$[\alpha]^{20}_D = -49°$). Elemental anal. Calcd for $C_{19}H_{23}{}^2HO_9$ (397.40): C, 57.43; H, 6.34. Found: C, 57.52; H, 6.22. ^1H NMR (300 MHz, $C_6D_6/CDCl_3$, 1:1): δ 1.72, 1.78, 1.80 (3 s, OAc), 2.190 (d, 6-OH), 3.159 (dd, H-5), 3.440 (br, H-6), 4.394 (d, H-1), 4.471 (d, Ha-Bn), 4.742 (d, Hb-Bn), 5.072 (dd, H-4), 5.192 (dd, H-2), 5.236 (dd, H-3), 7.15-7.25 (m, Ar); $J_{1,2} = 7.7$, $J_{2,3} = J_{3,4} = 9.2$, $J_{4,5} = 9.5$, $J_{5,6} = 5.1$, $J_{Ha\text{-}Bn,Hb\text{-}Bn} = -12.4$ Hz. ^{13}C NMR (75.5 MHz, $CDCl_3$) (cf. ref 33 for parent ^1H isotopomer): δ 3 × 20.00 ($OCOCH_3$), 60.85 (t, C-6), 68.79 (C-4), 70.60 (CH_2(Bn)), 71.53 (C-2), 72.95 (C-3), 73.99 (C-5), 99.58 (C-1), 127.34-128.32 (m, Ar), 168.87, 169.51, 169.91 ($OCOCH_3$); $J_{C,D} = 21.9$ Hz.

Benzyl (6*S*)-[6-^{2}H]-2,3,4-Tri-*O*-acetyl-6-*O*-sulfo-β-D-glucopyranoside Triethylammonium Salt (18). Compound **17** (3.5 g, 8.8 mmol) was reacted in the same way as described for **6**, to give 4.7 g (8.1 mmol) of compound **18** (92%): mp 73-74 °C; $[\alpha]^{20}_D = -25.0°$ (c = 0.9 in $CHCl_3$). Elemental anal. Calcd for $C_{25}H_{38}{}^2HO_{12}NS$ (578.65): C, 51.89; H, 6.97; N, 2.42. Found: C, 51.47; H, 6.88; N, 2.35. ^1H NMR (300 MHz, $CDCl_3$): δ 1.352 (t, $CH_3(NEt_3)$), 1.982, 2.000, 2.028 (3 s, OAc), 2.351 (s, NH^+), 3.155 (q, $CH_2(NEt_3)$), 3.805 (dd, H-5), 4.137 (d, H-6), 4.558 (d, H-1), 4.625 (d, Ha-Bn), 4.887 (d, Hb-Bn), 5.017 (dd, H-2), 5.045 (dd, H-4), 5.163 (dd, H-3), 7.22-7.38 (m, Ar); $J_{1,2} = 7.9$, $J_{2,3} = 9.5$, $J_{3,4} = 9.4$, $J_{4,5} = 9.5$, $J_{5,6} = 5.5$, $J_{Ha\text{-}Bn,Hb\text{-}Bn} = -12.3$ Hz. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 8.63 ($CH_3(NEt_3)$), 3 × 20.60 ($OCOCH_3$), 46.50 ($CH_2(NEt_3)$), 65.52 (t, C-6), 68.77 (C-4), 70.59 (CH_2(Bn)), 71.31 (C-2), 72.14 (C-5), 73.00 (C-3), 99.24 (C-1), 127.59, 127.85, 128.38, 136.76 (Ar), 169.37, 169.61, 170.17 ($OCOCH_3$); $J_{C,D} = 21.1$ Hz.

Benzyl (6*S*)-[6-^{2}H]-6-*O*-Sulfo-β-D-glucopyranoside Sodium Salt (19). Compound **18** (3.4 g, 5.9 mmol) was reacted in the same way as described for **7**, to give 2.2 g (5.9 mmol) of **19** (100%): mp 255 °C dec; $[\alpha]^{20}_D = -36.7°$ (c = 0.8 in H_2O). Elemental anal. Calcd for $C_{13}H_{16}{}^2HO_9SNa$ (373.33): C, 41.82; H, 4.86. Found: C, 41.67; H, 4.81. ^1H NMR (300 MHz, D_2O): δ 3.157 (dd, H-2), 3.28 (dd, H-4), 3.33 (dd, H-3), 3.476 (dd, H-5), 4.042 (d, H-6), 4.364 (d, H-1), 4.593 (d, Ha-Bn), 4.771 (d, Hb-Bn), 7.21-7.35 (m, H-Ar); $J_{1,2} = 7.9$, $J_{2,3} = 9.5$, $J_{3,4} = 9.0$, $J_{4,5} = 9.7$, $J_{5,6} = 5.3$, $J_{Ha\text{-}Bn,Hb\text{-}Bn} = -11.8$ Hz. ^{13}C NMR (75.5 MHz, D_2O): δ 67.10 (t, C-6), 69.65 (C-4), 71.85 (CH_2(Bn)), 73.37 (C-2), 74.02 (C-5), 76.00 (C-3), 101.52 (C-1), 128.79, 129.04, 129.20, 136.92 (Ar); $J_{C,D} = 22.2$ Hz.

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Registry No. **3**, 4304-12-5; **4**, 56775-63-4; **5**, 29868-41-5; **6**, 123641-83-8; **7**, 123641-84-9; **8**, 123641-85-0; **9**, 123641-86-1; **10**, 123641-87-2; **11**, 86448-08-0; **13**, 123641-88-3; **14**, 123641-89-4; **15**, 123641-90-7; **16**, 123641-91-8; **17**, 123641-92-9; **18**, 123674-15-7; **19**, 123641-93-0.

