MHz) δ 5.083 (d, J = 8.5 Hz, H-1c), 4.858 (dd, J = 11.3, 8.5 Hz, H-2c), 4.475 (d, J = 7.9 Hz, H-1d), 4.179 (d, J = 2.1 Hz, H-4c), 4.040 (dd, J = 5.5, 2.1 Hz, H-4d), 3.914 (dd, J = 7.0, 5.5 Hz, H-3d), 3.200 (dd, J = 7.9, 7.0 Hz, H-2d), 1.231 and 1.129 (s, Me_2C); IR 1780; 1720 cm^{-1}. Anal. Calcd for $C_{54}H_{57}NO_{12}·0.5H_2O$: C, 70.41; H, 6.34; N, 1.52. Found: C, 70.55; H, 6.32; N, 1.47.

O-(2,6-Di-O-benzyl-3,4-O-isopropylidene-β-D-galactopyranosyl)-(1→3)-4,6-di-O-benzyl-2-deoxy-2-phthalimido-D-galactopyranose (39). Dry H_2 was passed through a stirred solution of $[Ir(COD)(PMePh_2)_2]PF_6$ (3 mg, 4 μmol) in THF (5 mL) until the faintly red solution became colorless. The flask was repeatedly evacuated and refilled with nitrogen in order to purge all of dissolved hydrogen. Then a solution of **5** (312 mg, 0.342 mmol) in THF was added. The mixture was stirred at rt for 1 h. Then were successively added water (1 mL), $NaHCO_3$ (0.5 g) and iodine (120 mg, 0.52 mmol). The mixture was stirred at rt for 1 h, and, then it was diluted with EtOAc and was washed with aqueous $Na_2S_2O_3$. The organic layer was processed as usual. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc (1:1)) to afford 223 mg (75%) of **39**: R_f = 0.39 (*n*-hexane/EtOAc (1:1)); ^1H NMR (500 MHz, 20:1 $CDCl_3/D_2O$) δ 5.370 (d, J = 3.5 Hz, H-1cα), 5.234 (dd, J = 11.9, 2.5 Hz, H-3cα), 5.156 (d, J = 8.2 Hz, H-1cβ), 5.072 (dd, J = 11.6, 3.5 Hz, H-2cα), 4.790 (dd, J = 11.3, 2.8 Hz, H-3cα), 4.715 (dd, J = 11.3, 8.2 Hz, H-2cβ), 1.244 and 1.141 (s, $Me_2Cα$), 1.229 and 1.131 (s, $Me_2Cβ$); IR 1675, 1710 cm^{-1}. Anal. Calcd for $C_{51}H_{53}NO_{12}$: C, 70.25; H, 6.13; N, 1.61. Found: C, 69.86; H, 6.18; N, 1.55.

O-(2,6-Di-O-benzyl-3,4-O-isopropylidene-β-D-galactopyranosyl)-(1→3)-4,6-di-O-benzyl-2-deoxy-2-phthalimido-α- and -β-D-galactopyranosyl Fluoride (40). Compound **39** (159 mg, 0.183 mmol) was treated with DAST (100 μL, 0.76 mmol) in toluene in the manner described in the preparation of **4a** to afford 147 mg (92%) of a 2:3 mixture of the α- and β-anomers of **40**. Compounds **40**: R_f = 0.37 and 0.32 (*n*-hexane/EtOAc (2:1)); ^1H NMR (500 MHz) δ 5.736 (dd, J = 53.9 and 8.1 Hz, H-1cβ), 5.678 (dd, J = 54.2, 2.5 Hz, H-1cα), 5.380 (dd, J = 11.7, 2.4 Hz, H-3cα), 5.047 (ddd, J = 30.4, 11.7, 2.5 Hz, H-2cα), 4.925 (td, J = 11.7, 8.1 Hz, H-2cβ), 4.719 (dd, J = 11.7, 2.4 Hz, H-3cβ), 4.247 (d, J = 2.9 Hz, H-4c), 4.095 and 4.046 (dd, J = 5.5, 1.8 Hz, H-4d), 4.054 and 3.933 (dd, J = 9.5, 6.6 Hz, H-3d), 1.258, 1.234, 1.174, and 1.140 (s, Me_2C). Anal. Calcd for $C_{51}H_{52}NO_{11}F$: C, 70.09; H, 6.00; N, 1.60. Found: C, 70.38; H, 6.06; N, 1.54.

