δ 3.9–2.85 (m, 25 H), 1.95 (s, 3 H), 1.25 (br s, 16 H). Anal. Calcd for $C_{23}H_{45}O_7N$: C, 61.7; H, 10.1; N, 3.1. Found: C, 61.3, H, 9.9; N, 3.0.

2-[9-(Ethylamino)-*n*-nonyl]-1,4,7,10,13,16-hexaoxacyclooctadecane (10). Reduction of 4.5 g (0.01 mol) of **9** with 2.0 g (0.06 mol) of lithium aluminium hydride was performed under the conditions described for **7**. The crude product was purified by extraction from a methylene chloride solution with 2 N aqueous hydrochloric acid and subsequent reprecipitation with tetraethylammonium hydroxide. Final extraction with methylene chloride afforded 3.4 g (78%) of **10**: colorless oil; $n^{20}{}_D$ 1.4750; ^1H NMR ($CDCl_3$) δ 3.93–3.3 (m, 21 H), 2.83 (s, 1 H), 2.70 (q, 2 H), 2.62 (t, 2 H), 1.20 (br s, 13 H), 1.13 (t, 3 H). Anal. Calcd for $C_{23}H_{47}O_6N$: C, 63.7; H, 10.9; N, 3.2. Found: C, 63.8; H, 11.0; N, 3.3.

Polymer-Supported Cryptands (6a,b) and Crown Ethers (14a–c, 15, 16). Chloromethylated polystyrenes 11, 1, 2, and 4.5% cross-linked with *p*-divinylbenzene, were commercially available. Resins **12** and **13** were prepared as previously described.[1] Functionalized cryptand **5** and crown ether **10** were linked to resins **11**–**13** by heating the amount of the resin corresponding to 1 mol equiv of covalent halogen with 1.2 mol equiv of **5** or **10** in the presence of dimethylformamide (DMF) (4 mL for 1 g of resin) and 2.0 mol equiv of sodium hydrogen carbonate for 7 days at 65 °C. Initially the mixture was carefully deaerated under vacuum. At the end of reaction the resins were successively washed with water, ethyl alcohol, ethyl ether, methylene chloride, ethyl ether, methylene chloride, and ethyl ether and then dried at 60 °C for 3 h.

Titration of Polyethers on the Resins. Method A. A 0.01 N solution of picric acid in 0.1 N aqueous sodium hydroxide was added dropwise to a stirred suspension of a weighed amount (0.3–0.5 g) of resin in 10 mL of water and 10 mL of methylene chloride. Picrate anion was absorbed by the methylene chloride swelled resin, decoloring the aqueous phase. The end point (persistent yellow color of the aqueous phase) was sharp with cryptands but was broad with crown ethers due to the lower binding constant of the latter (Table I); indeed, when titration was tested on the corresponding soluble ligands **20** and **21**, it gave 99.5 and 65% of the expected values, respectively.

Method B. A molar excess of a 1.0×10^{-3} M solution of potassium picrate in a 0.1 N aqueous solution of sodium hydroxide (10 mL, 1.5–3.0 mol equiv with respect to the polymer-bound polyether) was stirred at room temperature for 15 h with a weighed amount (1–5 mg) of resin suspended in 10 mL of water and 10 mL of methylene chloride. A given portion (4.0 mL) of the aqueous phase was diluted with 50 mL of 0.1 N sodium hydroxide and spectrophotometrically analyzed at 360 nm. The amount of polyether was established by the equation polyether (mequiv/g of resin) = $0.01 \times [(A_o - A)/A_o] \times 1/g$, where A_o and A are the observed absorbances without and with the resin, respectively, and g is the weighed amount of resin in grams. Method B was satisfactory for both polymer-supported cryptands and crown ethers, and results agreed with those expected on the basis of the weight increases upon functionalization of the resins (Table I).

Method C. A weighed amount of resin (0.2–0.5 g) was stirred at room temperature for 15 h with a chloroform suspension of excess solid potassium iodide. Swelling of resin occurred and potassium iodide was complexed by the polyether. After this time carbon tetrachloride was added to ensure better separation of the two solid phases and the supernatant resin was collected and washed with methylene chloride and ethyl ether. After being dried at 60 °C for 3 h, a weighed amount of resin was suspended in aqueous methanol and iodide ion was titrated[15] with silver nitrate. This method gave less accurate values compared with methods A and B (Table I).

