–d** and **20** react with acetylenedicarboxylic ester by C–N bond breaking and form pyrrole-2,3-dicarboxylic esters **18a–d** and **21**. Structures of each type of pyrroledicarboxylic ester are established by X-ray analysis.

Aziridines are of importance as natural products and as versatile synthetic intermediates.¹ They are used as chiral auxiliaries, reagents, and ligands² and as monomers for polymer synthesis;³ their synthesis and transformations are actively studied. Many preparative methods for aziridines involve a two-component reaction,¹ such as the aza-Darzens,⁴ utilization of carbenes⁵ or ylides,⁶ and the 1,2-dihalide route.⁷ Meanwhile, benzotriazole has emerged as a versatile synthetic auxiliary, capable of stabilizing both α -carbocations and α -carbanions.⁸ As a leaving group, benzotriazole can generate a carbocation,⁸ radical,⁹ or carbanion.¹⁰ Therefore, the preparation of benzotriazolyl-substituted aziridines could enable several different types of reactivity. Herein, we describe our preparation of 2-benzotriazolylaziridines and their utility in the synthesis of a variety of pyrroles.

Scheme 1



Results and Discussion

Syntheses of 2-Benzotriazolylaziridines. Two methods were developed for the preparation of benzotriazolyl-substituted aziridines **3a,b** and **8a–g** (Schemes 1 and 2), one involving a novel carbenoid intermediate **2** and the 1,2-dihalide route via **5**.

Attempts to lithiate 1-chloromethylbenzotriazole (**1**) and trap intermediate **2** were modeled on previous generations of carbenoids.¹¹ As a result of the electron-donating ability of the benzotriazolyl group, carbenoid **2** (Scheme 1) is not expected to be long-lived and needs to be rapidly trapped by an appropriate electrophile; to our knowledge, there are no reports on α -nitrogen substituted carbenoids.¹² However, we now find that 1-chloromethylbenzotriazole (**1**) can be lithiated in the presence of a diaryl imine and intermediate **2** can be captured to form aziridines **3a,b** in high yields (Scheme 1). For the

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(1) (a) Pearson, W. H.; Lian, B. W.; Bergmeier, S. C. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, 1996; Vol. 1A, p 1. (b) Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Am. Chem. Soc.* **1994**, *116*, 2742.

(2) Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599.

(3) Goethals, E. J. In *Comprehensive Polymer Science*; Allen, G., Bevington, J. C., Eds.; Pergamon: Oxford, 1989; Vol 3, p 837.

(4) (a) Reutrakul, V.; Prapansiri, V.; Panyachotipun, C. *Tetrahedron Lett.* **1984**, *25*, 1949. (b) Satoh, T.; Sato, T.; Oohara, T.; Yamakawa, K. *J. Org. Chem.* **1989**, *54*, 3973.

(5) Casarrubios, L.; Pérez, J. A.; Brookhart, M.; Templeton, J. L. *J. Org. Chem.* **1996**, *61*, 8358.

(6) Wang, D.-K.; Dai, L.-X.; Hou, X.-L. *Chem. Commun.* **1997**, 1231 and references therein.

(7) (a) Carlier, P.; Gelas-Mialhe, Y.; Vessiere, R. *Can. J. Chem.* **1977**, *55*, 3190. (b) Saoudi, A.; Hamelin, J.; Benhaoua, H. *J. Chem. Res. (S)* **1996**, 492.

(8) Katritzky, A. R.; Lan, X.; Yang, J. Z.; Denisko, O. V. *Chem. Rev.* **1998**, *98*, 409.

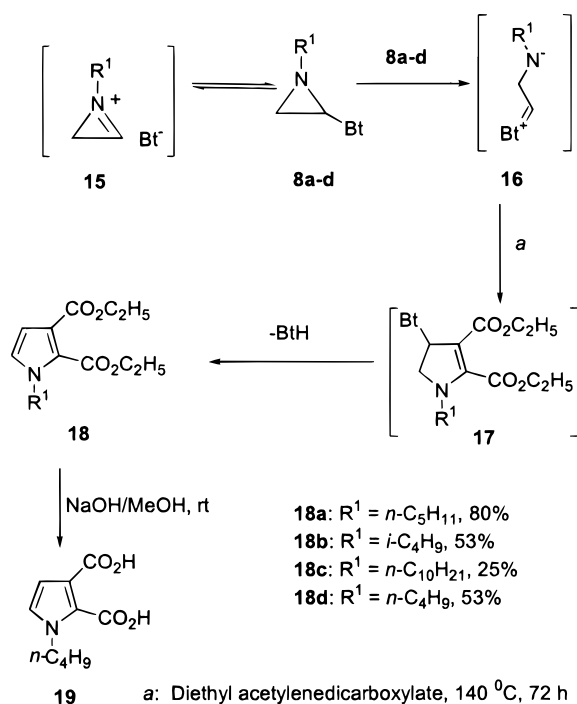
(9) Aurrecoechea, J. M.; López, B.; Fernández, A.; Arrieta, A.; Cossio, F. P. *J. Org. Chem.* **1997**, *62*, 1125 and references therein.

