Variable Substituent Response to Electron Demand and Substituent–Substituent Interactions in Protonation Equilibria of 1,1-Diphenylethylenes

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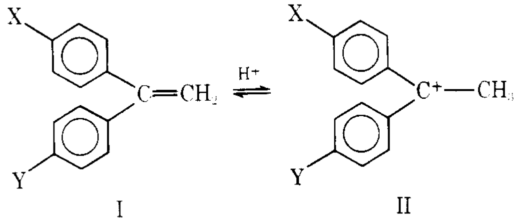
pK_{BH^+} values for protonation equilibria of 4- and 4,4′-substituted 1,1-diphenylethylenes have been measured in aqueous SO_4H_2 solutions. Nonadditivity of structural effects observed in disubstituted compounds indicates important substituent–substituent interactions (up to 1 pK unit), interpreted on the basis of a variable substituent response which depends upon the electron demand at the carbenium center in the protonated form (II). These effects are described by a free-energy relationship, including an interaction term expressed as a $\sigma^+_X\sigma^+_Y$ product: $pK = -9.72 - 3.66(\sigma^+_X + \sigma^+_Y) - 1.85\sigma^+_X\sigma^+_Y$. MO-INDO calculation of electronic energy changes from the olefin to the corresponding ion proves to be unable to accurately express these interactions as well as the strong electron transfer occurring in methoxy-substituted ions, and therefore appears to be in limited agreement with the experimental results.

Nonconstancy and nonadditivity of substituent effects in polysubstituted compounds have been reported in various reactivity data (rate or equilibrium constants).[1–4] For a better understanding of this phenomenon, particularly regarding its interrelation with the electronic structure of the involved substrates, we recently performed a NMR study on substituted 1,1-diphenylethylenes (I) and the corresponding diphenylmethylcarbenium ions (II).[5] Both ^1H and ^{13}C data indicate a strict additivity for the substituent effects on the chemical shifts in the neutral form (I).[5a,b] In contrast, important deviations appearing in ions II clearly point out a "variable response" of the substituents since the amount of electron migration from the substituents to the electron-deficient carbenium center is largely determined by the electron demand at this position (this conclusion is substantiated by a comparison with parent benzophenones and hydroxycarbenium ions).[5c,d] We report here further evidence of such substituent–substituent interactions (generated by this "variable response" pattern) in protonation equilibria constants (pK_{BH^+}) for these compounds (eq 1).



I II (1)

Indeed, owing to the increased resonance interactions in ions II, it may be expected that the substituent influences on these protonated forms, rather than the structural effects in the neutral initial state (I), would constitute the most important factor in the overall substituent effects quoted on the protonation equilibria constants. The pK_{BH^+} values would therefore largely reflect the pattern of electron delocalization in the corresponding carbenium ions (II).

Results and Discussion

The pK values are listed in Table I. They are all expressed in the H_c acidity scale,[6] which was claimed to be more appropriate than the H_R' scale[7] for the protonation of carbon bases.

From these results, it appears that for monosubstituted compounds substituent effects are well described by a Hammett-like relationship using the Brown–Okamoto σ^+ substituent constants[8,9] (eq 2).

$$pK_{BH^+} = -(9.62 \pm 0.09) - (3.4 \pm 0.3)\sigma^+ \qquad (2)$$

$$\text{correlation coefficient } \rho = 0.989$$

$$\text{standard deviation (SD)} = 0.24$$

However, for disubstituted compounds strong deviations from the additivity of substituent influences are observed, as exemplified on a pK vs. $\Sigma\sigma^+$ plot (Figure 1). For instance, two methoxy groups (compound **10**) induce a variation of only 4.8 pK units (compared to the unsubstituted 1,1-diphenylethylene, **1**), whereas a single OCH_3 group results in a pK change of 2.9 in **3**. Likewise, 4-OCH_3, 4′-NO_2 diphenylethylene (**12**) is observed to be 1 pK unit more basic than diphenylethylene, whereas on the basis of the preceding σ^+ correlation it would be inferred that the influence of the NO_2 and OCH_3 groups nearly counterbalances. More generally, the influence of a variable substituent (Y) in 4-OCH_3, 4′-Y diphenylethylenes appears to be strongly attenuated in comparison to the effects observed in the corresponding monosubstituted compounds (bearing only variable Y groups) as shown by the decreased slope of the pK, σ^+_Y correlation (eq 3) as compared to eq 2.