Benzyl O-(2,6-Di-O-benzyl-3,4-O-isopropylidene-β-D-galactopyranosyl)-(1→3)-O-(4,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-galactopyranosyl)-(1→4)-O-[methyl (5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosid)onate-(2→3)]-O-(2,6-di-O-benzyl-β-D-galactopyranosyl)-(1→4)-3,6-di-O-benzyl-2-O-pivaloyl-β-D-glucopyranoside (42). To a cold (−20 °C) stirred mixture of $AgOSO_2CF_3$ (22 mg, 86 μmol), Cp_2HfCl_2 (32 mg, 84 μmol), molecular sieve 4A (0.2 g), and toluene (0.5 mL) was added a solution of **40** (56.4 mg, 64.5 μmol), **41** (57.0 mg, 42.2 μmol), and toluene (1.5 mL). The stirred mixture was gradually warmed to rt and was kept there for 3 h. After workup in the manner described in the preparation of **1** (method C), the residue was purified by column chromatography on silica gel (toluene/acetone/Et_3N (79:20:1 then 59:40:1)) to afford 52.1 mg (56%) of **42** and 12.0 mg (13%) of its α-isomer. Compound **42**: R_f = 0.16 (toluene/acetone (3:1)); $[α]_D$ +22.0° (*c* 1.3); ^1H NMR (500 MHz) δ 5.421 (m, H-8g), 5.261 (dd, J = 8.6, 2.8 Hz, H-7g), 5.177 (d, J = 8.2 Hz, H-1c), 5.137 (d, J = 10.4 Hz, N*H*Ac), 4.934 (dd, J = 11.8, 2.8 Hz, H-3c), 4.871 (dd, J = 11.3, 8.2 Hz, H-2c), 4.077 (dd, J = 9.8, 2.5 Hz, H-3b), 4.050 (dd, J = 5.0, 2.0 Hz, H-4d), 3.680 (s, OMe), 3.226 (t, J = 7 Hz, H-2d), 2.884 (dd, J = 12.8, 4.0 Hz, H-3geq), 2.831 (dd, J = 9.8, 7.3 Hz, H-2b), 2.089, 2.014, 1.890, 1.838, and 1.668 (s, 5 Ac), 1.234 and 1.142 (s, Me_2C), 1.189 (s, Me_3C); IR 1745, 1720 cm^{-1}. Anal. Calcd for $C_{123}H_{138}N_2O_{35}$: C, 67.02; H, 6.31; N, 1.27. Found: C, 66.99; H, 6.36; N, 1.24.

α-Isomer of **42**: R_f = 0.24; $[α]_D$ +48.4° (*c* 1.1); ^1H NMR (500 MHz) δ 5.627 (m, H-8g), 5.490 (dd, J = 11.4, 3.0 Hz, H-3c), 5.250 (dd, J = 8.5, 2.5 Hz, H-7g), 5.115 (d, J = 4.0 Hz, H-1c), 5.033 (dd, J = 8.8, 8.1 Hz, H-2a), 4.948 (dd, J = 11.4, 4.0 Hz, H-2c), 3.487 (s, OMe), 3.317 (dd, J = 8.8, 8.1 Hz, H-2b), 3.178 (dd, J = 8.1, 7.0 Hz, H-2d), 2.701 (dd, J = 12.5, 4.5 Hz, H-3geq), 2.072, 1.966, 1.815, 1.676, and 1.617 (s, 5 Ac), 1.230 and 1.096 (s, Me_2C), 1.096 (s, Me_3C). Anal. Found: C, 66.93; H, 6.36; N, 1.17.