Supplementary Material Available: 2D (^{13}C, ^1H) COSY spectrum of **6** (1 page). Ordering information is given on any current masthead page.

(33) Vignon, M. R.; Vottero, J. A. *Tetrahedron Lett.* **1976**, 2445.
(34) Meyer, B. GESA program. *Carbohydr. Res.* In preparation.
(35) Conformational preferences were calculated by using the equation of Gerlt and Youngblood.[28] $2.7x_{gt} + 1.3x_{gg} + 11.7x_{tg} = J_{5,6S}$; $11.5x_{gt} + 1.3x_{gg} + 5.8x_{tg} = J_{5,6R}$; and $x_{gt} + x_{gg} + x_{tg} = 1$.
(36) Nishida, Y.; Ohrui, H.; Meguro, H. *Tetrahedron Lett.* **1984**, *25*, 1575.

Preparation of Carboalkoxyalkylphenylalanine Derivatives from Tyrosine

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In order to provide the means for the synthesis of peptides incorporating stable and relatively nonpolar mimics of tyrosine phosphates and sulfates, procedures for the conversion of tyrosine derivatives to the corresponding carboalkoxyalkylphenylalanines have been developed. For the synthesis of carboalkoxyethylphenylalanines, a benzyl or benzhydryl ester of *N*-(Boc)tyrosine triflate (**2**) is coupled with an acrylate ester or preferably a 3-(trialkylstannyl)acrylate in the presence of bis(triphenylphosphine)palladium dichloride to give a carboalkoxyethenylphenylalanine derivative. Hydrogenation affords the corresponding *N*-(Boc)carboalkoxyethylphenylalanine. For the preparation of carboalkoxymethylphenylalanines, an ester of **2** is coupled with allyltributyl tin in the presence of bis(triphenylphosphine)palladium dichloride and lithium chloride to give an ester of 4-allylphenylalanine. A two-stage oxidation using ruthenium tetroxide/sodium periodate followed by sodium chlorite in phosphate buffer gives a carboxymethylphenylalanine. Appropriate esterification of the newly formed carboxylic acid and selective deesterification of the α-carboxylate then completes the synthesis of *N*-(Boc)-carboalkoxymethylphenylalanine.

Tyrosine phosphorylation by tyrosine kinases represents an important control point for cell growth and differentiation.[1] In addition, a number of neurohormones and secretory peptides such as gastrin,[2] cholecystokinin,[3] fibronectin,[4] and leucosulfakinin[5] contain a sulfated tyrosine which is necessary for expression of their biological activity. In view of the ionic character and instability of tyrosine phosphates and sulfates,[6] it would be of interest to have access to analogues incorporating less polar and more stable mimics of these groups for structure-activity studies and development of antagonists or agonists of the parent

(1) Krebs, E. G. *Biochem. Soc. Trans.* **1985**, *13*, 813. Hunter, T.; Cooper, J. A. *Ann. Rev. Biochem.* **1985**, *54*, 897. Weinberg, R. A. *Science* **1985**, *230*, 770. Goustin, A. S.; Leof, E. B.; Shipley, G. D.; Moses, H. L. *Cancer Res.* **1986**, *46*, 1015.
(2) Gregory, H.; Hardy, P. M.; Jones, D. S.; Kenner, G. W.; Sheppard, R. C. *Nature* **1964**, *204*, 931.
(3) Mutt, V.; Jorpes, J. E. *Eur. J. Biochem.* **1968**, *6*, 156.
(4) Liu, M.-C.; Lipmann, F. *Proc. Natl. Acad. Sci. U.S.A.* **1985**, *82*, 34.
(5) Nachamn, R. J.; Holman, G. M.; Haddon, W. F.; Ling, N. *Science* **1986**, *234*, 71. Nachamn, R. J.; Holman, G. M.; Cook, B. J.; Haddon, W. R.; Ling, N. *Biochem. Biophys. Res. Commun.* **1986**, *140*, 357. Nachman, R. J.; Holman, G. M.; Haddon, W. F.; Hayes, T. K. *Peptide Research* **1989**, *2*, 171.
(6) Bettelheim, F. R. *J. Am. Chem. Soc.* **1954**, *76*, 2838.

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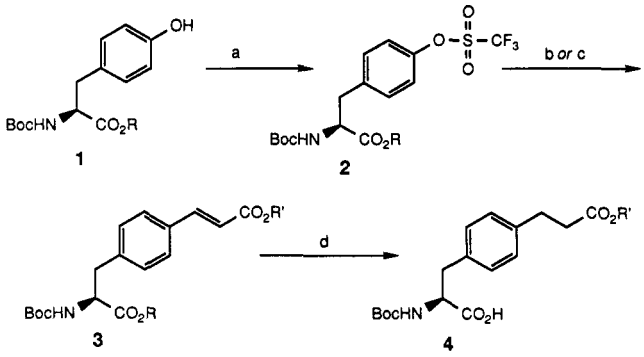
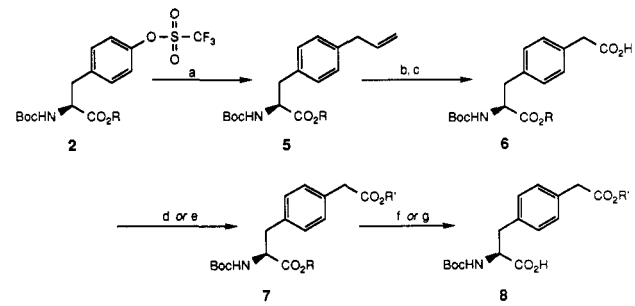
Scheme I[a]



Series a, R = $CH(C_6H_5)_2$, R' = $C(CH_3)_3$
b, R = $CH_2C_6H_5$, R' = CH_3

[a] (a) Phenyltriflimide, NEt_3, CH_2Cl_2, (85–96%); (b) *tert*-butyl acrylate, $[(C_6H_5)_3P]_2PdCl_2$, NEt_3, DMF, 90 °C, 24 h (54%); (c) (*E*)-methyl 3-(tributylstannyl)acrylate, $[(C_6H_5)_3P]_2PdCl_2$, LiCl, DMF, 90 °C, 1 h (65%); (d) H_2, Pd(C), C_2H_5OH (89–94%).