$$\text{4-OCH}_3\text{, 4'-Y diphenylethylenes: } pK = -(6.74 \pm 0.09) - (2.29 \pm 0.16)\sigma^+_Y \qquad (3)$$

$$\rho = 0.989 \quad SD = 0.19$$

These observations are consistent with the assumption of a variable substituent response, a function of the electron demand, in the ions which, on the basis of NMR results, are discussed elsewhere[5c,d] in terms of a concerted π-inductive mesomeric mechanism. The decrease in resonance interactions between the carbenium center and the nitro-substituted phenyl ring in **12**, for instance, enhances the electron migration from the OCH_3 group via the other phenyl group. In contrast, in **10** the electron donation from one of the two methoxy groups opposes strong electron transfer from the other, thereby leading (for each group) to an apparently decreased effect when it is compared to the monosubstituted derivative **3**. In accordance with the NMR results,[5d] as the electron-releasing or -withdrawing power of the substituents becomes

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Table I. pK_{BH^+} of Substituted 1,1-Diphenylethylenes at 298 K

compd no.	X	$\sigma^+{}_X{}^a$	Y	$\sigma^+{}_Y{}^a$	$-1.85\sigma^+{}_X\sigma^+{}_Y$	$-pK_{calcd}{}^b$	$-pK_{obsd}{}^c$	ΔE,[d] kcal/mol
1	H	0	H	0	0	9.72	9.60	351.0
2	CH_3	−0.311	H	0	0	8.58	8.60	354.0
3	OCH_3	−0.778	H	0	0	6.87	6.70	356.7
4	F	−0.073	H	0	0	9.45	9.65	349.3
5	Cl	0.114	H	0	0	10.14	10.25	
6	CF_3	0.612	H	0	0	11.96	11.40	341.3
7	NO_2	0.790	H	0	0	12.61	12.30[e]	337.3
8	CH_3	−0.311	CH_3	−0.311	−0.179	7.62	8.10	356.9
9	CH_3	−0.311	OCH_3	−0.778	−0.448	6.18	6.15	359.5
10	OCH_3	−0.778	OCH_3	−0.778	−1.120	5.15	4.80	362.1
11	OCH_3	−0.778	CF_3	0.612	0.881	8.23	7.90	347.5
12	OCH_3	−0.778	NO_2	0.790	1.121	8.56	8.55	343.6
13	OCH_3	−0.778	Br	0.150	0.216	7.21	7.40	
14	F	−0.073	F	−0.073	−0.009	9.20	9.60	347.6
15	Cl	0.114	Cl	0.114	−0.024	10.58	10.55	
16	Br	0.150	Br	0.150	−0.043	10.86	11.10	

[a] From ref 8. [b] Calculated according to eq 4. [c] Expressed in H_c acidity scale.[6] [d] Difference of MO-INDO electronic energy (olefin minus parent ion) in kcal/mol. [e] Tentative assignment. Owing to the instability of the corresponding ion, accurate extension of the H_c scale was not intended beyond concentrations of 14 M SO_4H_2. Half-protonation corresponds to 15.55 M SO_4H_2. The quoted pK value was not used in the statistical treatments (eq 2 and 3); however, it fits well into the correlations obtained.

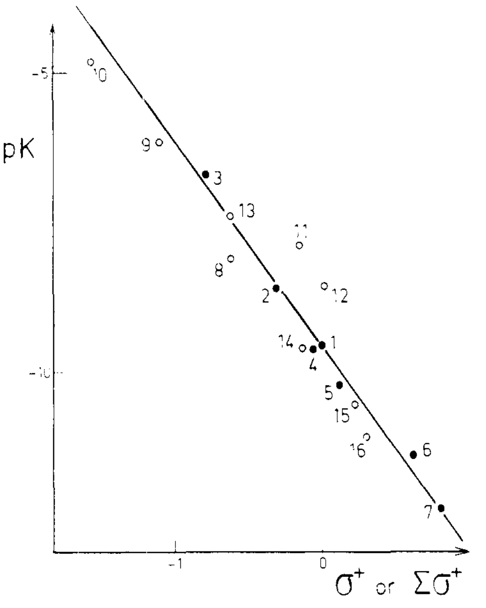

Figure 1. Plot of pK vs. $\sigma^+{}_X$ (monosubstituted compounds, ●) or $\Sigma\sigma^+ = \sigma^+{}_X + \sigma^+{}_Y$ (disubstituted compounds, ○). The numbers refer to the compounds in Table I.

greater, the observed deviations from a strict additivity of substituent influences appear to be more important, thereby leading either to a *saturation* of the effects for two donor groups or to an *exaltation* from one donor and one acceptor group.