Kinetic Measurements. Kinetics were run in a 4-mL flask, maintained at the appropriate temperature within ±0.1 °C, with magnetic stirring, following already described procedures.[1] Resins were first conditioned for 3–15 h at the reaction temperature in the presence of all reagents except one; the last reagent was added at zero time. The stirring speed, 1300 ± 50 rpm, was controlled by using a strobe light. The amounts of reagents for each kind of reaction studied are indicated in Tables II and III. The reactions were followed by GLC analysis (5% SE-30 on Chromosorb) and results were corrected by calibration with standard mixtures. The pseudo-first-order rate constants (k_{obsd}) were obtained by plotting ln [substrate] vs. time and determining the slope of the straight lines by the least-squares method.

Registry No. **1**, 76665-94-6; **1** bisformate, 76684-18-9; **2a**, 61013-92-1; **2b**, 76665-95-7; **3**, 61013-91-0; **4**, 76665-96-8; **5**, 76684-20-3; **7**, 61013-93-2; **8a**, 76665-97-9; **8b**, 76665-98-0; **9**, 76665-99-1; **10**, 61013-89-6; **20**–$NaBF_4$ complex, 56725-51-0; **21**, 74339-04-1; 10-undecenenitrile, 53179-04-7; 1,10-diaza-18-crown-6, 23978-55-4; triethylene glycol ditosylate, 19249-03-7; chloroacetic acid, 79-11-8.

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Analysis of Carbon-13 Nuclear Magnetic Resonance Shifts in Terms of Substituent Parameters: Statistical Comparison of Dual and Single Substituent Parameter Treatments

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A systematic comparison is made, by using six different scales of substituent parameters, of the α-, β-, and γ-carbon-13 chemical shifts for the olefinic moiety in four series of styrene derivatives. There is no systematic significant superiority, in general, of a dual substituent parameter (DSP) treatment with respect to the simpler single substituent parameter (MSP) treatment. In the case of the γ-carbons, with the former type of analysis, the inductive effect is found to be more sensitive than the resonance effect to configurational differences.

Many studies deal with linear free energy relationships (LFER),[1] applied to NMR chemical shifts, especially to ^{13}C values, with a view either to gain some insight into the determining factors of the chemical shift, or, and perhaps more profitably, to use the chemical shift as a semiempirical measure of substituent effects. We single out, from this vast corpus, those investigations which have focussed upon the olefinic carbons (C_α and C_β) in the styrene series **1**.[2-9] Correlations have been reported for

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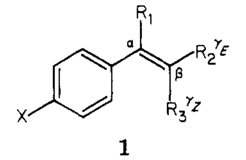
[1] J. Shorter, "Correlation Analysis in Organic Chemistry", Clarendon Press, Oxford, 1973.

0022-3263/81/1946-2130$01.25/0 © 1981 American Chemical Society



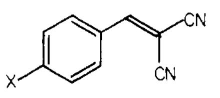
1

C_α[6] or for the allylic γ carbons,[5] but, by and large, the bulk of the reported LFER apply to C_β.[2-9] Conversely, several groups have determined new σ^+ values from the β-carbon chemical shifts.[3,4,8]

Recently, this last practice has come under criticism:[10] rather than relying upon the use of a single parameter, such as σ^+, a more correct procedure appears to be a dual substituent parameter treatment (DSP), applied to a σ_R^+ basis; observation of a successful monoparametric correlation (MSP) would result from the accidental equality of the ρ_I and ρ_R coefficients in the full DSP regression.

Intuitively, a DSP approach should be more successful than the simpler MSP approach in correlating the data. Is it really the case?

We have set about to answer this question in as objective a way as possible by examining the quality of adjustment (GOF) in both approaches. For this purpose, we shall examine the ^{13}C chemical shifts in various positions for the substituted styrenes **2**–**5**.