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Application of the Ring–Chain-Transfer Concept to the Synthesis of 4-(ω-Aminoalkyl)imidazole Analogues of Histamine[1]

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Reaction of semicyclic 2-aza-3-(methylthio)-3-propeniminium iodides **1** with CH-acidic methylamines **2** gives rise to the formation of 4-(ω-aminoalkyl)imidazole **5** or corresponding hydroiodides. In this ring-transformation reaction the imidazole ring as well as the aminoalkyl substituent are formed within one procedure. The compounds obtained represent novel analogues of histamine.

Naturally occurring histamine (4-(2-aminoethyl)-imidazole) has important functions in biochemical processes. Analogues of histamine such as isohistamine (4-(3-aminopropyl)imidazole) or corresponding derivatives have gained practical interest because of their antihistamine activity in order to treat certain diseases, i.e., ulceral diseases in men. Such compounds are usually synthesized starting from a 1-functionalized ω-aminoalkane with the heterocyclic ring being formed in the final step. We became interested in applying a novel type of ring transformation by ring–chain-transfer[2,3] in order to provide

(1) Part VII on ring–chain-transfer reactions; for part VI see ref 2.

(2) Bohrisch, J.; Pätzel, M.; Mügge, C.; Liebscher, J. *Synthesis* **1991**, 1153.

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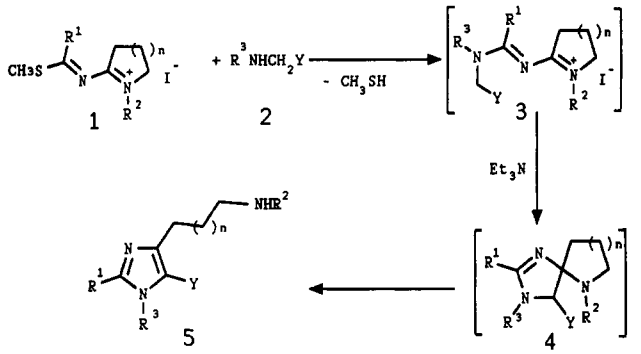
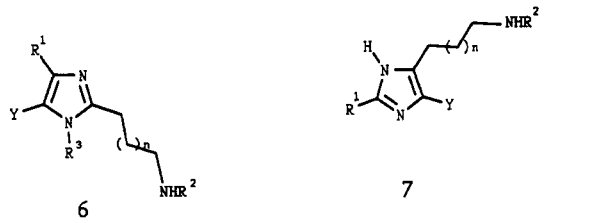
histamine analogues where the alkyl chain can also be longer than propyl and, furthermore, the terminal amino group is substituted by an alkyl substituent.

The general idea of this ring transformation is based on the reaction of semicyclic 2-aza-3-(methylthio)-propeniminium iodides 1[3] as heteroanalogues of imides with 1,2-bifunctional nucleophiles. In this way, for example, 5-(ω-aminoalkyl)-1,2,4-triazoles could be synthesized when hydrazines were used.[3]

We report now on the reaction of semicyclic 2-aza-3-(methylthio)propeniminium salts 1 with methylamines 2, which are substituted by electron-withdrawing alkoxycarbonyl or 4-nitrophenyl groups R^3 and hence are CH-acidic. Reaction was conducted by heating the reactants in ethanol in the presence of triethylamine. Under these conditions 4-(ω-aminoalkyl)imidazoles 5 are formed in satisfactory yields without intermediates being isolated. Usually, the 4-(ω-aminoalkyl)imidazoles separate as salts, e.g., hydroiodides or hydrotosylates. Presumably, primary attack of the amino group of 2 at the isothioamide C-atom of substrate 1 takes place giving condensation products 3 while methyl mercaptan is eliminated. Subsequent cyclization by interaction of the deprotonated methylene group with the amidinium C-atom gives a spiro intermediate 4 which finally opens the saturated N-containing ring.