These substituent–substituent interactions can be accounted for by using the "Quantitative Factorization Interaction Treatment" that we have previously developed for estimation of rate constants in the bromination of polysubstituted benzenes[2b] of pK's of benzophenones[2c] or of ^{13}C shifts of aryl- and arylhydroxycarbenium ions.[5d] Introduction into the pK vs. σ^+ relationship of an interaction term (expressed by a $\sigma^+{}_X\sigma^+{}_Y$ product), which represents the substituent effect deviations from additivity, leads to eq 4 by a least-squares treatment of all of the data in Table I.

$$pK_{BH^+} = -9.72 - (3.66 \pm 0.03)(\sigma^+{}_X + \sigma^+{}_Y) - (1.85 \pm 0.12)\sigma^+{}_X\sigma^+{}_Y \quad (4)$$

$$\rho = 0.989 \text{ and SD} = 0.28$$

This correlation appears to give quite a satisfactory representation of the substituent effects on the pK for both mono- and disubstituted compounds. It should also be noted that the coefficient of the $\sigma^+{}_X + \sigma^+{}_Y$ term in this relationship is nearly identical with that of the σ^+ term in eq 2 obtained for monosubstituted derivatives only.

Another striking point is the importance of the nonlinear interaction term ($1.85\sigma^+{}_X\sigma^+{}_Y$) expressing the deviations by substituent influences from a strict additivity whose value can reach 1 pK unit (with opposite signs) for 4-OCH_3, 4′-OCH_3 and 4-OCH_3, 4′-NO_2 diphenylethylenes.

It should be recalled that for the pK_{BH^+} of parent substituted benzophenones a similar treatment leads to values of 1.56 and 0.55, respectively, for the $\sigma^+{}_X + \sigma^+{}_Y$ and $\sigma^+{}_X\sigma^+{}_Y$ terms.[2c,10] This confirms that both the sensitivity to substituents effects and the importance of substituent–substituent interactions depend upon the demand of the carbenium center (a demand which is less in the protonated ketone where the oxygen atom can accommodate a fraction of the positive charge).

These substituent–substituent interactions can also be characterized by the *saturation ratio* (*SR*) defined by Freedman[11] as the ratio of the substituent effect observed in disubstituted compounds vs. the values calculated assuming additivity of the perturbations observed in monosubstitutions. Although *SR* is substituent dependent, it can be used for a given group to evaluate the extent of the interactions and to compare their magnitude in various physicochemical properties. For the OCH_3 group, for instance, *SR* calculated from the pK of compounds **1**, **3** and **10** is 0.8. This value appears to be intermediate between that observed for molecules I (~1 since additivity holds) and *SR* ≈0.6 derived from a previous NMR study[5] (^{13}C shifts of C_α or ^1H shifts of the methyl protons) in the protonated from (II).

In an alternative way, the pK values can also be compared to the differences in electronic energy (ΔE) between the neutral olefin and the corresponding ion evaluated by a semiempirical MO method[12] (INDO approximation was used here as it appears to have given consistent results for the description of carbenium ions[5c]). Such a comparison between the variations of electronic energy and the observed pK supposes of course that solvation energies remain constant or have variations proportional to those of ΔE throughout the entire family studied and, similarly, that substituent effects on enthalpic and entropic terms are proportional or that the reac-

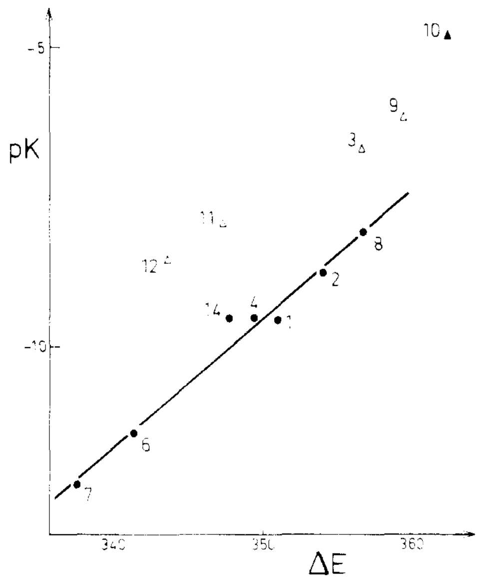

Figure 2. Plot of pK vs. ΔE (difference of INDO electronic energy between olefin and ions). Substituents bearing one or two methoxy groups are quoted (△ and ▲, respectively). See Table I for the numbering of the compounds.

