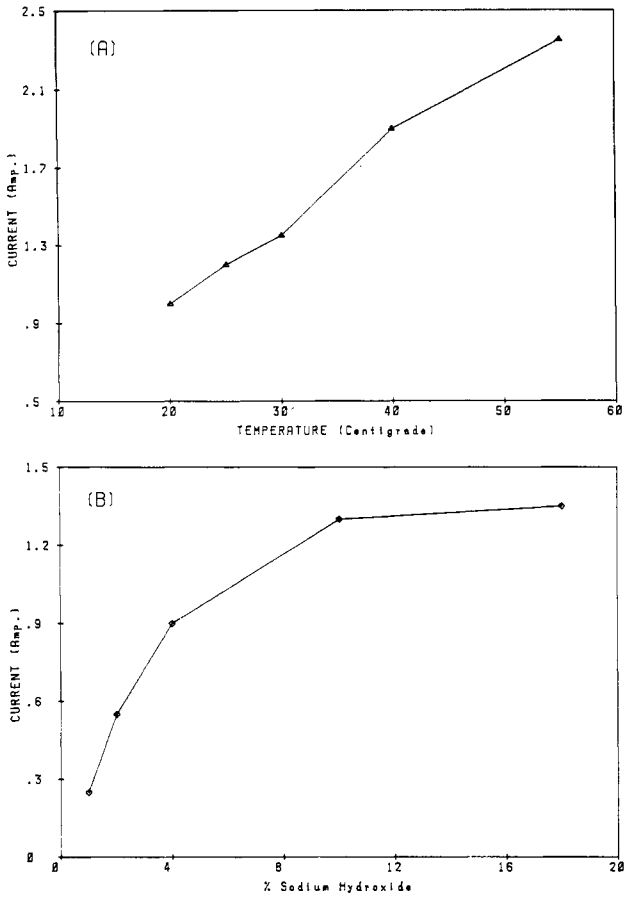

Figure 1. Influence of temperature and hydroxide concentration on rate of oxidation of glycerol. (A) Observed oxidation current as a function of temperature. Stirred solution of 5 g of glycerol/100 mL of 18% aqueous NaOH, electrolyzed at 0.2 V. vs. SCE. (B) Observed oxidation current as a function of hydroxide concentration. Stirred solution of 5 g of glycerol/100 mL solution, electrolyzed at 0.2 V vs. SCE, 30 °C.

in situ formed silver oxide on a silver electrode.

Results and Discussion

The oxidation of glycerol to glyceric acid occurs in aqueous basic medium when a potential of 0.2–0.6 V vs. a saturated calomel reference electrode (SCE) is applied to a silver foil working electrode. A potential of +0.2 V is most suitable for avoiding side reactions such as oxygen evolution or overoxidation of glycerol. Through measurement of the current, the oxidation rate is observed to be dependent on both hydroxide concentration and temperature and in general increases as either of these factors increase. The temperature effect was observed by using thermostated solutions. Interestingly, this effect is roughly linear over the region examined (Figure 1A). We have no plausible explanation for this at this time. We prefer temperatures below 45 °C because some decarboxylation seems to occur above this temperature as evidenced by CO_2 evolution upon acidification of the electrolyzed solution. The effect of hydroxide concentration is dramatic up to a concentration of about 10% above which the rate is not significantly altered (Figure 1B). In neutral or acidic media the desired oxidation does not occur. The oxidation takes place in either divided or undivided cells. The only reactions observed at the potentials used are the oxidation of glycerol at the anode and hydrogen evolution at the cathode. The oxidation is believed to be a typical heterogeneous electrocatalytic reaction involving in situ formed silver oxides at the anode surface. Mechanisms via such surface oxides have been proposed.[5] Although a silver mirror test for aldehyde was positive during the electrolysis, no aldehyde was detected in the isolated products. Other possible side products were negligible, as evidenced from the IR spectrum of the calcium salt and the almost stoichiometric yield of the salt referred to the starting amount of glycerol. As regards the speculated mechanism, it should be noted that when the black oxide surface of the anode was exposed to the solution, with the circuit open, the blackness quickly disappeared, most probably as a result of chemical reaction of the oxide with glycerol. However, this did not happen in the absence of glycerol.