(10) (a) Katritzky, A. R.; Qi, M. *J. Org. Chem.* **1997**, *62*, 4116. (b) Katritzky, A. R.; Qi, M.; Feng, D.; Nichols, D. A. *J. Org. Chem.* **1997**, *62*, 4121.

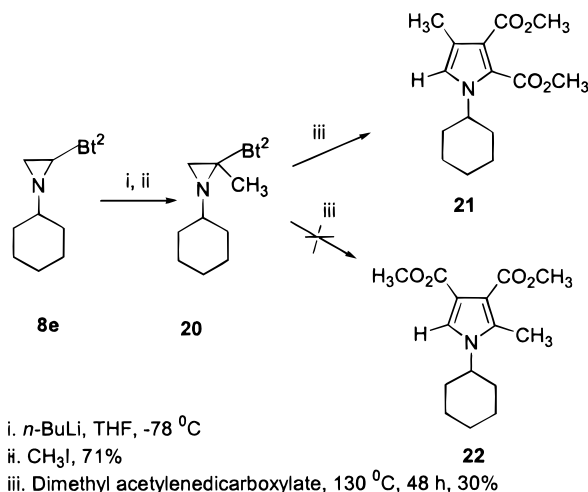
(11) (a) Siegel, H. *Top. Curr. Chem.* **1982**, *106*, 55. (b) Kobrich, G. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 473.

(12) Boche, G.; Lohrenz, J. C. W.; Opel, A. In *Lithium Chemistry, A Theoretical and Experimental Overview*; Sapsee, A.-M., Schleyer, P. V. R., Eds.; John Wiley & Sons: New York, 1995; p195.

Scheme 5



Scheme 6



14a,b in good yields (Scheme 4), presumably via formation of an azomethine ylide (**13**) followed by a polar [2 + 3] cyclization and aromatization by loss of benzotriazole. The structure of the diester **14b** was confirmed by X-ray crystallography (Figure 1), thereby unambiguously locating the positions of the two methoxycarbonyl substituents in the 3 and 4 positions of the pyrrole ring. Compound **14b** crystallizes with two independent molecules in the asymmetric unit, which show significant differences in the conformations of the various substituents attached to the pyrrole ring (for details, see supporting materials). Because the pyrrole-ring H5 and the ¹H and ¹³C signals of each of the two methoxycarbonyl groups of **14a** and **14b** appeared in similar positions in the NMR spectra (Table 1), we deduced that compound **14a** has the same type of structure as **14b**.

1-Alkyl-2-(benzotriazol-2-yl)aziridines (**8a–d**) required a higher temperature (140 °C) and longer times for complete reaction with diethyl acetylenedicarboxylate; these reactions also form pyrrole-dicarboxylic esters, but

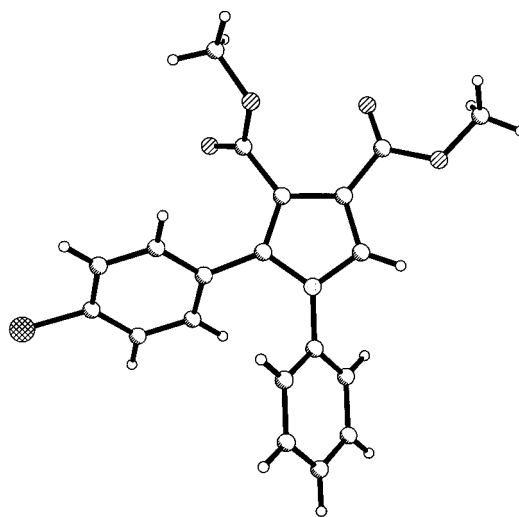


Figure 1. Perspective view of one of the two independent molecules in the unit cell of the X-ray crystal structure of **14b**.