tion is isentropic.[13] As indicated in Figure 2, a definite trend to correlation is observed between pK and ΔE.[14] However, systematic deviations appear for all of the compounds bearing an OCH_3 group (the corresponding points would in fact nearly lie on a distinct correlation parallel to that drawn for the substrates with only CH_3, NO_2, F, and CF_3 substituents). Examination of these results suggests that some caution is necessary if one attempts an extensive use of such a treatment in view of an accurate representation of substituent effects on the observed pK_{BH^+} as indicated in the following remarks.

(i) Substituent effects derived from the calculated INDO ΔE values would appear to be nearly additive, irrespective of the strong substituent–substituent interactions experimentally noted.

(ii) The deviations observed for the methoxy-substituted compounds indicate that the calculation performed predicts too small values of substituent effects for the OCH_3 group; comparing, for instance, points 1 and 3 in Figure 2, it may be seen that the variation of the calculated ΔE (5.7 kcal) suggests, when compared to the partial ΔE, pK relation, a pK change of 1.2, whereas the observed effect is of 2.9 pK units.

It seems, therefore, that INDO calculation underestimates the stabilization due to the OCH_3 substituent in the protonated forms (II). This result is fully consistent with our previous NMR observation;[5c,d] we have recently shown, by comparison of NMR shifts with π-electron densities, that the standard INDO parametrization is not well-suited to express the strong electron release from the OCH_3 group toward the electron-deficient center occurring in the corresponding ions, although it gives better results for neutral molecules or systems where the electron transfer is less important.[15]

It should also be observed that substituent effects derived from the calculated ΔE values are predicted to be 3.4 times as large as the observed variations. Such a discrepancy is, however, much less critical than the preceding remarks, since, for lack of an absolute evaluation, proportionality relationships are often of valuable interest for the prevision of substituent effects. This discrepancy might be related to the above assumptions about solvation energy or entropic terms. In all likelihood it is probably related to the inadequacy of the INDO method to correctly scale energy changes, particularly for σ electrons. Wiberg and Danen[16] have already stated that semiempirical MO methods (such as CNDO or INDO) overestimate energy changes between related species by a factor of ca. 3, which is in good agreement with the present observation.

Conclusion

The pK_{BH^+} values measured in aqueous SO_4H_2 solutions for disubstituted 1,1-diphenylethylenes indicate important substituent–substituent interactions. They can be accounted for by the assumption of a variable response of the substituents to the electron demand of the deficient carbenium center in the protonated forms (II), which is in accordance with our previous NMR conclusions.

Rather than the semiempirical MO-INDO method (whose standard parametrization does not seem to be well-suited to a study of strong electron transfer), free-energy relationships, including an interaction term expressed by factorization, give an accurate representation of the experimental pK. The present results, as well as neighboring NMR observations, strongly support the assumption that the extent of such substituent–substituent interactions is closely interrelated to the electron demand at the carbenium center.

In extending our study, this remark prompts us to use the substituent–substituent interactions pointed out in kinetic data as a probe of electron delocalization for the purpose of gaining some insight about the electronic structure of the transition states in electrophilic addition reactions of arylalkenes. This work is now under way.

Experimental Section

The pK values have been determined by usual spectrophotometric methods[2c,17] in aqueous SO_4H_2 solutions. Extrapolation to 0 time was performed for unstable ions (diphenylethylene or structures bearing an electron-withdrawing group). The preparation of the compounds has been reported elsewhere.[2a,17] For INDO calculations (and particularly the geometrical parameters used), see ref 5c,d.