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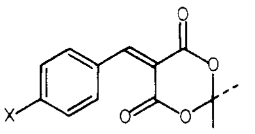
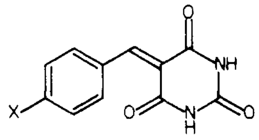


3



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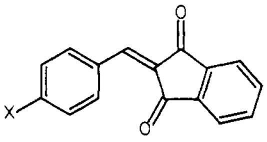

5

Procedure

Heeding the recommendation that "these are counsels of perfection, and cannot always be adhered to strictly, but the limitation of supposed correlations should always be clearly stated",[1] we shall first delineate the constraints of this study. We have restricted it to the para derivatives **2**–**5**, further excluding from consideration those substituents X which could serve as hydrogen-bond donors, might become ionized, or for which a complete set of σ, σ^+, σ_I, σ_R^{BA}, σ_R^0, σ_R^+, σ_R^- parameters is unavailable. The literature is replete with σ scales presenting corrected, adjusted, or recalculated values.[11-13] In order for our results to be more easily comparable to others, we have opted in favor of the most widespread parameter basis, viz., for DSP parameters the original basis proposed by Ehrenson, Brownlee, and Taft[14] and for the MSP parameters a basis from the compilation by Gordon and Ford.[15] In addition, our data base for a given series will refer only to a *homogeneous* set of experimental values, determined under the same conditions of concentration, solvent, and temperature.

The linear and multilinear regressions were performed with statistical subroutines on an IBM 370-158 computer. In the absence of a standard and agreed-upon index of the quality of adjustment,[1,14,16] we hold as essential the reliance upon the simplest statistical criteria. Hence, we shall use two estimate factors. (a) The first is a tendency estimator, the linear regression coefficient r in the MSP treatment *or* the multiple regression coefficient R in the DSP treatment. For this estimator, the hypothesis of the existence of a nonaccidental correlation[1] has been tested at the 99% confidence level by comparison with tables of Student t values[17] or Snedecor F values.[18] (b) The second is an estimate of the dispersion, f, in the interbasis comparison within a given series of molecules. We use there the Ehrenson formulation,[16] with a modification. The equation below is taken from this article:[16]

$$\text{“}f = \frac{(\sum_i \delta_i^2/n)^{1/2}}{(\sum_i P_{i,\mathrm{obsd}}^2/n)^{1/2}}$$

P_i is log k_i, log k_i/k_0, or otherwise, dependent upon the LFER form used, and δ_i is the observed to calculated P_i value difference. The numerator ... should be quickly recognized as the root-mean-square (rms) deviation of the fitted set and the denominator as the rms of observed values." If this definition is applied without modification to NMR chemical shifts, the f values become dependent upon the choice of an origin for the chemical shift scale and upon the location of the range of measurement with respect to a predetermined zero. In order to bypass this difficulty, we normalize measurement of the P_i values by referring them to the *unsubstituted* molecular system: the substituent chemical shift (SCS)[10] is defined as $P_i = \delta_X - \delta_H$, using an obvious notation. In using the f statistic, we consider as significant a difference between two parameter bases when it corresponds in the $\mathcal{R}$ tables[16] to a confidence level of 99% or higher.

Experimental Section

The NMR data on compounds **2** have been obtained in the same manner as previously reported.[4] The measurements on the Meldrum acid derivatives **3** have been performed in like manner by using as a reference the Me_2SO-d_6 signal (δ 39.6). These para-substituted derivatives **3** have been prepared by a reliable method[19] and have been identified by their melting points and from their ^{13}C spectrum. Molecules **3** with p-CH_3 (mp 127–128 °C. Anal. Calcd: C, 68.28; H, 5.73. Found: C, 68.87; H, 5.84), with p-F (mp 137–140 °C. Anal. Calcd: C, 62.40; H, 4.43. Found: C, 62.57; H, 4.37), with p-Br (mp 170–172 °C. Anal. Calcd: C, 50.19; H, 3.56. Found: C, 50.12; H, 3.55), and with p-CN (mp