Table 1. Selected ¹³C and ¹H NMR Chemical Shifts (ppm) of Products **14a,b**, **21**, and **18a–d**

	14a	14b	21	18a	18b	18c	18d
C2			123.1	128.5	120.9	124.3	124.9
C3			119.7	120.8	118.9	120.7	120.7
C4			119.5	110.0	109.7	110.0	109.9
C5			120.3	124.9	125.5	124.8	124.2
CO	163.6	163.5	162.0	161.8	161.9	161.5	161.5
	165.5	165.4	166.2	164.3	165.0	164.8	164.8
H5	7.51(s)	7.47(s)	6.69(s)	6.69(d)	6.69(d)	6.69(d)	6.68(d)
H4				6.46(d)	6.47(d)	6.47(d)	6.46(d)

now with the methoxycarbonyl groups at the 2 and 3 positions (**18a–d**, Scheme 5). The ¹H and ¹³C NMR spectra of each of compounds **18a–d** show two non-equivalent methoxycarbonyl groups and two nonequivalent pyrrole-ring protons signals (Table 1). For example, for compound **18d**, the ¹H NMR spectrum had two different ring protons (δ_H 6.46 ppm, d, 1H, *J* = 2.4 Hz and 6.68 ppm, d, 1H, *J* = 2.4 Hz); the ¹³C NMR spectrum showed the presence of two carbonyl groups (δ_C 161.5 and 164.8 ppm) and four different peaks of the pyrrole ring carbon (δ_C 109.9, 120.7, 124.2, 124.9 ppm). If the carboxyl groups were at the 3 and 4 positions, symmetrical ¹H and ¹³C NMR patterns would be expected for compounds **18a–d**; thus, the reaction of **8a–d** is demonstrated to proceed in a different orientation from the reaction of **3a,b**.

The structure of pyrrole **18d** was established by the hydrolysis of **18d** to give the crystalline acid **19**; X-ray crystallography of **19** (Figure 2) showed the 2,3-orientation of the carboxyl groups. Compound **19** also crystallizes with two independent molecules in the asymmetric unit, which have different conformations of the *N*-butyl group. In the unit cell molecule of **19** shown in Figure 2, the *N*-butyl substituent has a 1-anti, 2-gauche conformation, whereas in the other unit cell molecule of **19**, the *N*-butyl has a 1-gauche, 2-anti conformation. In each of the molecules in the unit cell of **19**, an intramolecular hydrogen bond exists between the two carboxylate groups, with the result that all the carboxyl groups are coplanar with the attached pyrrole ring. The remaining OH hydrogens of **19** are involved in intermolecular hydrogen bonds to the carbonyl oxygens of adjacent molecules.

The assignment of pyrrole-ring ¹H and ¹³C NMR features of compounds **18a–d** were based on literature

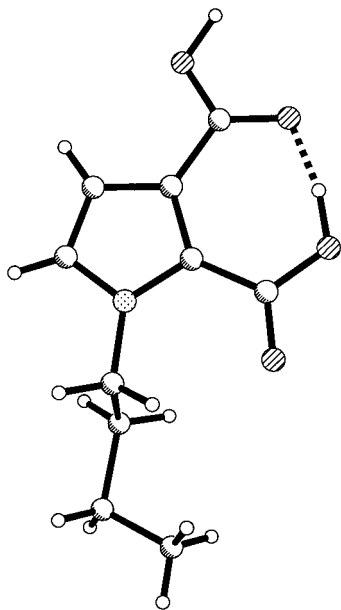


Figure 2. Perspective view of one of the two independent molecules in the unit cell of the X-ray crystal structure of **19**.

analogies.^{4,16} The four ring carbons have two types of ¹³C NMR signals: (i) C2, C3 and (ii) C4, C5 signals. C2 and C5 (linked directly to nitrogen) appeared downfield (i.e., at higher ppm) relative to those for C3 and C4, and thus we assign the ¹³C NMR peaks as in Table 1. The ring protons H5 appear at higher ppm than proton H4, as also shown in Table 1.