Experimental Section

An undivided three-electrode cell was employed, with a Princeton Applied Research Corp. potentiostat, Model 371 (20 V compliance and current limit of 7 A). Typically, 12 g (0.13 mol) of glycerol was dissolved in 100 mL of water containing 10 g (0.25 mol) of NaOH. The solution was electrolyzed at an anodic potential of 0.2 V vs. SCE at 25–35 °C with constant stirring. A cylindrical silver foil, ~100 cm^2 exposed area, served as anode and a graphite rod, cocentric with the anode, as cathode. The reference electrode, Luggin capillary, was almost touching the inner part of the anode. After the theoretical coulombs had passed (~10 h, initial current ~4 A, final current ~0.08 A) the electrolysis was stopped. The solution was brought to pH 8 with concentrated HCl, and the water was evaporated at 50–80 °C from a petri dish. The white crystals thus obtained were washed with 35 mL of acetone and then with 35 mL of methanol and were dried at ~50 °C. Thus, 25 g of white crystals were obtained, consisting of sodium glycerate and sodium chloride. From this mixture glyceric acid can be recovered upon acidification as a syrupy liquid. However, great care should be exercised during water removal in order to avoid interesterification of the glyceric acid.

The infrared spectrum of the calcium salt of the produced glyceric acid was identical with a standard spectrum (*Aldrich Library of Infrared Spectra*). The identity of the Ca salt was confirmed by melting point [mp 130–135 °C (lit. mp 137–139 °C)]: ^1H NMR (decoupled in D_2O) δ 8.41 (OH, s), 4.62 (CH(OH), 1 H, s), 3.91 (CH_2OH, 2 H, s) [lit. for glyceric acid (polysol), δ 5.41 (OH, s), 4.12 (CH(OH), 1 H, t), 3.72 (CH(OH), 2 H, d)]; ^{13}C NMR (decoupled in D_2O) δ 62.3 (CH_2OH), 171.8 (CH(OH)), 180.4 (CO_2H).

Acknowledgment. We acknowledge the help of Dr. Edwin G. E. Jahngen in obtaining and interpreting the NMR data.

Registry No. NaOH, 1310-73-2; glycerol, 56-81-5; sodium glycerate, 70333-81-2; glyceric acid, 473-81-4.

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Activation and Coupling of Pyrrole-1-carboxylic Acid in the Formation of Pyrrole *N*-Carbonyl Compounds: Pyrrole-1-carboxylic Acid Anhydride

Dale L. Boger*[1] and Mona Patel

Department of Chemistry and Medicinal Chemistry, Purdue University, West Lafayette, Indiana 47907

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The preparation of pyrrole *N*-carbonyl compounds typically are based on the nucleophilic coupling of 1,1′-carbonyldipyrrole[2] or the selective N-acylation of pyrrole

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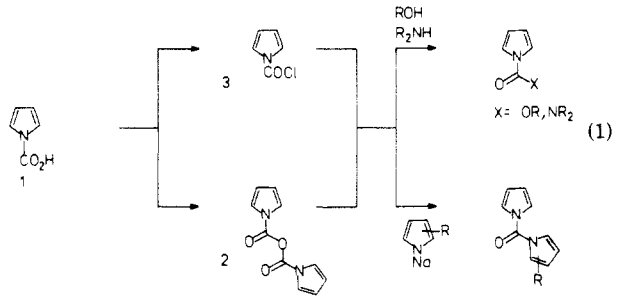
with conventional, readily accessible acylating agents[3] Consequently, in the instances when the nucleophilic displacement reaction with 1,1'-carbonyldipyrrole would be expected to be nonselective or unreactive[4] and for systems for which no activated acylation reagent is available, the pyrrole *N*-carbonyl derivatives currently are inaccessible.

In conjunction with efforts to develop an effective, intramolecular, mixed 2,2'-bipyrrole coupling suitable for use in the total synthesis of the prodigiosenes[5] we required a direct, controlled, and selective method for the preparation of mixed, electron-deficient 1,1'-carbonyldipyrrole compounds. Herein, we describe several methods for the carboxylate activation of pyrrole-1-carboxylic acid (**1**),[6] the preparation of pyrrole-1-carboxylic acid anhydride (**2**), and their use in selective, controlled coupling reactions with representative alcohols, amines, phenols, anilines, and pyrroles leading to the preparation of the corresponding pyrrole *N*-carbonyl compounds (eq 1).



(1)