The novel 4-(ω-aminoalkyl)imidazoles 5 are colorless crystalline solids. Their structure is in accordance with the results of elemental analysis and with their spectral data. Isomeric structures such as 3 or 4 can be ruled out since the typical pattern of the methylene groups of ω-aminoalkyl chains is found in the proton NMR spectra obtained from products 5.[3,4] Furthermore, fragment peaks of m/e = NR^2H, R^2NHCH_2, and $R^2NHCHCH_2$ are found in the mass spectra, which are characteristic for ω-aminoalkyl heteroaromatics.[3,4] Finally, isomeric 2-(ω-aminoalkyl)imidazoles 6 can be ruled out by ^{1}H-NMR where the



proximity of the aryl substituent R^1 and the group R^3 in compound **5a** (R^1 = 4-$CH_3OC_6H_4$, R^2 = CH_3, n = 1) is proved by NOE-difference signals. ^{13}C-NMR data of compound **5b** are also in accordance with the proposed structure. In the ^{13}C-NMR spectra of N-unsubstituted (aminoalkyl)imidazoles 5 (R^3 = H) in DMSO-d_6, however, some peaks are missing under normal measuring conditions. Most of them appear after much longer accumulation or in DMF-d_7 solution especially at higher temperatures. This phenomenon can be interpreted by the existence of an equilibrium of the two annular tautomers 5 (R^3 = H) and 7. Similar behavior of other N-unsubstituted imidazoles is known.[5] Lowering the measuring temperature to −30 °C causes broadening of some signals but no separation to new peaks.

Table I

	n	R^2	R^3	R^1	Y	X
5a	1	Me	H	4-MeOPh	COOEt	I
5b	1	Me	Me	4-MeOPh	COOEt	I
5c	1	Me	H	4-MeOPh	COOBzl	Tos
5d	1	Me	H	thien-2-yl	COOEt	
5e	1	Me	H	4-MeOPh	4-NO_2Ph	I/Cl
5f	2	Et	H	4-ClPh	COOMe	I
5g	3	Me	H	4-ClPh	COOMe	I

The synthesis of imidazoles 5 demonstrates once more the great utility of the principle of ring–chain transformations of bridged 1,3-dicarbonyl heteroanalogues as a general route to ω-aminoalkyl heteroaromatics, where the heterocyclic ring as well as the aminoalkyl chain is formed within one synthetic procedure. In the present case the imidazole ring is built up from a C–N–C-synthon (1) and a C–N-synthon (2). This connection scheme has been used so far only in a few cases[6] by applying *N*-cyanodithiocarboxylates[7] or *N*-cyanoimido esters[8] in the synthesis of imidazoles lacking the aminoalkyl chain.

Experimental Section

Melting points were determined on a Boetius hot-stage apparatus and are uncorrected. The ^{1}H-NMR spectra were measured with a TESLA BS 587 (80 MHz) FT-spectrometer. The ^{13}C-NMR spectra were recorded on a Bruker AC 300. Mass spectra were taken with a Hewlett-Packard 599 SA spectrometer operating at an ionizing voltage of 70 eV.

Starting materials 1 were synthesized according to ref 3.

General Procedure for Synthesis of Imidazoles 5 (Table I). A mixture of 2-aza-3-(methylthio)-3-propeniminium iodide 1[3] (10 mmol), amino acid ester 2 (10.5 mmol), or in the case of **5e** 4-nitrobenzylamine 2 (1.52 g, 10 mmol), and 25 mL of ethanol was briefly refluxed. After the mixture was cooled to room temperature triethylamine (1.0 g, 10 mmol) was added and the mixture was further refluxed for 30 min. Some solvent was evaporated and the residue cooled. The precipitated product was filtered off by suction and recrystallized.