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Table I. Chemical Shifts[a] of the α-, β-, γ_E-, and γ_Z-Carbons in Probe Molecules 2-5

substituent	2[b] (solvent $CDCl_3$)				3[c] (solvent Me_2SO-d_6)				4[d] (solvent Me_2SO-d_6)				5[d] (solvent $CDCl_3$)			
	α	β	γ_E	γ_Z	α	β	γ_E	γ_Z	α	β	γ_E	γ_Z	α	β	γ_E	γ_Z
F	158.44	82.47	113.64	112.54	155.3	114.0	162.2	158.9	153.6	118.6	163.3	161.7	145.4	128.7	190.1	189.1
H	159.85	82.67	113.65	112.54	156.5	115.6	162.2	159.1	154.8	119.0	163.3	161.5	146.7	129.1	190.0	188.8
NO_2	157.55	87.47	*e*	*e*					151.1	122.3	162.5	161.1				
CN	156.50	87.24	113.00	112.11	154.1	118.4	*e*	*e*	151.7	121.8	162.6	161.1	143.3	131.9	189.2	188.5
Cl	158.07	83.55	113.38	112.28					153.1	119.6	163.1	161.5	145.0	129.5	189.8	188.9
OCH_3	158.91	78.45	114.71	113.41	156.6	111.4	164.0	163.1	154.9	115.5	163.8	162.1	146.7	126.5	190.7	189.4
$N(CH_3)_2$	158.04	72.21	115.54	114.94	156.6	103.1	164.2	160.9	154.1	109.6	164.6	162.6	147.4	123.0	191.6	189.9
CH_3					156.4	114.1	162.3	159.2	155.1	117.7	163.5	161.7	147.1	128.3	190.5	189.1
Br					155.1	116.2	161.8	158.9	153.1	119.7	163.1	161.4	145.7	129.7	189.8	188.9

[a] In parts per million downfield from Me_4Si. [b] Published in part in ref 4. [c] This work. [d] Data from ref 5. [e] In view of their poor sensitivity, these signals are confused with the instrumental noise (see ref 3).

Table II. Correlations Retained for Probe Molecules 2-5 on the Basis of Both *r* (or *R*) and *f* – ℛ Statistics