Representative results derived from the subjection of pyrrole-1-carboxylic acid (**1**)[6] to a range of procedures for carboxylate activation followed by coupling with nucleophiles are detailed in Table I. Standard (oxalyl chloride, catalytic *N,N*-dimethylformamide, tetrahydrofuran, 25 °C)[7] and less convenient approaches to the generation of pyrrole-1-carboxylic acid chloride (**3**) including the use of *N,N*-dimethyl-1-chloro-2-methyl-1-propenylamine,[8,9] phosgene iminium chloride,[10] and triphenylphosphine–carbon tetrachloride[11] occasionally proved successful in providing the pyrrole *N*-carbonyl compounds although the instability of the acid chloride **3** precluded many successful coupling reactions. Of these methods, the use of oxalyl chloride for the generation of pyrrole-1-carboxylic acid chloride (**3**) proved most convenient, while the use of the Ghosez reagent [$Me_2C{=}C(Cl)NMe_2$][8,9] proved most effective. In the alternative carboxylate activation procedures tested, including the use of dicyclohexylcarbodiimide (DCC),[12] 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (EDCI·HCl),[13] *N*-methyl-2-chloropyridinium iodide,[14] diphenyl phosphorazidate [DPPA, $(PhO)_2P(O)N_3$],[15] bis(2-oxo-3-oxazolidinyl)phosphinic chloride (BOP-Cl),[16] and diethyl azodicarboxylate–triphenylphosphine,[17] the intermolecular coupling of **1** with poor nucleophiles proceeds with the competitive or intermediate generation of pyrrole-1-carboxylic acid anhydride (**2**; eq 1).

The preparation [**1**, 0.5 equiv of EDCI·HCl, methylene chloride, 25 °C, 15 min, 87%], isolation–purification, and characterization of pyrrole-1-carboxylic acid anhydride (**2**) followed by its stoichiometric use in coupling reactions proved to be the most effective and dependable procedure for formation of the pyrrole *N*-carbonyl compounds derived from unreactive or nonnucleophilic coupling substrates (cf. Table I). In the instances of the use of nonnucleophilic coupling substrates including phenols (Table I, entries 3–5), alcohols (Table I, entries 9,10), or electron-deficient pyrroles (Table I, entries 1,2), the pyrrole *N*-carbonyl compound formation was observed effectively only with the use of the preformed sodium salts of the coupling substrates. As a consequence of the ease of removal of the water soluble reagent and reaction byproducts, the procedure employing the use of 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (EDCI·HCl) for pyrrole-1-carboxylic acid activation and anhydride formation (**1** → **2**) followed by the in situ coupling with suitable substrates has proven to be the most convenient procedure studied.

The application of the reagent, pyrrole-1-carboxylic acid anhydride (**2**), in the preparation of substrates suitable for mixed, 2,2'-bipyrrole coupling and their implementation in the total synthesis of prodigiosenes is currently in progress.

Experimental Section

Proton nuclear magnetic resonance spectra (^1H NMR) were recorded on a Varian XL-200, and chemical shifts are reported in parts per million relative to internal tetramethylsilane (0.00 ppm). Infrared spectra (IR) were recorded on a Perkin-Elmer 1710 Fourier transform spectrometer and a Perkin-Elmer 1420 spectrometer. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Electron impact mass spectra (EIMS) and chemical ionization mass spectra (CIMS) were recorded on a Finnegan 4000 spectrometer. High-resolution mass spectra (HRMS) were recorded on a Kratos MS-50 spectrometer. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl and *N,N*-dimethylformamide (DMF) was distilled from calcium hydride. Methylene chloride (CH_2Cl_2) was distilled from phosphorus pentoxide. All extraction and chromatographic solvents, ethyl ether (Et_2O), ethyl acetate (EtOAc), and hexane, were distilled prior to use. 1-[3-(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (EDCI·HCl) and dicyclohexylcarbodiimide (DCC) were obtained from Aldrich Chemical Co. All reactions were performed under a positive atmosphere of nitrogen (N_2) or argon.

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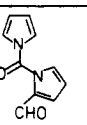
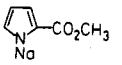
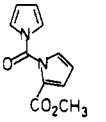
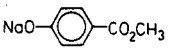
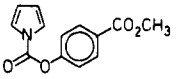
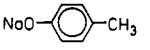
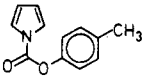
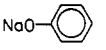
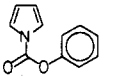
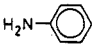
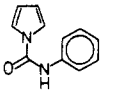
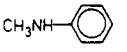
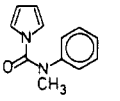
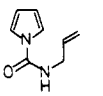
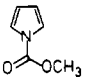
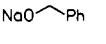
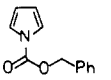
Table I. Activation and Coupling of Pyrrole-1-carboxylic Acid (1) and Pyrrole-1-carboxylic Acid Anhydride (2)

entry	(activation) reagent (equiv)	conditions	coupling substrate	conditions	product[a]	% yield[b]
						
1	2 (1.2)		4a	THF, 25 °C, 15 min	5a	63
						
2	1 (4.0), $(COCl)_2$ (8), DMF (catalytic)	THF, 25 °C, 15 min	4b	THF, 25 °C, 15 min	5b	89
	1 (2.0), DCC[c] (1.95),	CH_2Cl_2, 25 °C, 5 min	4b	THF, 25 °C, 15 min	5b	67
	2 (1.2)		4b	THF, 25 °C, 15 min	5b	69
						