Ethyl 2-(4-methoxyphenyl)-4-[3-(methylamino)propyl]-imidazole-5-carboxylate hydroiodide (5a): yield 57%; mp 224–6 °C (EtOH); ^{1}H-NMR (DMSO-d_6) δ 1.50 (t, J = 7 Hz, 3 H) Me, 2.25 (m, 2 H) CH_2, 2.75 (s, 3 H) NMe, 3.22 (m, 4 H) 2 CH_2, 4.03 (s, 3 H) OMe, 4.50 (q, J = 7 Hz, 2 H) CH_2, 7.19 (d, J = 8 Hz, 2 H) C_6H_4, 8.21 (d, J = 8 Hz, 2 H) C_6H_4; ^{13}C-NMR (DMF-d_7) 14.5, 24.4*, 26.0, 33.4, 49.2, 55.7, 60.4, 114.7, 123.0, 123.9*, 127.9, 144.8*, 147.4, 161.0, 162.4, measured at 23 °C, signals marked with * broaden when measured at about −25 °C and become more sharp on heating to 70 °C; ^{13}C-NMR (DMSO-d_6) δ 14.3, 25.2, 32.5, 47.8, 55.3, 59.6, 114.1, 122.1, 127.2, 159.9, measured at 23 °C, after long accumulation broad signals appear at 23, 146, 162 ppm; MS m/e (relative intensity) 317 (M^+ − HI, 5), 273 (22), 260 (100), 214 (56), 134 (58), 44 (90). Anal. Calcd for $C_{17}H_{24}IN_3O_3$: C, 45.85; H, 5.43; N, 9.43. Found: C, 45.86; H, 5.42; N, 9.47.

Ethyl 2-(4-methoxyphenyl)-1-methyl-4-[3-(methylamino)propyl]imidazole-5-carboxylate hydroiodide (5b): yield 67%; mp 151–2 °C (EtOH); ^{1}H-NMR (400 MHz, DMSO-d_6)

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δ 1.49 (t, J = 7 Hz, 3 H), Me, 2.05 (quin, J = 7 Hz, 2 H) CH_2, 2.68 (s, 3 H) NMe, 2.97 (t, J = 7 Hz, 2 H) CH_2, 3.05 (t, J = 7 Hz, 2 H) CH_2, 3.89 (s, 3 H) N(im)Me (gave a NOE with the signal at 7.70 ppm), 3.91 (s, 3 H) OMe (gave a NOE with the signal at 7.18 ppm), 4.38 (q, J = 7 Hz, 2 H), CH_2, 7.18 (d, J = 9 Hz, 2 H) C_6H_4, 7.70 (d, J = 9 Hz, 2 H) C_6H_4; ^{13}C-NMR (DMSO-d_6) δ 14.1, 24.6, 25.7, 32.4, 34.6, 48.0, 55.3, 60.0, 113.9, 119.4, 121.5, 130.6, 140.6, 150.2, 159.9, 160.2; MS m/e (relative intensity) 331 (M^+ – HI, 2) 287 (16), 274 (67), 215 (56), 202 (100), 134 (14). Anal. Calcd for $C_{18}H_{26}IN_3O_3$: C, 47.06; H, 5.70; N, 9.15. Found: C, 46.86; H, 5.83; N, 8.83.

Benzyl 2-(4-methoxyphenyl)-4-[3-(methylamino)propyl]-imidazole-5-carboxylate tosylate (5c): yield 78%; mp 149–51 °C (EtOH); ^{1}H-NMR (DMSO-d_6) δ 2.11 (m, 2 H) CH_2, 2.38 (s, 3 H) Me, 2.74 (s, 3 H) NMe, 3.11 (m, 4 H) 2 CH_2, 3.98 (s, 3 H) OMe, 5.55 (s, 2 H) CH_2, 7.14–8.02 (m, 13 H) 2 C_6H_4, C_6H_5. Anal. Calcd for $C_{29}H_{33}N_3O_6S$: C, 63.14; H, 6.03; N, 7.62; S, 5.81. Found: C, 62.77; H, 6.25; N, 7.48; S, 5.86.