Scheme II[a]



Series b, R = $CH_2C_6H_5$, R' = CH_3
c, R = CH_3, R' = $C(CH_3)_3$

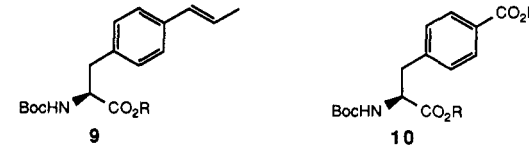
[a] (a) Allyltributylstannane, $[(C_6H_5)_3P]_2PdCl_2$, DMF, 90 °C, 0.5 h (87–92%); (b) catalytic $RuCl_3$, $NaIO_4$, CCl_4, CH_3CN, H_2O, 25 °C, 1 h; (c) $NaClO_4$, NaH_2PO_4, 2-methyl-2-butene, $(CH_3)_3COH$, 0 °C, 2 h (73%); (d) CH_3I, K_2CO_3, DMF, 25 °C, 2 h (90%); (e) DMF–di-*tert*-butyl acetal toluene, 80 °C, 4 h (65%); (f) H_2, Pd(C), C_2H_5OH, (91%); (g) NaOH, CH_3OH, 25 °C, 2 h (78%).

agents as potential therapeutics. As part of an effort to address the stability problem, recent reports have described methods for the preparation of phosphono-,[7] phosphonomethyl-,[8] and sulfomethylphenylalanine[8] derivatives. In our own work, we have considered the possibility that tyrosine phosphates and sulfates might be productively substituted by carboxyalkylphenylalanines. Thus we have developed procedures for the conversion of suitably protected tyrosine derivatives to the corresponding carboalkoxyalkylphenylalanines which are appropriately functionalized for incorporation into peptide analogues by solid-phase synthesis.

The process starts with the tyrosine triflate derivatives **2** which are readily available from the corresponding protected tyrosines **1** by reaction with phenyl triflimide.[9] For the synthesis of carboxyethylphenylalanines **4** (Scheme I), we first investigated the palladium-catalyzed coupling of **2** with *tert*-butyl acrylate under the general conditions described by Chen,[10] but found that relatively long reaction times were required and the isolated yield of **3a** was only modest (54%). After considerable experimentation, we found that 3-(tributylstannyl)acrylates[11] couple more rapidly and give somewhat better yields. For example, in DMF at 90 °C, methyl 3-(tributylstannyl)acrylate reacted completely with **2b** in the presence of bis(triphenylphosphine)palladium dichloride and lithium chloride in 1 h to give a 65% yield of **3b**.

Hydrogenation of **3a** and **3b** afforded the acids **4a** and **4b**, respectively, in nearly quantitative yields. To ascertain whether racemization occurred during these transformations, the end products were hydrolyzed with 6 N hydrochloric acid, esterified with 2-propanol in hydrochloric acid, and acylated with perfluoropropanoic anhydride prior to gas chromatographic analysis on a Chirasil-Val chiral column.[12] Employing conditions under which a racemic mixture gave two peaks of equal area, **4a** and **4b** were each determined to consist of ≥96.5% of a single optical isomer. Since 1–2% racemization typically occurs during the hydrolysis procedure, it is apparent that the synthetic steps proceed with minimal racemization.

For the preparation of carboalkoxymethylphenylalanines, **2b** and **2c** were coupled with allyltributyl tin in the presence of bis(triphenylphosphine)palladium dichloride and lithium chloride to give the allylphenylalanines **5b** and **5c** in high yield (Scheme II). At 90 °C, the reaction was complete within 30 min. Analysis of the products by ^1H NMR spectroscopy indicated that less than 5% of the material had suffered isomerization of the allylic double bond into conjugation with the aromatic ring to give **9**. Attempted direct oxidation of the allyl group of **5** to the corresponding acetic acid **6** using sodium metaperiodate in the presence of a catalytic amount of ruthenium chloride gave a mixture consisting of the desired acid and the intermediate aldehyde in an approximately 1:1 ratio as determined by ^1H NMR spectroscopy. While Sharpless indicates that cleaner oxidations can be achieved using periodic acid in the place of sodium periodate,[13] concern over the integrity of the protecting groups prompted us to resort to a two-stage oxidation using ruthenium chloride/periodate followed by sodium chlorite in phosphate buffer[14] to give the acids **6b** and **6c**, each in 73% yield. Since the separation of **5** from the small quantities of its isomer **9** was extremely tedious, it was more practical to oxidize the mixture to provide the acetic acids **6** together with small amounts of the corresponding benzoic acids **10**, which were readily separable by flash chromatography.