The formation of pyrroles **18a–d** probably involves the pathway in Scheme 5. In contrast to aziridines **3a,b**, aziridines **8a–d** have no aryl group at the C3 position to stabilize the azomethine ylide intermediate (cf. **13**, Scheme 4).¹⁷ Evidently, at a higher temperature, the electronic effects of the amino and Bt moieties of **8a–d** can combine to break either the C–N bond or the C–Bt bond, which would form species **15** and **16**, respectively.¹⁸ Whereas **15** is expected to simply equilibrate with aziridine **8a–d**, **16** should react with acetylene to give pyrrolines **17**, which can aromatize to afford pyrroles **18a–d** by the loss of benzotriazole.

The reaction of **20** with dimethyl acetylenedicarboxylate could take two paths (C–C or C–N scission) to form **21** or **22**, however, we only obtained one product. Comparison of the chemical shift of the H5 signal in the ¹H NMR spectrum of this product with the corresponding values for **18a–d** (Table 1) suggested structure **21**. This was confirmed by the observation of an NOE enhancement of the methyl group signal upon irradiation of the signal for H5. Thus the reaction between **20** and dimethyl acetylenedicarboxylate proceeded by the same pathway as the reaction between **8a–d** and diethyl acetylenedicarboxylate through the C–N scission as shown in Scheme 5.

The scission of a C–N bond is of course the normal reaction of aziridines with diverse nucleophiles (R₂CuLi, NaN₃, KSCN, NaI, KCN, allylsilane, RMgBr, RLi, amine, alcohol, phosphite, ylide, *et al.*) to form primary or second-

ary amines.¹⁶ However, to our knowledge, no previous examples of [2 + 3] cycloadditions are known in which the aziridine provides a N–C–C component.^{17,19}

To summarize, we have developed two routes for the synthesis of 2-benzotriazolylaziridines. These aziridines possess multiple reaction centers and have interesting synthetic potential, as exemplified by our preliminary studies of their utility in the preparation of polysubstituted pyrroles.

Experimental Section

General Comments. Melting points were measured on a hot-stage microscope and are uncorrected. ¹H and ¹³C NMR data were collected on a 300 MHz NMR spectrometer (300 and 75 MHz, respectively) using CDCl₃ as solvent. Compounds **1**,²⁰ **4**,²¹ and **9**²¹ were prepared by the literature methods quoted.

General Procedure for the Synthesis of 1,3-Diaryl-2-(benzotriazol-1-yl)aziridines (3). A mixture of 1-(chloromethyl)benzotriazole (**1**, 1.0 g, 6 mmol) and an imine (6 mmol) in THF–HMPA (4:1) was cooled to –20 °C, and lithium bis-(trimethylsilyl)amide (7.2 mmol, 1.0 M in THF) was added over 15 min. The mixture was stirred at room temperature for another 12 h. Water was added, and the mixture was extracted with ether. After the organic layers were dried and concentrated, the crude product was purified by chromatography on silica gel (eluent: hexanes–EtOAc–Et₃N, 100:3:1) to give **3**.

1,3-Diphenyl-2-(benzotriazol-1-yl)aziridine (3a). The *cis* and *trans* isomers (*cis/trans* = 57/43) were separated by column chromatography. *cis*-1,3-Diphenyl-2-(benzotriazol-1-yl)aziridine, white solid, mp 129–131 °C; ¹H NMR δ_H 3.92 (d, 1H, *J* = 4.9 Hz), 5.28 (d, 1H, *J* = 4.9 Hz), 6.67–7.48 (m, 12H), 7.83 (d, 1H, *J* = 8.3 Hz), 7.96 (d, 1H, *J* = 8.4 Hz); ¹³C NMR δ_C 47.9, 56.8, 111.1, 114.7, 119.6, 119.8, 123.9, 124.1, 127.2, 127.6, 128.1, 128.2, 129.2, 129.7, 149.3, 150.7. Anal. Calcd for C₂₀H₁₆N₄: C, 76.90; H, 5.16; N, 17.94. Found: C, 76.92; H, 5.17; N, 17.47. *trans*-1,3-Diphenyl-2-(benzotriazol-1-yl)aziridine: viscous colorless oil; ¹H NMR δ_H 4.76 (d, 1H, *J* = 1.9 Hz), 5.48 (d, 1H, *J* = 1.9 Hz), 6.82–7.58 (m, 12H), 7.86 (d, 1H, *J* = 9.0 Hz), 8.06 (d, 1H, *J* = 8.7 Hz); ¹³C NMR δ_C 45.5, 56.6, 109.9, 113.4, 120.3, 120.6, 123.3, 124.3, 127.7, 128.1, 128.5, 129.0, 133.2, 133.5, 145.4, 146.2.