3	1 (2.0), EDCI·HCl[d] (1.95)	CH_2Cl_2, 25 °C, 15 min	4c	THF, 25 °C, 15 min	5c	82
	2 (1.2)		4c	THF, 25 °C, 15 min	5c	88
						
4	1 (2.0), EDCI·HCl[d] (1.95)	CH_2Cl_2, 25 °C, 15 min	4d	THF, 25 °C, 15 min	5d	87
	2 (1.2)		4d	THF, 25 °C, 15 min	5d	99
						
5	1 (2.0), EDCI·HCl[d] (1.95)	CH_2Cl_2, 25 °C, 15 min	4e	THF, 25 °C, 15 min	5e	74
	2 (1.2)		4e	THF, 25 °C, 15 min	5e	79
						
6	1 (2.0), EDCI·HCl[d] (1.95)	CH_2Cl_2, 25 °C, 15 min	4f	THF, 25 °C, 15 min	5f	84
	2 (1.2)		4f	THF, 25 °C, 15 min	5f	93
						
7	1 (2.0), EDCI·HCl[d] (1.95)	CH_2Cl_2, 25 °C, 15 min	4g	CH_2Cl_2, 25 °C, 15 min	5g	82
	2 (1.2)		4g	THF, 25 °C, 15 min	5g	89
						
8	1 (2.0), EDCI·HCl[d] (1.95)	CH_2Cl_2, 25 °C, 15 min	4h	CH_2Cl_2, 25 °C, 15 min	5h	94
	2 (1.2)		4h	THF, 25 °C, 15 min	5h	95
						
9	1 (2.0), EDCI·HCl[d] (1.95)	CH_2Cl_2, 25 °C, 15 min	4i	sodium, methoxide, CH_2Cl_2, 25 °C, 15 min	5i	76
	2 (1.2)		4i	sodium methoxide, THF, −20 °C, 15 min	5i	69
						
10	2 (1.2)		4j	THF, 25 °C, 15 min	5j	59
	2 (1.2)		4j	THF, −20 °C, 30 min	5j	57

[a] All products exhibited the expected or previously reported ^1H NMR, IR, and MS characteristics consistent with the assigned structure. All new compounds gave satisfactory CHN analysis or HRMS information. [b] All yields are based on purified material isolated by chromatography (SiO_2). [c] DCC = Dicyclohexylcarbodiimide. The use of EDCI·HCl leads to the protonation of the coupling substrate with no observable coupling reaction. [d] EDCI·HCl = 1-[3-(Dimethylamino)-propyl]-3-ethylcarbodiimide hydrochloride.

Pyrrole-1-carboxylic Acid (1).[6] A solution of 2.5 M *n*-BuLi in hexane (30.87 mmol, 12.35 mL) was added to a 0 °C solution of pyrrole (2.13 mL, 30.87 mmol) in dry ether (120 mL). The resulting mixture was warmed at reflux for 1 h, cooled, and poured onto a slurry of crushed dry ice (excess) in ether and extracted with water. The aqueous layer was acidified to pH 1 with 5% aqueous hydrochloric acid and extracted with ether (2 × 150 mL). The combined ether extracts were dried over anhydrous sodium sulfate and concentrated in vacuo to afford pyrrole-1-carboxylic acid (**1**, 2.25 g, 3.43 g theoretical, 66%) as a white solid: mp 116–117 °C (hexane) (lit.[6] mp 118 °C); ^{1}H NMR ($CDCl_3$) δ 8.15 (s, 1 H), 7.30 (t, 2 H, J = 2 Hz), 6.30 (t, 2 H, J = 2 Hz); IR (KBr) ν_{max} 3160 (br), 2900, 1710, 1460, 1330, 1310, 1190, 1080, 940, 910, 890, 860, 750 cm^{-1}.

Pyrrole-1-carboxylic Acid Anhydride (2). 1-[3-(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (EDCI·HCl, 189 mg, 0.9 mmol) was added to a 25 °C solution of pyrrole-1-carboxylic acid (**1**, 200 mg, 1.8 mmol) in dry CH_2Cl_2 (6 mL), and the resulting mixture was stirred at 25 °C for 15 min. The reaction mixture was diluted with water (10 mL) and extracted with ether (2 × 50 mL). The combined ether extracts were dried over anhydrous sodium sulfate and concentrated in vacuo. The resulting white solid was *rapidly* passed through a short plug of silica gel (60–200 mesh) under a positive pressure of nitrogen (2 cm × 10 cm, ether eluant) to afford pyrrole-1-carboxylic acid anhydride (**2**, 160 mg, 183 mg theoretical, 87%) as a white solid: mp 87 °C (hexane); ^{1}H NMR ($CDCl_3$) δ 7.31 (t, 2 H, J = 1 Hz), 6.37 (t, 2 H, J = 1 Hz); IR (KBr) ν_{max} 3140, 1810, 1750, 1475, 1395, 1330, 1300, 1160, 1075, 1060, 1020, 935, 875, 860, 730 cm^{-1}; EIMS, m/e (relative intensity) 204 (M^+, 25) 160 (11), 159 (14), 132 (1), 118 (2), 104 (1), 95 (3), 94 (base), 66 (84), 51 (1); CIMS (2-methylpropane), m/e 205 (M^+ + H, base); HRMS, m/e 204.0537 ($C_{10}H_8N_2O_3$ requires 204.0535).