The choice of protecting group for the newly formed acid depends on the ester group already present as well as the intended strategy for peptide synthesis. In the present work, the methyl ester **7b** was formed in high yield from the Boc-benzyl ester **6b** by treatment with iodomethane in DMF over potassium carbonate. Alternatively, the *tert*-butyl ester **7c** was available through reaction of the Boc-methyl ester **6c** with excess dimethylformamide di-

(7) Petrakis, K. S.; Nagabhushan, T. L. *J. Am. Chem. Soc.* **1987**, *109*, 2831.
(8) Marseigne, I.; Roques, B. P. *J. Org. Chem.* **1988**, *53*, 3621.
(9) Hendrickson, J. B.; Bergeron, R. *Tetrahedron Lett.* **1973**, 4607.
(10) Chen, Q.-Y.; Yang, Z.-Y. *Tetrahedron Lett.* **1986**, *27*, 1171.
(11) Leusink, A. J.; Budding, H. A.; Marsman, J. W. *J. Organomet. Chem.* **1967**, *9*, 285.
(12) Frank, H.; Nicholson, J. T.; Bayer, E. *J. Chromatography* **1978**, *167*, 187. Frank, H.; Woiwode, W.; Nicholson, G.; Bayer, E. *Justus Leibigs Ann. Chem.* **1981**, 354.
(13) Chong, J. M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1560, see footnote 4.
(14) Bal, B. S.; Childers, W. E.; Pinnick, H. W. *Tetrahedron* **1981**, *37*, 2091.

tert-butyl acetal in toluene.[15] In the former case, catalytic hydrogenation served to free the protected amino acid **8b**, and in the latter case, base-mediated hydrolysis was employed to prepare **8c**. Compounds **8b** and **8c** were determined to be ≥98% and ≥99% optically pure, respectively, by gas chromatography, again indicating that very little racemization occurred during the synthetic steps.

The chemical approaches outlined in this report provide a general entry into protected phenylalanine derivatives for use in the solid-phase synthesis of peptides bearing carboxyalkylphenylalanines in the place of tyrosine phosphates and sulfates. Minor modifications to these procedures should permit the synthesis of intermediates with suitable carboxyl protecting groups to accommodate various peptide synthetic strategies. Our results on the incorporation of **4** and **8** into polypeptides will be reported in a separate communication.

Experimental Section

Melting points were determined on a Büchi 510 melting point apparatus and are uncorrected. Proton magnetic resonance spectra were recorded on a Varian XL-100, XL-200, or XL-400 spectrometer, and shifts are reported in ppm downfield from tetramethylsilane used as an internal reference. Electron impact (EI, 70 ev) and fast ion bombardment (FAB) mass spectra were taken on VG ZAB-1F or VG 7070E-HF mass spectrometers. Preparative high-pressure liquid chromatography (HPLC) was performed on silica gel Prep-Pak 500 cartridges using a Water Associates Prep LC 500A. Flash silica gel chromatography employed Kiesel gel 60, 230–400 mesh as supplied by E. Merck, Darmstadt under a nitrogen pressure of 2–5 psi. DMF was dried over Linde 3A sieves, and triethylamine was distilled from calcium hydride. Concentration refers to removal of solvent under aspirator pressure using a Büchi rotary evaporator.

To determine the enantiomeric purities of **4a**, **4b**, **8a**, and **8b**, a 1-mg sample of the test substance was dissolved in 0.5 mL of 6 N HCl and sealed under vacuum. The vial was heated at 110 °C for 18 h and allowed to cool. The hydrolysate was evaporated to dryness and then heated in a sealed reaction vessel in 3 N HCl in 2-propanol for 1 h at 110 °C. The reaction mixture was evaporated to dryness and dissolved in 0.3 mL of ethyl acetate and 0.2 mL of pentafluoropropionic anhydride. After heating in a sealed reaction vessel for 10 min at 150 °C, the solvent and excess reagent were evaporated under a stream of nitrogen. The residue was dissolved in 1.0 mL of CH_2Cl_2 and was analyzed by gas chromatography on a Hewlett-Packard 5710A instrument equipped with a 50 m × 0.28 mm Chirasil-Val III capillary column. The column temperature was programmed from 90 °C to 200 °C at a rate of 4 °C/min using hydrogen as the carrier gas and FID detection.[12]

(*S*)-α-[[(1,1-Dimethylethoxy)carbonyl]amino]-4-[[(trifluoromethyl)sulfonyl]oxy]benzenepropanoic acid diphenylmethyl ester (2a) was prepared as described for **2c** below. From 17.0 g (38 mmol) of **1a**, there was obtained 13.7 g (62%) of **2a**: mp 110–112 °C; $[\alpha]^{25}_D$ −14.23° (*c* = 0.12, EtOH); EI MS *m/z* 523 ($M^+ - C_4H_9$); ^{1}H NMR ($CDCl_3$) δ 1.30 (s, 9 H, $C(CH_3)_3$), 3.00 (m, 1 H, β-CH*H*), 3.07 (m, 1 H, β-C*H*H), 4.66 (m, 1 H, α-CH), 5.01 (d, 1 H, *J* = 3.5 Hz, NH), 6.91 (s, 1 H, $CHAr_2$), 6.70 (m, 4 H, ArH), 7.5 (m, 10 H, ArH). Anal. Calcd for $C_{28}H_{28}F_3NO_7S$: C, 58.03; H, 4.87; N, 2.42; S, 5.53. Found: C, 58.26; H, 4.82; N, 2.49; S, 5.63.