2-(1,2-Dibromoethyl)benzotriazole (5a). Br₂ (4 g, 25 mmol) was added to a solution of 2-vinylbenzotriazole (2.0 g, 13.8 mmol) in CCl₄ (100 mL) at room temperature, and the mixture was stirred for 45 min. The reaction mixture was washed with saturated NaHCO₃ and concentrated to afford **5a** (93%) as a white solid, mp 62–65 °C; ¹H NMR δ_H 4.28 (dd, 1H, *J* = 3.7, 11.2 Hz), 4.88 (dd, 1H, *J* = 11.2 Hz), 6.98 (dd, 1H, *J* = 3.7, 11.2 Hz), 7.46–7.49 (m, 2H), 7.90–7.94 (m, 2H); ¹³C NMR δ_C 31.8, 60.7, 118.7, 128.0, 144.9. Anal. Calcd for C₈H₇Br₂N₃: C, 31.93; H, 2.31; N, 13.51. Found: C, 31.97; H, 2.25; N, 13.73.

General Procedure for the Synthesis of 1-Alkyl-2-(benzotriazol-2-yl)aziridines (8). A mixture of 2-(1,2-dibromoethyl)benzotriazole (**5a**, 1.3 g, 4.0 mmol), an appropriate alkylamine (10 mmol), NaOH (0.5 g, 12 mmol), ether (6 mL), and HMPA (4 mL) was stirred at room temperature for 24 h under nitrogen. Water was added, and the mixture was extracted with ether. After the organic layer was dried and concentrated, the crude product was purified by column chromatography on neutral Al₂O₃ (eluent: hexanes–EtOAc, 100:3) to afford **8**.

(17) In the transformation of aziridines to pyrroles, most literature (see ref 4a and 16) only reported the reaction between phenyl-substituted aziridines and diethyl acetylenedicarboxylate.

(18) We have observed for open-chain compounds of type Bt–C–N similar competition between C–N and C–Bt bond scission; see ref 10b.

(19) The scission of both C–N and C2–C3 bonds of aziridines and its cyclization with isothiocyanates have been reported; see (a) Nomura, R.; Nakano, T.; Nishio, Y.; Ogawa, S.; Ninagawa, A.; Matsuda, H. *Chem. Ber.* **1989**, *122*, 2407. (b) Lown, J. W.; Matsumoto, K. *Can. J. Chem.* **1970**, *48*, 3399. (c) Lown, J. W.; Dallas, G.; Malony, T. W. *Can. J. Chem.* **1969**, *47*, 3557.

(20) Burckhalter, J. H.; Stephens, V. C.; Hall, L. A. R. *J. Am. Chem. Soc.* **1952**, *74*, 3868.

(21) Katritzky, A. R.; Li, J.; Malhotra, N. *Liebigs Ann. Chem.* **1992**, 843.

1-Pentyl-2-(benzotriazol-2-yl)aziridine (8a). Colorless oil; ^1H NMR δ_{H} 0.89 (t, 3H, $J = 6.7$ Hz), 1.33–1.35 (m, 4H), 1.68–1.70 (m, 2H), 1.96 (d, 1H, $J = 5.4$ Hz), 2.44–2.48 (m, 1H), 2.65–2.68 (m, 1H), 2.97 (d, 1H, $J = 1.7$ Hz), 4.58–4.65 (m, 1H), 7.35–7.38 (m, 2H), 7.83–7.86 (m, 2H); ^{13}C NMR δ_{C} 13.9, 22.4, 28.8, 29.3, 34.5, 57.0, 59.5, 118.1, 126.5, 144.2. Anal. Calcd for $\text{C}_{13}\text{H}_{18}\text{N}_4$: C, 67.78; H, 7.88; N, 24.34. Found: C, 67.33; H, 7.66; N, 24.53.

General Procedure for the Synthesis of Aziridines 12 and 20. To a solution of **3b** or **8e** (1.0 mmol) in THF (20 mL, -78°C) was added $n\text{-BuLi}$ (1.1 mmol), and the mixture was then stirred for 20 min. 1-Bromobutane or iodomethane (1.0 equiv) was added to the reaction mixture, which was kept overnight. The reaction mixture was treated with saturated NaHCO_3 solution and extracted with ether. After column chromatography on neutral alumina (eluent: hexanes–EtOAc, 100:3), the pure product was obtained.