Ethyl 4-[3-(methylamino)propyl]-2-(thien-2-yl)-imidazole-5-carboxylate (5d): yield 76%; mp 177–8 °C (EtOH); ^{1}H-NMR (300 MHz, DMSO-d_6) δ 1.31 (t, J = 6 Hz, 3 H) CH_3, 1.75 (quint, J = 7 Hz, 2 H) CH_2, 2.30 (s, 3 H) NCH_3, 2.50 (t, J = 7 Hz, 2 H) CH_2, 2.90 (t, J = 7 Hz, 2 H) CH_2, 4.25 (q, J = 6 Hz, 2 H) CH_2, 4.65 (br, 1 H) NH, 7.12 (dd, $J_{4'5'}$ = 6 Hz, $J_{3'4'}$ = 4 Hz, 1 H) 4'-H, 7.55 (dd, $J_{3'4'}$ = 4 Hz, $J_{3'5'}$ = 1 Hz, 1 H) 3'-H, 7.65 (dd, $J_{4'5'}$ = 6 Hz, $J_{3'5'}$ = 1 Hz, 1H) 5'-H; ^{13}C-NMR (DMSO-d_6) δ 14.3, 24.3, 28.6, 35.7, 50.9, 59.3, 124.4, 124.7, 126.6, 127.8, 133.8, 141.8, 144.4, 162.1; MS m/e (relative intensity) 293 (M^+ – HI, 11), 236 (99), 203 (49), 190 (100), 176 (21), 162 (47), 110 (48), 44 (62). Anal. Calcd for $C_{14}H_{19}N_2SO_2$: C, 57.34; H, 6.48; N, 14.34; S, 10.92. Found: C, 57.25; H, 6.65; N, 14.39; S, 10.88.

2-(4-Methoxyphenyl)-5-(4-nitrophenyl)-4-[3-(methylamino)propyl]imidazole hydroiodide/hydrochloride (5e): mp 157–8 °C; ^{1}H-NMR (DMSO-d_6) δ 2.05 (m, 4 H) 2 CH_2, 2.52 (s, 3 H) NMe, 3.05 (m, 2 H), CH_2, 4.02 (s, 3 H) OMe, 4.57 (br, 2 H) 2 NH, 7.14 (d, J = 8 Hz, 2 H) C_6H_4, 8.18 (m, 6 H) C_6H_4.

Methyl 2-(4-chlorophenyl)-4-[4-(ethylamino)butyl]-imidazole-5-carboxylate hydroiodide (5f): yield 61%; mp 217–9 °C (EtOH); ^{1}H-NMR (DMSO-d_6) δ 1.24 (t, J = 7 Hz, 3 H) Me, 1.62 (m, 4 H) 2 CH_2, 2.77 (m, 6 H) 3 CH_2, 3.79 (s, 3 H) OMe, 7.52 (d, J = 9 Hz, 2 H) C_6H_4, 7.91 (d, J = 9 Hz, 2 H) C_6H_4; MS m/e 335 (M^+, 16), 278 (10), 250 (100), 218 (58), 138 (46), 58 (96). Anal. Calcd for $C_{17}H_{23}ClIN_3O_2$: C, 44.03; H, 4.99; N, 9.06. Found: C, 44.15; H, 4.87; N, 9.05.