(*S*)-α-[[(1,1-Dimethylethoxy)carbonyl]amino]-4-[[(trifluoromethyl)sulfonyl]oxy]benzenepropanoic acid phenylmethyl ester (2b) was prepared as described for **2c** below. From 6.20 g (16.9 mmol) of **1b** there was obtained 7.37 g (87%) of **2b**: mp 61–62 °C; $[\alpha]^{25}_D$ −9.68° (*c* = 0.10, EtOH); FAB MS *m/z* (relative intensity) 504 (8) (M^+ + H), 448 (20), 404 (100); ^{1}H NMR ($CDCl_3$) δ 1.41 (s, 9 H, $C(CH_3)_3$), 3.06 (m, 1 H, β-CH*H*), 3.13 (m, 1 H, β-C*H*H), 4.63 (m, 1 H, α-CH), 5.02 (d, 1 H, *J* = 3.5 Hz, NH), 5.09 (d, 1 H, ArC*H*HO, *J* = 6 Hz), 5.20 (d, 1 H, ArCH*H*O, *J* = 6 Hz), 7.09 (s, 4 H, ArH), 7.26–7.31 (m, 2 H, ArH), 7.37–7.38 (m, 3 H, ArH). Anal. Calcd for $C_{22}H_{24}F_3NO_7S$: C, 52.48; H, 4.80; N, 2.78; F, 11.32; S, 6.37. Found: C, 52.68; H, 4.83; N, 2.67; F, 11.54; S, 6.67.

(*S*)-α-[[(1,1-Dimethylethoxy)carbonyl]amino]-4-[[(trifluoromethyl)sulfonyl]oxy]benzenepropanoic Acid Methyl Ester (2c). A solution of 19.23 g (65.0 mmol) of (*S*)-4-hydroxy-α-[[(1,1-dimethylethoxy)carbonyl]amino]benzenepropanoic acid methyl ester (**1c**) and 24.0 g (67.0 mmol) of phenyl triflimide in 175 mL of dry dichloromethane was cooled in an ice bath, and 9.7 mL (70 mmol) of triethylamine was added over 3 min. The resulting mixture was held at 0 °C for 1 h and allowed to warm to room temperature over 1 h. The reaction mixture was diluted with 500 mL of ether and washed successively with water (1 × 100 mL), 1 N sodium hydroxide solution (2 × 100 mL), water (1 X 100 mL), and saturated sodium chloride solution (1 × 100 mL). The organic phase was dried ($MgSO_4$) and concentrated to an oil which was purified by preparative liquid chromatography, eluting with 20% ethyl acetate–hexane. The pure fractions were combined and concentrated to give 26.78 g (96%) of **2c** as a colorless oil which crystallized on standing: mp 48–49 °C; $[\alpha]^{25}_D$ −43.13° (*c* = 1.02, EtOH); FAB MS *m/z* (relative intensity) 450 (M^+ + Na) (22), 428 (M^+ + H) (25), 372 (100); ^{1}H NMR ($CDCl_3$) δ 1.40 (s, 9 H, $C(CH_3)_3$), 3.02 (m, 1 H, β-C*H*H), 3.14 (m, 1 H, β-CH*H*), 3.70 (s, 3 H, OCH_3), 4.59 (m, 1 H, α-CH), 5.01 (d, 1 H, *J* = 3.5 Hz, NH), 7.20 (s, 4 H, ArH). Anal. Calcd for $C_{16}H_{20}F_3NO_7S$: C, 44.97; H, 4.72; N, 3.28; F, 13.34; S, 7.50. Found: C, 44.96; H, 4.48; N, 3.42; F, 13.64; S, 7.77.

(*S*)-(*E*)-α-[[(1,1-Dimethylethoxy)carbonyl]amino]-4-[3-(1,1-dimethylethoxy)-3-oxo-1-propenyl]benzenepropanoic Acid Diphenylmethyl Ester (3a). Argon was passed through a solution of 3.0 g (5.2 mmol) of **2a**, 1.5 mL (10.2 mmol) of *tert*-butyl acrylate, and 4.0 mL (30 mmol) of triethylamine in 50 mL of DMF for 15 min, and 120 mg (0.20 mmol) of bis(triphenylphosphine)palladium dichloride was added. The well-stirred suspension was then heated at 90 °C for 24 h, and the mixture was concentrated. The residue was purified by flash chromatography on silica gel, eluting with 8:1 dichloromethane–hexane to give 1.6 g (54%) of **3a**: mp 135–137 °C; $[\alpha]^{25}_D$ −5.35° (*c* = 0.97, EtOH); EI MS *m/z* 484 ($M^+ - C_4H_9$); ^{1}H NMR ($CDCl_3$) δ 1.41 (s, 9 H, $C(CH_3)_3$), 1.54 (s, 9 H, $C(CH_3)_3$), 3.10 (br s, 2 H, β-CH_2), 4.72 (m, 1 H, α-CH), 4.98 (br s, 1 H, NH), 6.39 (d, *J* = 12 Hz, 1 H, =CH), 6.88 (m, 3 H, ArH, $CHAr_2$), 7.28 (m, 12 H, ArH), 7.50 (d, 1 H, *J* = 12 Hz, =CH). Anal. Calcd for $C_{34}H_{39}NO_6$: C, 73.23; H, 7.05; N, 2.51. Found: C, 73.31; H, 6.91; N, 2.48.