General Procedure for the Preparation of Pyrrole *N*-Carbonyl Compounds Using Oxalyl Chloride and Catalytic Dimethylformamide for Generation of Pyrrole-1-carboxylic Acid Chloride (3): Preparation of 5b. Oxalyl chloride (0.78 mL, 6.2 mmol) was added to a 25 °C solution of **1** (348 mg, 3.1 mmol) in tetrahydrofuran (2 mL) containing catalytic *N*,*N*-dimethylformamide (15 μL), and the reaction mixture was allowed to stir at 25 °C until evolution of gases ceased (ca. 10 min). The reaction mixture was concentrated in vacuo, and the crude acid chloride **3** was taken up in tetrahydrofuran (2 mL). The sodium salt of **4b** [generated in THF (2 mL) at 25 °C from methyl pyrrole-2-carboxylate (200 mg, 1.6 mmol) and NaH (77 mg of 50% dispersion in mineral oil, 1.6 mmol)] was added. The reaction mixture was stirred at 25 °C for 15 min, poured into water, and extracted with ether (3 × 50 mL). The combined ether extracts were dried over anhydrous sodium sulfate and concentrated in vacuo. Chromatography (SiO_2, 3 cm × 20 cm, 25% ether–hexane eluant) afforded **5b** (260 mg, 292 mg theoretical, 89%) as a pale yellow solid: mp 61 °C (hexane); ^{1}H NMR ($CDCl_3$) δ 7.2 (m, 1 H), 7.0 (m, 3 H), 6.3 (m, 3 H), 3.7 (s, 1 H); IR (KBr) ν_{max} 3140, 2940, 1730, 1710, 1540, 1470, 1440, 1400, 1350, 1280, 1240, 1120, 1090, 1070, 1030, 980, 940, 890, 860, 790, 760, 740 cm^{-1}; EIMS, m/e (relative intensity) 218 (M^+, 16), 187 (5), 159 (2), 153 (5), 152 (base), 137 (1), 125 (3), 111 (4), 94 (23), 80 (19), 66 (38); CIMS (2-methylpropane), m/e 219 (M^+ + H); HRMS, m/e 218.0685 ($C_{11}H_{10}N_2O_3$ requires 218.0691).

General Procedure for the Preparation of Pyrrole *N*-Carbonyl Compounds Using EDCI·HCl as the Activating Agent: Preparation of 5d. EDCI·HCl (163 mg, 0.87 mmol) was added to a 25 °C solution of **1** (100 mg, 0.9 mmol) in dry CH_2Cl_2 (3 mL), and the reaction mixture was allowed to stir at 25 °C for 15 min. The sodium salt of cresol [generated in THF (2 mL) at 25 °C from cresol (0.45 mmol, 49 mg) and NaH (0.45 mmol, 21 mg of 50% mineral oil dispersion)] was added, and the resulting mixture was stirred at 25 °C for 15 min. The reaction mixture was treated with 5% aqueous hydrochloric acid and extracted with ether (2 × 25 mL). The combined ether extracts were dried over anhydrous sodium sulfate and concentrated in vacuo. Chromatography (SiO_2, 2 cm × 10 cm ether eluant) afforded **5d** (79 mg, 90 mg theoretical, 87%) as a white solid: mp 74–75 °C (hexane); ^{1}H NMR ($CDCl_3$) δ 7.4 (t, 2 H, J = 2 Hz), 7.25 (d, 2 H, J = 5 Hz), 7.15 (d, 2 H, J = 5 Hz), 6.3 (t, 2 H, J = 2 Hz), 2.37 (s, 3 H); IR (KBr) ν_{max} 3140, 2920, 1750, 1510, 1470, 1400, 1330, 1310, 1210, 1190, 1170, 1140, 1070, 940, 750 cm^{-1}; EIMS, m/e (relative intensity) 201 (M^+, 30), 157 (68), 156 (20), 129 (7), 115 (7), 94 (base), 91 (31), 77 (17), 67 (12), 66 (64), 51 (9); CIMS (2-methylpropane), m/e 202 (M^+ + H, base); HRMS, m/e 201.0795 ($C_{12}H_{11}NO_2$ requires 201.0790).