1-Phenyl-2-butyl-2-(benzotriazol-1-yl)-3-(4-chlorophenyl)aziridine (12). White solid, mp $60\text{--}61^\circ\text{C}$; ^1H NMR δ_{H} 0.76 (t, 3H, $J = 6.9$ Hz), 1.19–1.35 (m, 3H), 1.56–1.60 (m, 1H), 1.88–1.93 (m, 1H), 2.13–2.18 (m, 1H), 3.78 (s, 1H), 7.05 (br s, 5H), 7.20 (t, 1H, $J = 7.2$ Hz), 7.27 (d, 2H, $J = 7.5$ Hz), 7.34 (t, 1H, $J = 7.5$ Hz), 7.46 (t, 2H, $J = 7.5$ Hz), 7.80 (d, 1H, $J = 8.4$ Hz), 8.01 (d, 1H, $J = 8.1$ Hz); ^{13}C NMR δ_{C} 13.7, 22.4, 27.7, 33.8, 50.3, 64.1, 110.7, 119.9, 120.1, 123.7, 127.5, 128.0, 128.3, 128.7, 129.5, 132.7, 133.2, 133.7, 145.0, 146.8. Anal. Calcd for $\text{C}_{24}\text{H}_{23}\text{ClN}_4$: C, 71.54; H, 5.75. Found: C, 71.67; H, 5.98.

General Procedure for the Synthesis of Substituted Pyrroles 14. A mixture of an appropriate benzotriazolylaziridine (**3a** or **3b**, 2.2 mmol) and dialkyl acetylenedicarboxylate (2.8 mmol) was stirred at 100°C for 48 h. Then the mixture was purified by column chromatography on silica gel (eluent: hexanes–EtOAc– Et_3N , 100:3:1) to afford pure **14**.

Diethyl 2-(4-chlorophenyl)-1-phenyl-1H-pyrrole-3,4-dicarboxylate (14b).^{4a} White solid, mp $120\text{--}121^\circ\text{C}$; ^1H NMR δ_{H} 3.75 (s, 3H), 3.82 (s, 3H), 7.04–7.06 (m, 2H), 7.12 (d, 2H, $J = 8.6$ Hz), 7.18 (d, 2H, $J = 8.6$ Hz), 7.28–7.30 (m, 3H), 7.47 (s, 1H); ^{13}C NMR δ_{C} 51.3, 51.8, 115.4, 116.8, 125.7, 127.9, 128.0, 128.1, 129.2, 131.4, 131.5, 133.9, 134.2, 138.0, 163.5, 165.4. Anal. Calcd for $\text{C}_{20}\text{H}_{16}\text{ClNO}_4$: C, 64.96; H, 4.36; N, 3.79. Found: C, 64.71; H, 4.23; N, 3.93.

General Procedure for the Synthesis of Substituted Pyrroles 18. A mixture of an appropriate benzotriazolylaziridine (**8**, 2.2 mmol) and diethyl acetylenedicarboxylate (2.8 mmol) was stirred at 140°C for 72 h. Then the mixture was purified by column chromatography on silica gel (eluent: hexanes–EtOAc– Et_3N , 100:1:1) to afford pure **18**.

Diethyl 1-pentyl-1H-pyrrole-2,3-dicarboxylate (18a). Colorless oil; ^1H NMR δ_{H} 0.89 (t, 3H, $J = 6.9$ Hz), 1.22–1.39 (m, 10H), 1.72–1.77 (m, 2H), 4.14 (t, 2H, $J = 7.1$ Hz), 4.25–4.36 (m, 4H), 6.46 (d, 1H, $J = 2.7$ Hz), 6.69 (d, 1H, $J = 2.7$ Hz); ^{13}C NMR δ_{C} 13.9, 14.1, 14.3, 22.2, 28.7, 31.2, 49.2, 60.4, 61.1, 110.0, 120.8, 124.9, 128.5, 161.8, 164.3. Anal. Calcd for $\text{C}_{15}\text{H}_{23}\text{NO}_4$: C, 64.04; H, 8.24; N, 4.98. Found: C, 63.73; H, 8.70; N, 5.38.