(*S*)-α-[[(1,1-Dimethylethoxy)carbonyl]amino]-4-(3-methoxy-3-oxo-1-propenyl)benzenepropanoic Acid Phenylmethyl Ester (3b). A stream of argon was passed through a solution of 1.00 g (1.99 mmol) of **2b**, 1.12 g (3.00 mmol) of methyl (*E*)-3-(tributylstannyl)acrylate, and 0.25 g (6.0 mmol) of LiCl in 10 mL of DMF for 15 min, and 70 mg (0.10 mmol) of bis(triphenylphosphine)palladium dichloride was added. The reaction mixture was immersed in an oil bath, which has been preheated to 95 °C, and was stirred at this temperature for 1.5 h. The resulting dark solution was diluted with 100 mL of ether and was washed with 2 × 20 mL of water, 1 × 20 mL 5% KF in water, and 1 × 20 mL of saturated NaCl and was dried ($MgSO_4$). The residue obtained after concentration was purified by flash chromatography over 100 g of silica gel, eluting with 4:1 hexane–ethyl acetate to afford 0.57 g (65%) of **3b**, as a white solid: mp 81–82 °C; $[\alpha]^{25}_D$ −30.0° (*c* = 0.97, EtOH); EI MS *m/z* (relative intensity) 408 (<1), 366 (<1), 334 (<1), 322 (13), 304 (10), 91 (100), 57 (50); ^{1}H NMR ($CDCl_3$) δ 1.41 (s, 9 H, $C(CH_3)_3$), 3.10 (m, 2 H, β-CH_2), 3.81 (s, 3 H, OCH_3), 4.63 (m, 1 H, α-CH), 5.00 (m, 1 H, NH), 5.09 (d, 1 H, *J* = 12 Hz, ArC*H*HO), 5.18 (d, 1 H, *J* = 12 Hz, ArCH*H*O), 6.39 (d, 1 H, *J* = 16 Hz, =CH), 7.04 (d, 2 H, *J* = 7.6 Hz, ArH), 7.30 (m, 2 H, ArH), 7.36 (m, 5 H, ArH), 7.64 (d, 1 H, *J* = 16 Hz, =CH). Anal. Calcd for $C_{21}H_{31}NO_6$: C, 64.10; H, 7.94; N, 3.56. Found: C, 63.89; H, 7.76; N, 3.47.

(*S*)-α-[[(1,1-Dimethylethoxy)carbonyl]amino]-4-[3-(1,1-dimethylethoxy)-3-oxopropyl]benzenepropanoic Acid (4a). A solution of 1.6 g (2.8 mmol) of **3a** in 20 mL of *tert*-butyl alcohol was hydrogenated over 300 mg of 10% palladium on carbon. Upon the consumption of 2 equiv of hydrogen, the mixture was filtered through a pad of Celite and washed with 50 mL of ethanol, and the combined filtrate was concentrated. The residue was purified by recrystallization from hexanes to give 1.0 g (94%) of **4a**: mp

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88.5–90 °C; $[\alpha]^{25}_D$ +21.2° (c = 0.90, EtOH); EI MS m/z 393 (M^+); ^1H NMR ($CDCl_3$) (major rotamer) δ 1.41 (s, 18 H, 2 $C(CH_3)_3$), 2.51 (t, 2 H, J = 7 Hz, CH_2), 2.87 (t, 2 H, J = 7 Hz, CH_2), 3.13 (m, 2 H, β-CH_2), 4.60 (m, 1 H, α-CH), 4.94 (m, 1 H, NH), 7.12 (s, 4 H, ArH). Anal. Calcd for $C_{21}H_{31}NO_6$: C, 64.10; H, 7.94; N, 3.56. Found: C, 63.89; H, 7.76; N, 3.47.

(*S*)-α-[[(1,1-Dimethylethoxy)carbonyl]amino]-4-(3-methoxy-3-oxopropyl)benzenepropanoic Acid (4b). A solution of 0.57 g (1.30 mmol) of **3b** in 15 mL of ethanol was hydrogenated over 60 mg of 10% palladium on carbon. Upon the consumption of 2 equiv of hydrogen, the mixture was filtered through a pad of Celite and washed with ethanol, and the filtrate was concentrated. The residue was purified by flash chromatography over 50 g of silica gel, eluting with 50:49:1 hexane–ethyl acetate–acetic acid to give 0.41 g (89%) of **4b** as a colorless oil: $[\alpha]^{25}_D$ +15.9° (c = 1.06, EtOH); EI MS m/z 295 ($M^+ - C_4H_9$) (5), 275 (4), 234 (45), 177 (100); ^1H NMR ($CDCl_3$) δ 1.42 (s, 9 H, $C(CH_3)_3$), 2.62 (t, 2 H, J = 7.6 Hz, CH_2), 2.93 (t, 2 H, J = 7.6 Hz, CH_2), 3.08 (m, 1 H, β-C*H*H), 3.15 (m, 1 H, β-CH*H*), 3.67 (s, 3 H, OCH_3), 4.57 (m, 1 H, α-CH), 4.91 (m, 1 H, NH), 7.12 (m, 4 H, ArH). Anal. Calcd for $C_{18}H_{25}NO_6$: C, 61.52; H, 7.17; N, 3.99. Found: C, 61.47; H, 7.23; N, 3.87.

(*S*)-α-[[(1,1-Dimethylethoxy)carbonyl]amino]-4-(2-propenyl)benzenepropanoic acid phenylmethyl ester (5b) was prepared as described below for **5c**. From 2.25 g (4.47 mmol) of **2c** there was obtained 1.61 g (91%) of **5b** which solidified after chromatography: mp 74–76 °C; $[\alpha]^{25}_D$ +37.0° (c = 1.09, EtOH); EI MS m/z (relative intensity) 395 (M^+) (1), 278 (20), 160 (24), 57 (100); ^1H NMR ($CDCl_3$) δ 1.41 (s, 9 H, $C(CH_3)_3$), 3.05 (m, 2 H, β-CH_2), 3.34 (d, 2 H, J = 7 Hz, $ArCH_2CH$=), 4.59 (m, 1 H, α-CH), 4.96 (m, 1 H, NH), 5.06 (m, 2 H, =CH_2), 5.12 (d, 1 H, J = 12 Hz, OC*H*HAr), 5.16 (d, 1 H, J = 12 Hz, OCH*H*Ar), 5.94 (m, 1 H, CH=), 6.97 (d, 2 H, J = 7 Hz, ArH), 7.06 (d, 2 H, J = 7 Hz, ArH), 7.26–7.36 (m, 5 H, ArH). Anal. Calcd for $C_{24}H_{28}NO_4$: C, 64.09; H, 7.99; N, 4.15. Found: C, 63.90; H, 8.15; N, 4.07.