General Procedure for the Preparation of Pyrrole *N*-Carbonyl Compounds Using Pyrrole-1-carboxylic Acid Anhydride (2): Preparation of 5h. Allylamine (0.03 mL, 0.46 mmol) was added to a 25 °C solution of pyrrole-1-carboxylic acid anhydride (**2**, 0.56 mmol, 114 mg) in THF (2 mL), and the resulting reaction mixture was allowed to stir for 15 min. The reaction mixture was poured onto 5% aqueous sodium bicarbonate and extracted with ether (2 × 25 mL). The combined ether extracts were dried over anhydrous sodium sulfate and concentrated in vacuo. Chromatography (SiO_2, 2 cm × 15 cm, ether eluant) afforded **5h** (66 mg, 69 mg theoretical, 95%) as a pale yellow solid: mp 64–65 °C (hexane); ^{1}H NMR ($CDCl_3$) δ 7.2 (t, 2 H, J = 2 Hz), 6.2 (t, 2 H, J = 2 Hz), 5.91 (ddtd, 1 H, J = 17, 11, 6, 1 Hz), 5.28 (d, 1 H, J = 17 Hz), 5.19 (d, 1 H, J = 11 Hz), 4.02 (dt, 2 H, J = 6, 1 Hz); IR (film) ν_{max} 3150, 2960, 1700, 1540, 1470, 1440, 1400, 1340, 1310, 1200, 1170, 1070, 1030, 980, 925, 800, 770, 740 cm^{-1}; EIMS, m/e (relative intensity) 150 (M^+, 12), 135 (1), 108 (1), 106 (1), 80 (1), 79 (1), 68 (1), 67 (base), 56 (1), 54 (2); CIMS (2-methylpropane), m/e 151 (M^+ + H, base); HRMS, m/e 150.0792 ($C_8H_{10}N_2O$ requires 150.0793).

5a: ^{1}H NMR ($CDCl_3$) δ 9.7 (s, 1 H), 7.35 (t, 1 H, J = 2 Hz), 7.23 (t, 1 H, J = 2 Hz), 7.15 (t, 2 H, J = 2 Hz), 6.45 (t, 1 H, J = 2 Hz), 6.35 (t, 2 H, J = 2 Hz); IR (KBr) ν_{max} 3146, 3136, 3097, 2925, 2850, 2362, 1745, 1728, 1664, 1550, 1473, 1437, 1407, 1351, 1268, 1231, 1162, 1101, 1082, 1026, 962, 898, 787 cm^{-1}; EIMS, m/e (relative intensity) 188 (M^+, 50), 171 (14), 159 (2), 131 (3), 122 (29), 104 (3), 99 (66), 67 (21), 66 (66), 51 (11), 39 (base); CIMS (2-methylpropane), m/e 189 (M^+ + H, base); HRMS, m/e 188.0577 ($C_{10}H_8N_2O_2$ requires 188.0586).

5c: mp 132–133 °C (hexane–EtOAc); ^{1}H NMR ($CDCl_3$) δ 8.15 (d, 2 H, J = 9 Hz), 7.4 (t, 2 H, J = 2 Hz), 7.35 (d, 2 H, J = 9 Hz), 6.35 (t, 2 H, J = 2 Hz), 3.9 (s, 3 H); IR (KBr) ν_{max} 3140, 2950, 2920, 1750, 1715, 1600, 1460, 1435, 1400, 1350, 1320, 1265, 1210, 1155, 1150, 1110, 1080, 1020, 1010, 945, 880, 755, 740, 690 cm^{-1}; EIMS, m/e (relative intensity) 245 (M^+, 17), 201 (27), 142 (3), 135 (2), 120 (3), 107 (3), 103 (3), 94 (base), 92 (6), 77 (2), 67 (14), 66 (58); CIMS (2-methylpropane), m/e 246 (M^+ + H, base); HRMS, m/e 245.0698 ($C_{13}H_{11}NO_4$ requires 245.0688).

5e: mp 45–46 °C (hexane); ^{1}H NMR ($CDCl_3$) δ 7.4 (t, 2 H, J = 2 Hz), 7.55–7.15 (m, 5 H), 6.35 (t, 2 H, J = 2 Hz); IR (KBr) ν_{max} 3139, 1752, 1543, 1406, 1319, 1263, 1220, 1165, 1081, 1003, 948, 869, 760, 738 cm^{-1}; EIMS, m/e (relative intensity) 187 (M^+, 45), 143 (60), 116 (10), 115 (32), 94 (base), 75 (52), 67 (15), 66 (61), 65 (15), 51 (22); CIMS (2-methylpropane), m/e 188 (M^+ + H, base); HRMS, m/e 187.0632 ($C_{11}H_9NO_2$ requires 187.0633).