position (no. of points)	equation	*R* or *r*	*f*
	(a) Molecule 2		
α (7)	none		
β (7)	$SCS = 0.03 + 6.42\sigma_I + 6.10\sigma_R^+$	$R = 0.999$	0.04
	$SCS = 0.37 + 6.32\sigma^+$	$r = 0.995$	0.09
γ_E (6)	$SCS = 0.04 - 1.32\sigma_I - 1.30\sigma_R^+$	$R = 0.991$	0.12
	$SCS = 0.35 - 2.10\sigma$	$r = 0.965$	0.24
	$SCS = -0.01 - 1.32\sigma^+$	$r = 0.977$	0.20
γ_Z (6)	$SCS = 0.06 - 1.22\sigma_I - 1.26\sigma_R^+$ [a]	$R = 0.976$	0.20
	$SCS = 0.38 - 2.01\sigma$	$r = 0.942$	0.30
	$SCS = 0.03 - 1.28\sigma^+$	$r = 0.966$	0.24
	(c) Molecule 4		
α (9)	$SCS = -0.20 - 4.23\sigma_I - 1.12\sigma_R^{BA}$	$R = 0.902$	0.31
	$SCS = -0.31 - 4.12\sigma_I - 1.96\sigma_R^0$	$R = 0.922$	0.28
	$SCS = -0.28 - 3.82\sigma_I - 1.96\sigma_R^-$	$R = 0.962$	0.19
β (9)	$SCS = 0.07 + 4.43\sigma_I + 5.21\sigma_R^+$	$R = 0.994$	0.10
	$SCS = 0.01 + 5.19\sigma^+$	$r = 0.990$	0.14
γ_E (9)	$SCS = -0.02 - 0.98\sigma_I - 0.79\sigma_R^+$	$R = 0.999$	0.04
γ_Z (9)	$SCS = 0.04 - 0.59\sigma_I - 1.18\sigma_R^{BA}$	$R = 0.986$	0.16
	$SCS = 0.00 - 0.49\sigma_I - 0.67\sigma_R^+$	$R = 0.995$	0.09
	(b) Molecule 3		
α (7)	$SCS = -0.24 - 3.12\sigma_I - 1.15\sigma_R^{BA}$	$R = 0.950$	0.25
	$SCS = -0.28 - 3.13\sigma_I - 1.78\sigma_R^0$	$R = 0.962$	0.22
	$SCS = -0.17 - 3.16\sigma_I - 1.60\sigma_R^-$	$R = 0.973$	0.18
β (7)	$SCS = 0.19 + 4.52\sigma_I + 6.86\sigma_R^+$	$R = 0.987$	0.14
	$SCS = -1.88 + 10.17\sigma$	$r = 0.940$	0.30
	$SCS = -0.29 + 6.29\sigma^+$	$r = 0.987$	0.14
γ_E (6)	$SCS = -0.11 - 1.97\sigma_I - 2.60\sigma_R^{BA}$	$R = 0.993$	0.11
	$SCS = -0.19 - 2.41\sigma_I - 4.18\sigma_R^0$	$R = 0.980$	0.18
	$SCS = -0.14 - 1.25\sigma_I - 1.28\sigma_R^+$	$R = 0.993$	0.10
	$SCS = -0.06 - 2.31\sigma$	$r = 0.975$	0.20
	$SCS = -0.19 - 1.32\sigma^+$	$r = 0.981$	0.17
γ_Z (6)	$SCS = -0.10 - 1.19\sigma_I - 1.14\sigma_R^+$	$R = 0.987$	0.14
	$SCS = 0.07 - 2.06\sigma$	$r = 0.960$	0.24
	$SCS = -0.16 - 1.18\sigma^+$	$r = 0.964$	0.23
	(d) Molecule 5		
α (8)	$SCS = -0.07 - 4.38\sigma_I - 1.79\sigma_R^{BA}$	$R = 0.955$	0.25
	$SCS = -0.14 - 4.46\sigma_I - 2.84\sigma_R^0$	$R = 0.973$	0.19
	$SCS = -0.03 - 4.21\sigma_I - 0.84\sigma_R^+$	$R = 0.932$	0.31
	$SCS = -0.03 - 4.54\sigma_I - 2.55\sigma_R^-$	$R = 0.986$	0.14
β (8)	$SCS = 0.16 + 3.53\sigma_I + 3.71\sigma_R^+$	$R = 0.999$	0.05
	$SCS = 0.24 + 3.8\sigma^+$	$r = 0.996$	0.08
γ_E (8)	$SCS = 0.15 - 1.53\sigma_I - 1.72\sigma_R^{BA}$	$R = 0.990$	0.14
	$SCS = 0.16 - 1.64\sigma_I - 2.40\sigma_R^0$	$R = 0.968$	0.24
	$SCS = 0.09 - 1.28\sigma_I - 0.93\sigma_R^+$	$R = 0.994$	0.10
γ_Z (8)	$SCS = 0.09 - 0.54\sigma_I - 1.17\sigma_R^{BA}$	$R = 0.989$	0.12
	$SCS = 0.10 - 0.62\sigma_I - 1.64\sigma_R^0$	$R = 0.965$	0.22
	$SCS = 0.05 - 0.37\sigma_I - 0.63\sigma_R^+$	$R = 0.992$	0.10
	$SCS = 0.11 - 0.61\sigma^+$	$r = 0.990$	0.12

[a] This correlation does not satisfy *both* criteria, as *R* implies only a confidence level of 97.5%; we, however, mention it for comparison sake, as it gives rise to the most favorable dispersion as measured by *f*.

131-132 °C) had not been described previously, to our knowledge.

Results

We have gathered into Tables I-III the ^{13}C NMR chemical shifts used in the present analysis together with the various attempts at correlation, which are evaluated with the two objective criteria of the *r* (or *R*) and of the *f* statistics.