Dimethyl 1-cyclohexyl-4-methyl-1H-pyrrole-2,3-dicarboxylate (21). Prepared from **20** and dimethyl acetylenedicarboxylate at 130°C for 72 h in 30% yield, colorless oil; ^1H NMR δ_{H} 1.18–1.26 (m, 1H), 1.36–1.61 (m, 4H), 1.74 (d, 1H, $J = 13.2$ Hz), 1.88 (d, 2H, $J = 12.6$ Hz), 2.06 (d, 2H, $J = 12.0$ Hz), 2.15 (s, 3H), 3.84 (s, 3H), 3.85 (s, 3H), 4.47–4.55 (m, 1H), 6.69 (s, 1H); ^{13}C NMR δ_{C} 10.8, 25.4, 25.7, 34.4, 51.5, 51.8, 56.7, 119.5, 119.7, 120.3, 123.1, 162.0, 166.2. Anal. Calcd for $\text{C}_{15}\text{H}_{21}\text{NO}_4$: C, 64.50; H, 7.58; N, 5.01. Found: C, 64.75; H, 7.45; N, 5.91.

1-Butyl-1H-pyrrole-2,3-dicarboxylic acid (19). Compound **18d** (0.1 g) in methanol (1 mL) and aqueous NaOH (2 N, 1 mL) were stirred at room temperature for 24 h. The reaction mixture was acidified to pH = 2 with aqueous saturated HCl solution and extracted with EtOAc (3×20 mL). The organic layer was washed with aqueous saturated NaCl solution and dried over MgSO_4 . Removal of the solvent under vacuum afforded **19**; mp $120\text{--}123^\circ\text{C}$; ^1H NMR δ_{H} 0.95 (t, 3H, $J = 5.6$ Hz), 1.35–1.37 (m, 2H), 1.78–1.81 (m, 2H), 4.50 (t, 2H, $J = 6.6$ Hz), 6.88 (br, 2H); ^{13}C NMR δ_{C} 13.6, 19.8, 33.4, 51.1, 113.2, 118.2, 128.4, 170.7.

X-ray Crystallography. Data were collected with a Siemens SMART CCD area detector, using graphite monochromatized Mo K α radiation ($\lambda = 0.71073$ Å). The structures were solved by direct methods and refined on F^2 using all data by full-matrix least-squares procedures. Hydrogen atoms were included in calculated positions, except for the OH hydrogens which were located from a difference map.

Crystal Data for **14b** at -110°C : $\text{C}_{20}\text{H}_{16}\text{ClNO}_4$, $M = 369.79$, monoclinic, space group $P2_1/c$; $a = 11.4672(6)$, $b = 38.103(2)$, $c = 8.1776(4)$ Å; $\beta = 103.718(1)^\circ$; $V = 3471.1(3)$, $Z = 8$, $F(000) = 1536$, $D_x = 1.415$ g cm^{-3} ; colorless block, $0.64 \times 0.52 \times 0.11$ mm; μ , 0.246 mm^{-1} , $2\theta_{\text{max}}$ 53° ; 6767 unique reflections, 473 parameters, $wR = 0.0943$ for all data, $R = 0.0377$ for 5415 data with $I > 2\sigma(I)$.

Crystal Data for **19** at -115°C : $\text{C}_{10}\text{H}_{13}\text{NO}_4$, $M = 211.21$, triclinic, space group $P-1$; $a = 7.767(2)$, $b = 11.193(3)$, $c = 13.039(4)$ Å, $\alpha = 75.336(5)^\circ$, $\beta = 86.921(4)^\circ$, $\gamma = 80.660(4)^\circ$; $V = 1081.9(5)$, $Z = 4$, $F(000) = 448$, $D_x = 1.297$ g cm^{-3} ; colorless plate, $0.62 \times 0.38 \times 0.02$ mm, μ , 0.101 mm^{-1} , $2\theta_{\text{max}}$ 47° ; 3124 unique reflections, 271 parameters, $wR = 0.1620$ for all data, $R = 0.0586$ for 1728 data with $I > 2\sigma(I)$.

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Supporting Information Available: Text providing detailed analysis data (^1H , and ^{13}C NMR and microanalysis) of compounds **3b**, **8b–g**, **10**, **11**, **14a**, **18b–d**, and **20** and eight tables of crystal data for compounds **14b** and **19** (17 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.