5f: mp 151–152 °C (hexane–EtOAc); ^{1}H NMR ($CDCl_3$) δ 7.6–7.0 (m, 5 H), 7.3 (t, 2 H, J = 2 Hz), 6.35 (t, 2 H, J = 2 Hz); IR (KBr) ν_{max} 3337, 3139, 3108, 2924, 1690, 1602, 1543, 1463, 1337, 1288, 1246, 1177, 1092, 1076, 954, 907, 875, 842, 812, 747, 713, 691, 623 cm^{-1}; EIMS, m/e (relative intensity) 186 (M^+, 14), 97 (1), 94 (7), 83 (1), 77 (9), 67 (base); CIMS (2-methylpropane) m/e 187 (M^+ + H, base); HRMS, m/e 186.0794 ($C_{11}H_{10}N_2O$ requires 186.0793).

5g: ^{1}H NMR ($CDCl_3$) δ 7.4–7.2 (m, 3 H), 7.1 (dd, 2 H, J = 6, 1 Hz), 6.8 (t, 2 H, J = 2 Hz), 6.0 (t, 2 H, J = 2 Hz), 3.46 (s, 3 H); IR (film) ν_{max} 3140, 3100, 3060, 2940, 1660, 1600, 1490, 1460, 1420, 1395, 1360, 1300, 1120, 1090, 1070, 1045, 1025, 1010, 930, 845, 750, 730, 695 cm^{-1}; EIMS, m/e (relative intensity) 200 3.46 38), 134 (37), 106 (45), 91 (4), 79 (4), 78 (4), 77 (54), 66 (26), 64 (5), 63 (5), 39 (base); CIMS (2-methylpropane), m/e 201 (M^+ + H, base); HRMS, m/e 200.0953 ($C_{12}H_{12}N_2O$ requires 200.0950).

5i: ^{1}H NMR ($CDCl_3$) δ 7.26 (t, 2 H, J = 2 Hz), 6.24 (t, 2 H, J = 2 Hz), 3.96 (s, 3 H); IR (film) ν_{max} 3140, 2960, 1750, 1540, 1480, 1440, 1340, 1310, 1200, 1170, 1070, 1030, 980, 920, 800, 770, 740 cm^{-1}; EIMS, m/e (relative intensity) 125 (M^+, base), 94 (7), 80 (78), 66 (24); CIMS (2-methylpropane), m/e 125 (M^+ + H, base); HRMS, m/e 125.0481 ($C_6H_7NO_2$ requires 125.0477).

5j: ^{1}H NMR ($CDCl_3$) δ 7.35 (m, 5 H), 7.2 (t, 2 H, J = 2 Hz), 6.16 (t, 2 H, J = 2 Hz), 5.3 (s, 2 H); IR (film) ν_{max} 3140, 3120, 2920, 2840, 1740, 1580, 1470, 1400, 1375, 1330, 1300, 1210, 1160, 1020, 960, 775, 735, 690 cm^{-1}; EIMS, m/e (relative intensity) 201 (M^+, 1), 157 (9), 92 (5), 91 (base), 77 (2), 66 (11), 55 (1); CIMS (2-

methylpropane), m/e 202 ($M^+ + H$); HRMS, m/e 201.0781 ($C_{12}H_{11}NO_2$ requires 201.0790).

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Reexamination of the Notion of π-Electron Delocalization Energy as a Theoretical Index to the Empirical Resonance Energy

Masahiro Kataoka* and Takeshi Nakajima[1]

Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980, Japan

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As early as in 1959, using the modified Hückel MO (HMO) method in which the effect of the σ-bond compression is taken into account, Longuet-Higgins and Salem[2] pointed out that in [4n + 2] annulenes the total bond energy of π electrons decreases along the bond-alternation mode. However, this important result has, until recently, escaped the attention it deserves. Recently, Epiotis[3] reaffirmed the above result, and Shaik and Hiberty[4] raised the question whether it is really the π system that drives benzene to be a symmetric hexagonal species. Very recently, Hiberty et al.[5] presented computational evidence that the symmetrical hexagonal structure of benzene is driven by the σ framework alone, the π system being found to favor a distorted and localized structure (see also ref 6 and 7). In these circumstances, the traditional view that the π-electron delocalization energy (DE) is useful as a theoretical index to the empirical resonance energy (RE) turns out to be erroneous and meaningless. Note that DE is the quantity defined in the framework of the constant-β HMO approximation, and it favors energetically the symmetric hexagonal benzene and a delocalized symmetric species in general. Nevertheless, it is well-known that in alternant hydrocarbons, the π-electron DE value has an excellent correlation with the empirical RE.[8] The aim of this paper is to understand the physical basis behind the above apparent correlation and to rationalize the π-electron DE value as an index to be used in predicting the stabilities and geometries of conjugated hydrocarbons.