While most of the experimental results are consistent with several LFER, there are also some unambiguous findings, which we list as follows. (1) In molecules **2**, C_α chemical shifts *cannot* be accounted for by *any* of the six LFER models which were tested. (2) In molecules **4**, the γ_E-carbon shows a *single* satisfactory correlation with the DSP treatment based upon σ_R^+ values.[10] (3) There is a trend for the smallest normalized dispersion, as measured from the individual *f* values (considered without any filtering on the base of the *r* or *R* implied confidence level), to occur with the DSP, σ_R^- treatment for the α-carbons, and with the DSP, σ_R^+ model for the other positions, the only exception being the β-carbons of **3**, for which DSP, σ_R^+ and MSP, σ^+ are equivalent. (4) The substituent effects *alternate* along the α, β, γ_E and α, β, γ_Z paths. This is consonant with a related observation by Membrey and Doucet[6] of alternation in sign of the substituent effects in the *trans*-chalcone series; these authors have also noted the quasi-equivalence of various LFER at the 1-position of their system. (5) Lastly, we found a remarkable feature: as indicated in Table IV, one can extract from the results of the DSP, σ_R^+ treatment for the γ_E and γ_Z carbons the ratios of the relative sensitivities to *inductive* and to *resonance* contributions, $(\rho_I)_E/(\rho_I)_Z$ and $(\rho_R)_E/(\rho_R)_Z$ for these two comparable centers, which differ only in the geometry. In the series of systems **2**–**5**, while the resonance term $(\rho_R)_E/(\rho_R)_Z$ is relatively invariant and close to unity, $(\rho_I)_E/(\rho_I)_Z$ *is more than tripled.* On the assumption that the DSP, ρ_R^+ treatment achieves a correct separation between inductive and resonance effects, the former finding

Table III. Synopsis of the Correlations Attempted[a]

probe molecule	position	DSP				MSP	
		σ_R^{BA}	σ_R^0	σ_R^+	σ_R^-	σ	σ^+
2	α	−	−	−	−·	−	−
2	β	−	−	+·	−	−	+
2	γ_E	−	−	+·	−	+	+
2	γ_Z	−	−	−·	−	+	+
3	α	+	+	−	+·	−	−
3	β	−	−	+·	−	+	+·
3	γ_E	+	+	+·	−	+	+
3	γ_Z	−	−	+·	−	+	+
4	α	+	+	−	+·	−	−
4	β	−	−	+·	−	−	+
4	γ_E	−	−	+·	−	−	−
4	γ_Z	+	−	+·	−	−	−
5	α	+	+	+	+·	−	−
5	β	−	−	+·	−	−	+
5	γ_E	+	+	+·	−	−	−
5	γ_Z	+	+	+·	−	−	+

[a] A plus sign indicates a correlation satisfying to *both* r (or R) and $f - \mathcal{R}$ statistics at the 99% level, a minus sign indicates a correlation failing to satisfy one or both of the preceding criteria, and a dot indicates a correlation giving minimal dispersion on the basis of f value.

Table IV. Sensitivities to Inductive and to Resonance Contributions in the DSP (σ_R^+) Treatment of the SCS of the γ Positions

probe molecule	γ_E		γ_Z		rel sensitivity γ_E/γ_Z	
	ρ_I	ρ_R	ρ_I	ρ_R	R_I[a]	R_R[b]
2	−1.32	−1.30	−1.22	−1.26	1.08	1.03
3	−1.25	−1.28	−1.19	−1.14	1.05	1.12
4	−0.98	−0.79	−0.49	−0.67	2.00	1.18
5	−1.28	−0.93	−0.37	−0.63	3.46	1.48

[a] $R_I = \rho_I^E/\rho_I^Z$. [b] $R_R = \rho_R^E/\rho_R^Z$.

would seem to indicate that the geometry remains coplanar in all of the styrenes **2**–**5** (or that the distribution of conformers remains the same for all these systems). We fail to fully understand the latter finding; i.e., why the two allylic carbons γ_E and γ_Z respond in such different manner to an inductive alteration in the electronic charge distribution.

Discussion

The rather comprehensive "basis set" of substituents we have used differs somewhat, albeit nonexcessively, from that recommended as the most appropriate for a DSP treatment.[14] It is true that the two statistical criteria r (or R) and f used throughout this study are not completely independent from one another, but one would be hard pressed to avoid this problem when characterizing deviations arising from use of one and the same model.