Registry No.—**1,** 530-48-3; **2,** 948-55-0; **3,** 4333-75-9; **4,** 395-21-1; **5,** 18218-20-7; **6,** 345-88-0; **7,** 22057-84-7; **8,** 2919-20-2; **9,** 13392-76-2; **10,** 4356-69-8; **11,** 68036-77-1; **12,** 28358-68-1; **13,** 34564-83-5; **14,** 6175-14-0; **15,** 2642-81-1; **16,** 10605-43-3.

References and Notes

(1) S. Nishida, *J. Org. Chem.*, **32**, 2697 (1967).

(2) (a) A. F. Hegarty, J. S. Lomas, W. V. Wright, E. D. Bergmann, and J. E. Dubois, *J. Org. Chem.*, **37**, 2222 (1972); (b) J. E. Dubois, J. J. Aaron, P. Alcais, J. P. Doucet, F. Rothenberg, and R. Uzan, *J. Am. Chem. Soc.*, **94**, 6823 (1972); (c) G. Goethals, J. P. Doucet, P. Bauer, and R. Uzan, *Spectrochim. Acta, Part A*, **31a**, 1501 (1975).

(3) F. G. Bordwell and G. J. McCollum *J. Org. Chem.*, **41**, 2391 (1976).

(4) S. Clementi, C. D. Johnson, and A. R. Katritzky, *J. Chem. Soc., Perkin Trans. 2*, 1294 (1974).

(5) (a) B. Ancian and J. P. Doucet, *J. Chim. Phys. Phys. Chim. Biol.*, **69**, 1211 (1972); (b) B. Ancian, to be published; (c) B. Ancian, J. P. Doucet, and J. E. Dubois, *J. Am. Chem. Soc.*, **98**, 4764 (1976); (d) B. Ancian, F. Membrey, and J. P. Doucet, *J. Org. Chem.*, **43**, 1509 (1978).

(6) M. T. Reagan, *J. Am. Chem. Soc.*, **91**, 5506 (1969). Although there are small systematic differences for individual pK values, the agreement is good for substituent effects in the common compounds studied.

(7) N. C. Deno, P. T. Groves, and G. Saines, *J. Am. Chem. Soc.*, **81**, 5790 (1959).

(8) H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, **80**, 4979 (1958).

(9) DSP treatment using Taft's constants σ_I and σ^+_R does not significantly improve the fit, and leads to nearly equal coefficients for the σ_I and σ^+_R terms (a further test of validity of the simplified σ^+ representations): pK $= -9.58 - (3.64 \pm 0.15)\sigma_I - (3.52 \pm 0.05)\sigma^+_R$, $\rho = 0.994$, and SD = 0.2.

(10) pK values are expressed in the H_0 scale for ketones and in the H_c scale for diphenylethylenes.

(11) H. H. Freedman in "Carbenium Ions", Vol. 4, G. A. Olah and P. v. R. Schleyer, Eds., Wiley, New York, N.Y., 1973, p 1553.

(12) M. J. S. Dewar, "The Molecular Orbital Theory of Organic Chemistry", McGraw Hill, New York, 1969.

(13) O. Exner, *Prog. Phys. Org. Chem.*, **11**, 41 (1973).

(14) For compounds **1–4**, **6–8**, and **14** (compounds without OCH_3 groups), pK $= -(83.9 \pm 5) + (0.213 \pm 0.014)\Delta E$, $\rho = 0.989$, and SD = 0.22.

(15) For instance, for the protonation of parent benzophenones, where the electron demand at the carbenium center is less (and so are the substituent–substituent interactions), charge densities calculated by semiempirical

MO methods give, as a first approximation, a fairly good representation of the p*K*: D. Beaupere, J. P. Seguin, R. Uzan, and J. P. Doucet, *Can. J. Chem.*, **54**, 297 (1976). Similarly, in a Δ*E*, p*K* plot, the methoxy-substituted compounds exhibit much smaller deviations than for 1,1-diphenylethylenes.

(16) (a) W. C. Danen, *J. Am. Chem. Soc.*, **94**, 4835 (1972); (b) K. C. Wiberg, *Tetrahedron*, **24**, 1083 (1968).

(17) B. Ancian, Doctoral Thesis, University of Paris VII, Paris, France, 1974.