The RE of a conjugated hydrocarbon is defined as

$$\mathrm{RE} = E_{\mathrm{tot}}(\mathrm{M}) - E_{\mathrm{tot}}(\mathrm{K}) \tag{1}$$

where $E_{\mathrm{tot}}(\mathrm{M})$ and $E_{\mathrm{tot}}(\mathrm{K})$ are the total energies of a delocalized symmetric structure and a Kekulé-type one in which isolated double bonds are linked by single bonds, respectively. According to Longuet-Higgins and Salem,[2] the total bond energy associated with a CC bond taken to be the sum of the σ-bond energy (f) and the π-electron energy is given by

$$E_{ij} = f_{ij} + 2P_{ij}\beta_{ij} = -(2/b)(\mathrm{d}P_{ij}/\mathrm{d}r_{ij})\beta_{ij} + \mathrm{const} \tag{2}$$

where P_{ij} is the π-bond order of the i–j bond and the resonance integral, $\beta_{ij}(r_{ij})$, has been assumed to be an exponential function of the form

$$\beta_{ij}(r_{ij}) = \beta_{\mathrm{b}} \exp[b(r_{\mathrm{b}} - r_{ij})] \tag{3}$$

where β_{b} and r_{b} are the values in benzene. Now, the equilibrium bond length, r_{ij}, is assumed to be related to P_{ij} by

$$r_{ij}/\text{Å} = r_0 - aP_{ij} \tag{4}$$

Differentiating this equation with respect to r_{ij} and substituting for $(\mathrm{d}P_{ij}/\mathrm{d}r_{ij})$ in eq 2, we obtain

$$E_{ij} = (2/ab)\beta_{ij} + \mathrm{const}$$

Summing E_{ij} over all the CC bonds, we obtain the total energy of an alternant hydrocarbon as

$$E_{\mathrm{tot}} = \frac{2}{ab}\sum_{i<j}^{\text{all bonds}} \beta_{ij} + N\alpha + E_{\mathrm{core}}{}^{\sigma} + \mathrm{const} \tag{5}$$

where α is the Coulomb integral of the C atom, N the number of π electrons, and $E_{\mathrm{core}}{}^{\sigma}$ the σ core energy. Further, substituting for r_{ij} in eq 3 from eq 4, we obtain

$$\beta_{ij} = B \exp(abP_{ij}) \tag{6}$$

where

$$B = \beta_{\mathrm{b}} \exp[b(r_{\mathrm{b}} - r_0)] \tag{7}$$

It should be noted that in order for benzene to keep D_{6h} symmetry, the condition $ab < 1$ must be fulfilled.[9]

Since $abP_{ij} < 1$ ($abP_{ij} \simeq 0.5$ in benzene), we now expand $\exp(abp_{ij})$ in power series of abP_{ij} and neglect the terms higher than the first power, thus obtaining

$$\beta_{ij} = B(1 + abP_{ij}) \tag{8}$$

Substituting eq 8 into eq 5, we then have

$$E_{\mathrm{tot}} = \sum_{i<j}^{\text{all bonds}} \left(2P_{ij}B + \frac{2}{ab}B\right) + N\alpha + E_{\mathrm{core}}{}^{\sigma} + \mathrm{const} \tag{9}$$

Using eq 9, we can write the total energy of a Kekulé-type structure with $P = 1$ for double bonds and $P = 0$ for single bonds as

$$E_{\mathrm{tot}}(\mathrm{K}) = 2nB + \sum_{i<j}^{\text{all bonds}} \frac{2}{ab}B + N\alpha + E_{\mathrm{core}}{}^{\sigma} + \mathrm{const} \tag{10}$$

where n is the number of double bonds. The RE can thus be written in the following form:

$$\mathrm{RE} = E_{\mathrm{tot}}(\mathrm{M}) - E_{\mathrm{tot}}(\mathrm{K}) = \left[\sum_{i<j}^{\text{all bonds}} 2P_{ij} - 2n\right]B \tag{11}$$

The last expression of eq 11, if B is replaced by β_{b}, is nothing but the expression of the DE defined in the constant-β HMO approximation. It is thus revealed that there does exist a proportionality between the RE and DE values. It should be remarked that the value of β that

(1) Present address: Tohoku Dental University, Koriyama 963, Japan.
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