The present work set about to test the superiority of multiple-parameter correlations over the single-parameter treatment. For this purpose, the chemical shifts of four carbons, α, β, γ_E, and γ_Z, in four styrene series are related to six different substituent parameter scales, in the formalisms of Hammett,[1] of Brown and Okamoto,[1] and of Ehrenson, Brownlee, and Taft.[10] We failed to find an overwhelming, or merely clear-cut, advantage for the multiple-parameter correlations.

Going now to the determination of substituent constants such as σ^+ from ^{13}C shifts in substituted styrenes, we note that certain benzylidenemalononitriles **2** are unpleasant and toxic (lachrymatory) materials. Hence, we would recommend using in their stead the much more inoccuous Meldrum acid derivatives **3**.

Recently, an extension was proposed of the minimal "basis set" of substituents:[10] this proposal finds additional support from our results. But this change would ipso facto restrict even more the number of probe molecules that can be used.

A happier prospect is the finding, which we emphasize again, that a less elaborate MSP treatment will provide in many cases at least equally good answers as the full DSP treatment.

This runs contrary to earlier conclusions in the literature.[10] These were based on an argument which may have been not entirely devoid of circularity: it is the σ_R^+ scale which is defined from the σ^+ scale, with a ratio $\lambda = \rho_I/\rho_R$ of unity for the original Brown and Okamoto data,[1] and not the reverse.[14] Observation of values differing from unity, in a DSP, σ_R^+ treatment combined with a satisfactory correlation for the MSP, σ^+ treatment, could very well indicate for instance that factors other than σ_I or σ_R^+ enter the σ^+ terms.

One should also point out that these authors[10] base their conclusion of the superiority for the DSP treatment, in the case of benzylidenemalononitriles (β-carbons), on a heterogeneous experimental basis, using data from two different studies and thus running the risk of introducing serious systematic errors.[20] Furthermore, their analysis of the C_α shifts for **2** gives a *positive* value to ρ_R, an astonishing result in view of the expected alternation in sign of the resonance effect.[6]

Future work in this field, following upon the lead from Happer et al.,[2] will exploit comparisons with classical treatments such as those of Yukawa–Tsuno or of Swain–Lupton;[1] it will also develop recent proposals such as using mixed scales,[7] going to triple[21] or DSP-NLR[22] parametrization, resorting to pattern recognition,[23] etc.

In conclusion, one should keep in mind that a correlation analysis can function at either the descriptive or at the explanatory level. In the latter case, it has to be used in conjunction with a physical model appropriate to the phenomenon. ^{13}C chemical shifts are quite complex; nevertheless, there is good theoretical understanding of their components, such as the prime importance of the excitation energy term, the determining influence of the local electronic charge, etc.[24-27] We also note, in this respect, that even though the DSP recipe has had numerous successes in accounting for ^{13}C chemical shifts, it has also met with failure.[11] We *do not* believe that it will be sufficient to relate ^{13}C shifts, in a semiempirical manner, to parameters such as σ, σ_I, and σ_R. We have reached the stage where one wants to go beyond such correlations and to try to understand the reasons for their success.

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Registry No. **2** (X = F), 2826-22-4; **2** (X = H), 2700-22-3; **2** (X = NO_2), 2700-23-4; **2** (X = CN), 36937-92-5; **2** (X = Cl), 1867-38-5;

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2 (X = OMe), 2826-26-8; **2** (X = $N(CH_3)_2$), 2826-28-0; **3** (X = F), 23160-10-3; **3** (X = H), 1214-54-6; **3** (X = CN), 53942-70-4; **3** (X = OMe), 15795-54-7; **3** (X = $N(CH_3)_2$), 15795-57-0; **3** (X = CH_3), 15795-51-4; **3** (X = Br), 15795-59-2; **4** (X = F), 71732-10-0; **4** (X = H), 27402-47-7; **4** (X = NO_2), 23536-26-7; **4** (X = CN), 57270-79-8; **4** (X = Cl), 27402-31-9; **4** (X = OCH_3), 49546-71-6; **4** (X = $N(CH_3)_2$), 1753-47-5; **4** (X = Me), 56504-51-9; **4** (X = Br), 49546-72-7; **5** (X = F), 16210-64-3; **5** (X = H), 5381-33-9; **5** (X = CN), 31316-87-7; **5** (X = Cl), 15875-54-4; **5** (X = OMe), 7421-76-3; **5** (X = NMe_2), 21889-13-4; **5** (X = Me), 15875-51-1; **5** (X = Br), 961-20-6.