(*S*)-α-[[(1,1-Dimethylethoxy)carbonyl]amino]-4-(2-propenyl)benzenepropanoic Acid Methyl Ester (5c). Argon was passed through a solution of 7.0 g (16.4 mmol) of **2c**, 5.7 g (16.5 mmol) of allyltributyl tin, and 1.42 g (4.0 mmol) of LiCl in 50 mL of DMF for 10 min, and 210 mg (0.30 mmol) of bis(triphenylphosphine)palladium dichloride was added. The bath temperature was raised to 90–95 °C for 40 min, and the mixture was allowed to cool. The mixture was diluted with ether, washed with water and saturated sodium chloride solution, and dried ($MgSO_4$). The residue obtained after filtration and evaporation was purified by preparative HPLC, eluting with 10% ethyl acetate–hexane to give 4.8 g (92%) of **5c**, mp 56–59 °C. Recrystallization of a portion from hexane gave the analytical sample: mp 59–60 °C; $[\alpha]^{25}_D$ +7.43° (c = 0.96, EtOH); ^1H NMR ($CDCl_3$) δ 1.41 (s, 9 H, $C(CH_3)_3$), 3.05 (m, 2 H, β-CH_2), 3.36 (d, 2 H, J = 7 Hz, $ArCH_2CH$=), 3.71 (s, 3 H, OCH_3), 4.57 (m, 1 H, α-CH), 4.95 (m, 1 H, NH), 5.07 (m, 2 H, =CH_2), 5.95 (m, 1 H, CH=), 7.05 (d, 2 H, J = 8 Hz, ArH), 7.12 (d, 2 H, J = 8 Hz, ArH). Anal. Calcd for $C_{18}H_{25}NO_4$: C, 67.69; H, 7.89; N, 4.39. Found: C, 67.56; H, 7.99; N, 4.35.

(*S*)-α-[[(1,1-Dimethylethoxy)carbonyl]amino]-4-(carboxymethyl)benzenepropanoic acid phenylmethyl ester (6b) was prepared according to the method described below for **6c**. From 0.79 g (2.0 mmol) of **5b** there was obtained 0.60 g (73%) of **6b** as a colorless oil: $[\alpha]^{25}_D$ −9.39° (c = 1.16, EtOH); FAB MS m/z 436 (M^+ + Na); ^1H NMR ($CDCl_3$) δ 1.41 (s, 9 H, $C(CH_3)_3$), 3.06 (m, 2 H, β-CH_2), 3.60 (s, 2 H, CH_2), 4.62 (m, 1 H, α-CH), 4.99 (m, 1 H, NH), 5.09 (d, 1 H, J = 8 Hz, OC*H*HAr), 5.17 (d, 1 H, J = 8 Hz, OCH*H*Ar), 7.03 (m, 2 H, ArH), 7.15 (m, 2 H, ArH), 7.29–7.36 (m, 5 H, ArH). Anal. Calcd for $C_{23}H_{27}NO_6$: C, 66.81; H, 6.58; N, 3.39. Found: C, 66.81; H, 6.59; N, 3.09.

(*S*)-4-(Carboxymethyl)-α-[[(1,1-dimethylethoxy)carbonyl]amino]benzenepropanoic Acid Methyl Ester (6c). To a solution of 4.00 g (12.5 mmol) of **5c** in 80 mL of carbon tetrachloride and 80 mL of acetonitrile was added a solution of 8.00 g (37 mmol) of sodium metaperiodate in 200 mL of water. The two-phase mixture was stirred mechanically, and 0.20 g (1.0 mmol) of ruthenium trichloride hydrate was added. The resulting dark mixture was stirred at room temperature for 1 h and was diluted with 500 mL of dichloromethane. The layers were separated, and the organic layer was washed with water and dried ($MgSO_4$). Filtration and evaporation gave 3.84 g of a dark oil, which was dissolved in 120 mL of *tert*-butyl alcohol and 40 mL of 2-methyl-2-butene. A solution of 12.6 g (140 mmol) of sodium chlorite and 12.6 g (90 mmol) of sodium dihydrogen phosphate in 80 mL of water was added, and the resulting mixture was stirred mechanically for 2 h. The mixture was diluted with 500 mL of ether, and the layers were separated. The organic phase was washed with 100-mL portions of water, 10% sodium thiosulfate, and saturated sodium chloride solution and was dried ($MgSO_4$). The residue obtained after filtration and evaporation was chromatographed over 150 g of silica gel, eluting with 40:59:1 ethyl acetate–hexane–acetic acid. The earlier fractions contained 0.63 g of a mixture from which **10** was obtained by crystallization from ether–hexane: mp 101–104 °C; $[\alpha]^{25}_D$ +4.00° (c = 1.0, EtOH); EI MS m/z (relative intensity) 267 (2), 206 (10), 164 (25), 88 (100); ^1H NMR ($CDCl_3$) δ 1.41 (s, 9 H, $C(CH_3)_3$), 3.10 (m, 1 H, β-CH*H*), 3.20 (m, 1 H, β-C*H*H), 3.72 (s, 3 H, OCH_3), 4.64 (m, 1 H, α-CH), 5.03 (m, 1 H, NH), 7.24 (d, 2 H, J = 7.7 Hz, ArH), 8.03 (d, 2 H, J = 7.7 Hz, ArH). Anal. Calcd for $C_{16}H_{21}NO_6$: C, 59.43; H, 6.55; N, 4.33. Found: C, 59.10; H, 6.67; N, 4.41.