Methyl 2-(4-chlorophenyl)-4-[5-(methylamino)pentyl]-imidazole-5-carboxylate hydroiodide (5g): yield 63%; mp 158–60 °C (i-PrOH); ^{1}H-NMR (DMSO-d_6) δ 1.82 (m, 6 H) 3 CH_2, 2.75 (s, 3 H) NMe, 3.09 (m, 4 H) 2 CH_2, 4.02 (s, 3 H) OMe, 7.73 (d, J = 8 Hz, 2H) C_6H_4, 8.32 (d, J = 8 Hz, 2 H) C_6H_4; MS m/e 335 (M^+, 2), 233 (28), 139 (25), 114 (14), 44 (100). Anal. Calcd for $C_{17}H_{23}ClIN_3O_2$: C, 44.03; H, 4.99; N, 9.06. Found: C, 43.76; H, 5.04; N, 9.23.

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Registry No. **1a**, 126336-72-9; **1d**, 138434-96-5; **1f**, 134471-61-7; **1g**, 126336-74-1; **2a**, 459-73-4; **2b**, 13200-60-7; **2c**, 1738-68-7; **2e**, 7409-30-5; **2f**, 616-34-2; **5a**, 138434-90-9; **5b**, 138434-91-0; **5c**, 138434-93-2; **5d**, 138434-94-3; **5e**, 138434-95-4; **5f**, 134471-58-2; **5g**, 134471-59-3.

Direct Observation of Tautomeric Forms of Deuteroporphyrin Derivatives by ^{1}H NMR Spectroscopy: Substituent Effects and Structure Implications

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A study of the position of tautomeric equilibrium in deuteroporphyrin IX methyl ester (**3**) and monosubstituted derivatives **4–7** using variable-temperature studies on the N,N-dideuteriated derivatives **8–12** is reported. The kinetic isotope effect on the prototropic exchange process is sufficiently large to allow the convenient observation of the individual tautomers by ^{1}H NMR spectroscopy. As in the case of 2-substituted 5,10,15,20-tetraphenylporphyrins **1**, the position of the tautomeric equilibrium in deuteroporphyrin derivatives is dependent on the substituent pattern on the porphyrin outer periphery. For the isomeric acetylporphyrins, 8-acetyldeuteroporphyrin IX dimethyl ester (**9**) and 3-acetyldeuteroporphyrin IX dimethyl ester (**10**), the acetyl group is the major influence in determining tautomer stability, i.e., both porphyrins are essentially one tautomer (>85% at 298 K) in which the acetyl group is not involved in the aromatic delocalization pathway. The more stable tautomer (59% at 298 K) of 3-(1-hydroxyethyl)deuteroporphyrin IX dimethyl ester (**11**) is that in which the hydroxyethyl substituent is directly substituted on the aromatic pathway. The vinylporphyrin (**12**) exists predominantly (56% at 298 K) as the tautomer in which the vinyl group is substituted on the β–β pyrrolic bond remote from the aromatic delocalization pathway. Conjugation of the vinyl group in **12** and the carbonyl group in the acetylporphyrins **9** and **10** with the β–β pyrrolic double bond probably contributes to the overall stability of the major tautomer of these porphyrins. This work serves to further emphasize that all nonsymmetric free-base porphyrins are necessarily a mixture of two tautomers of different energies which should be taken into account in interpreting the physical and chemical properties of these systems.

The fact that the symmetrically-substituted free-base porphyrin, 5,10,15,20-tetraphenylporphyrin, undergoes prototropic tautomerism between two equivalent forms (**1a** and **1b**, R = H) was shown by the ^{1}H NMR spectroscopy variable temperature studies of Storm and his co-workers.[1] The exchange process was conveniently observed and quantified in the temperature range 220–300 K, and the tautomerism was shown to involve a large kinetic isotope effect consistent with the coupled transfer of the two protons.[1,2]

This tautomeric process is a fundamental property of all free-base porphyrins. Indeed, all nonsymmetric free-base porphyrins are in fact a mixture of two tautomers whose populations depend on the substituents on the porphyrin outer periphery. In recent studies on 2-sub-

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