Chichibabin Amination of 1,*X*-Naphthyridines. Nuclear Magnetic Resonance Studies on the σ Adducts of Heterocyclic Systems with Nucleophiles[1]

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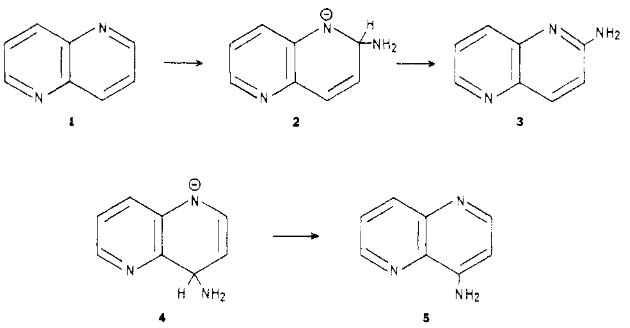
In the amination of 1,*X*-naphthyridines with potassium amide in liquid ammonia at about −35 to −40 °C the initial adduct formation is charge controlled. Thus, at these temperatures the site with the lowest electron density is most susceptible for amide attack (C-2 in 1,5-naphthyridine, C-2 in 1,6-naphthyridine, C-2 and C-8 in 1,7-naphthyridine, and C-2 in 1,8-naphthyridine), as proven by NMR spectroscopy. When the temperature was raised to about 10 °C, the site of addition has been found to change for 1,5- and 1,7-naphthyridine (NMR spectroscopy): from C-2 to C-4 in 1,5-naphthyridine and from C-2 and C-8 to C-8 only in 1,7-naphthyridine. In case of 1,6- and 1,8-naphthyridines no change was observed. Thus, the amination at about 10 °C is a process which is thermodynamically controlled. The several factors which contribute to the stability of these addition products have been discussed. It has been found that the anionic σ adducts 2(4,8)-aminodihydro-1,*X*-naphthyridinides can be easily oxidized with potassium permanganate into their corresponding 2(4,8)-amino-1,*X*-napthyridines.

The Chichibabin amination of the 1,*X*-naphthyridines has been described by several investigators.[2–4] However, contradictory results were sometimes reported, and product formation did not always follow the predictions based on calculated electron densities.[3,5,6] Moreover, 1:1 anionic σ adducts, formed on addition of the amide ion to the 1,*X*-naphthyridines,[7] were not always found to be the precursors of the products being obtained during the amination. We present here the results of detailed investigations on this subject, giving an explanation of the contradictory results which have been reported thus far.

Results and Discussion

(A) Amination of 1,5-Naphthyridine (1). The Chichibabin amination of **1** with sodamide at −33 °C was described first by Hart.[2] He claimed to have obtained 2-amino-1,5-naphthyridine (**3**). His results could not, however, be reproduced.[3,4] Paudler and Kress[3] reported that amination of **1** with potassium amide has to be carried out at *room temperature* in order to obtain the same compound (33%). It was shown later[4] that the amination product was not **3** but its isomer 4-amino-1,5-naphthyridine (**5**). When the reaction was carried out at 50 °C, the yield of **5** was considerably improved, but no further experimental details are available.[8] A few years ago it was shown by NMR spectroscopy that dissolving **1** at −40 °C in liquid ammonia containing a fourfold excess of potassium amide gives very rapid[7] formation of the 2-aminodihydro-1,5-naphthyridinide (**2**, Scheme I); no traces of **1** could be found, even if only a slight excess of potassium amide is used. On the basis of the Hammond postulate,[9,10] one has to conclude that, for reactions of this type, the transition state has a structure close to that of the starting material and thus that the attack of the amide ion is controlled by electron densities. This conclusion is in agreement with recent HMO calculations on nucleophilic substitution reactions in 1,*X*-naphthyridines; in these calculations the nature of the nucleophilic reagent[6] has also been taken into consideration.

Scheme I



Calculations[3,5,6] showed that position 2 in **1** has the lowest electron density and thus is most susceptible to a

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