The latter fractions were combined, diluted with toluene, evaporated to remove traces of acetic acid, and evacuated under high vacuum for 72 h to give 3.08 g (73%) of **6c** as a colorless oil: $[\alpha]^{25}_D$ +5.25° (c = 0.76, EtOH); EI MS m/z (relative intensity) 281 (<1), 220 (15), 178 (25), 88 (100); ^1H NMR ($CDCl_3$) δ 1.41 (s, 9 H, $C(CH_3)_3$), 3.09 (m, 2 H, β-CH_2), 3.62 (s, 2 H, $ArCH_2$), 3.71 (s, 3 H, OCH_3), 4.58 (m, 1 H, α-CH), 5.00 (m, 1 H, NH), 7.15 (d, 2 H, J = 8 Hz, ArH), 7.22 (d, 2 H, J = 8 Hz, ArH).

The dicyclohexylamine salt was recrystallized from CH_2Cl_2–hexane: mp 141–143 °C; FAB MS m/z 519 (M + H). Anal. Calcd for $C_{29}H_{46}N_2O_6$: C, 67.15; H, 8.94; N, 5.40. Found: C, 66.79; H, 9.16; N, 5.34.

(*S*)-α-[[(1,1-Dimethylethoxy)carbonyl]amino]-4-[2-(methyloxy)-2-oxoethyl]benzenepropanoic Acid Phenylmethyl Ester (7b). A solution of 0.579 g (1.40 mmol) of **6b** and 0.125 mL (2.0 mmol) of iodomethane in 5 mL of DMF was stirred for 3.5 h over 0.207 g (1.50 mmol) of anhydrous potassium carbonate. The reaction mixture was diluted with 50 mL of ether and was washed with 2 × 25 mL of water and 25 mL of brine and was dried ($MgSO_4$). Filtration and concentration afforded 0.585 g (98%) of **7b** as an oil, which was used directly in the next step. A portion was purified for analysis by silica gel chromatography, eluting with 15–30% ethyl acetate–hexane: $[\alpha]^{25}_D$ −9.13° (c = 1.1, EtOH); FAB MS m/z (relative intensity) 450 (90) (M^+ + Na), 4.28 (85) (M^+ + H); EI MS m/z (relative intensity) 310 (10), 292 (15), 192 (77), 91 (100); ^1H NMR ($CDCl_3$) δ 1.41 (s, 9 H, $C(CH_3)_3$), 3.06 (m, 2 H, β-CH_2), 3.58 (s, 2 H, CH_2), 3.69 (s, 3 H, OCH_3), 4.62 (m, 1 H, α-CH), 5.00 (m, 1 H, NH), 5.10 (d, 1 H, J = 6 Hz, OC*H*HAr), 5.17 (d, 1 H, J = 6 Hz, OCH*H*Ar), 6.99 (d, 2 H, J = 8 Hz, ArH), 7.14 (d, 2 H, J = 8 Hz, ArH), 7.30–7.37 (m, 5 H, ArH). Anal. Calcd for $C_{24}H_{29}NO_6$: C, 67.43; H, 6.84; N, 3.28. Found: C, 67.23; H, 6.78; N, 3.16.

(*S*)-α-[[(1,1-Dimethylethoxy)carbonyl]amino]-4-[2-(1,1-dimethylethoxy)-2-oxoethyl]benzenepropanoic Acid Methyl Ester (7c). A solution of 3.50 g (10.4 mmol) of **6c** in 40 mL of dry toluene and 10 mL of dimethylformamide di-*tert*-butyl acetal was heated to a bath temperature of 80 °C for 4 h. After cooling, the mixture was diluted with 100 mL of ether, washed with water and saturated sodium chloride solution, and dried ($MgSO_4$). The residue obtained after filtration and evaporation was chromatographed over 150 g of silica gel, eluting with 20% ethyl acetate–hexane to give 2.66 g (65%) of **7c** as a colorless oil: $[\alpha]^{25}_D$ +6.07° (c = 0.91, EtOH); FAB MS m/z 416 (M^+ + Na), 394 (M^+ + H); EI MS m/z (relative intensity) 393 (M^+) (<1), 322 (<1), 276 (4), 264 (4), 220 (15), 57 (100); ^1H NMR ($CDCl_3$) δ 1.42 (s, 9 H, $C(CH_3)_3$), 1.43 s, 9 H, $C(CH_3)_3$), 3.06 (m, 2 H, β-CH_2), 3.49 (s, 2 H, CH_2), 3.71 (s, 3 H, OCH_3), 4.58 (m, 1 H, α-CH), 4.97 (m, 1 H, NH), 7.07 (d, 2 H, J = 8 Hz, ArH), 7.20 (d, 2 H, J = 8 Hz, ArH). Anal. Calcd for $C_{21}H_{31}NO_6$: C, 64.10; H, 7.94; N, 3.56. Found: C, 63.80; H, 7.80; N, 3.55.

(*S*)-α-[[(1,1-Dimethylethoxy)carbonyl]amino]-4-[2-(methyloxy)-2-oxoethyl]benzenepropanoic Acid (8b). A solution of 0.580 g (1.36 mmol) of **7b** in 13 mL of ethanol was hydrogenated over 66 mg of 10% palladium on carbon for 2 h. The mixture was filtered through a pad of Celite, washed with ethanol, and concentrated to give a light yellow oil. The analytical sample was

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.

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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.

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