Stereochemistry of the Wagner–Meerwein Rearrangement of (−)-*endo*- and (+)-*exo*-5-Bicyclo[2.2.1]heptene-2-carboxylic Acids[1]

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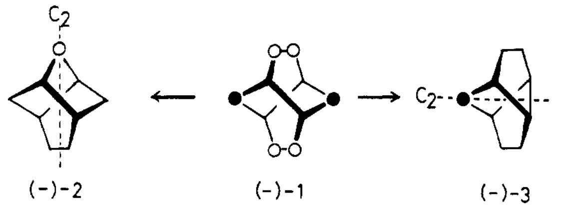
Stereochemistry of the acidic lactonization of *endo*- (4) and *exo*-5-bicyclo[2.2.1]heptene-2-carboxylic acid (14) has been studied with their optically active modifications. The (−)-endo isomer 4 and the (+)-exo isomer 14 both were found to give a mixture of the (−)-*endo*-lactone 15 and the (−)-*exo*-lactone 8 with retention of the optical purities of their parent acids (−)-4 and (+)-14. A scheme involving the Wagner–Meerwein rearrangement and the "6,2-hydride shift" has been suggested to explain these transformations.

D_2 symmetry inherent to gyrochiral[2] (−)-twistane (1)[3] ($C_{10}H_{16}$) demands that its six methylene groups be classified into two categories, each comprising two and four homotopic methylenes, respectively, as shown by closed and open circles in Chart I.

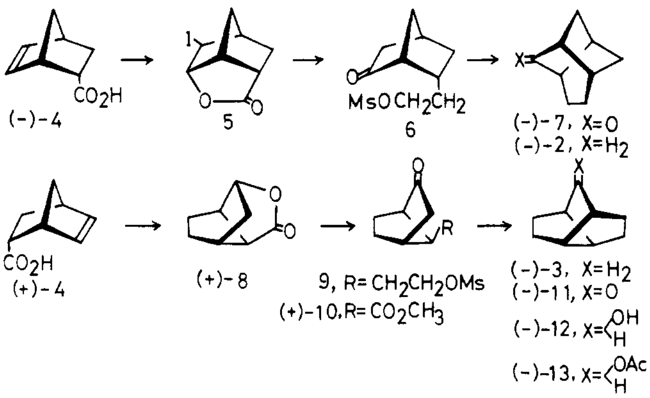
Chart I



Depending upon which methylene group is taken away, we have either (−)-*twist*-brendane (2)[4] or (−)-brexane (3),[2] both with C_2 symmetry, retaining one of original three C_2 axes of their parent tricyclic hydrocarbon.

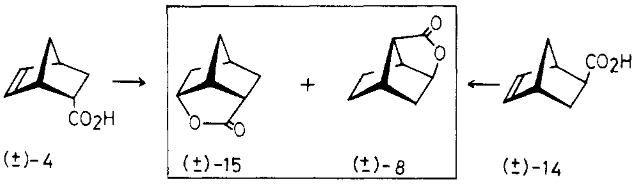
It is interesting to note that this structural relationship also reflects itself in their synthetic sequences which involve *endo*-5-bicyclo[2.2.1]heptene-2-carboxylic acid (4) as a common starting material (Chart II). Whereas the sequence of conversions for the synthesis of (−)-*twist*-brendane (2) was rather straightforward involving intramolecular alkylation of the keto mesylate 6 which in turn was derived from the (−)-unsaturated carboxylic acid 4 via the *endo*-iodolactone without skeletal rearrangement, the sequence leading to (−)-brexane (3) involved the acidic Wagner–Meerwein type rearrangement of (+)-4 to yield the (+)-*exo*-lactone 8 which was then transformed into (−)-brexan-2-one (11) via the keto mesylate 9.

Chart II



Beckmann,[5] who discovered this Wagner–Meerwein type rearrangement, reported another interesting observation, that being that both (±)-*endo*-carboxylic acid 4 (Chart III) and (±)-*exo*-carboxylic acid 14 afforded a mixture of (±)-*endo*-lactone 15 and (±)-*exo*-lactone 8. Although prolonged heating with strong acid converted the *endo*- and *exo*-carboxylic acids 4 and 14 completely into the *endo*-lactone 15, a difference between these diastereomeric starting materials was observed in the ratio of the two lactones 8 and 15 in their early reaction mixtures; the *endo*-lactone 15 was found to be rich in the early reaction mixture from the *endo*-carboxylic acid 4, while the reversed ratio was found in the early reaction mixture from the *exo*-carboxylic acid 14.

Chart III



In our preceding paper,[2] which reported the first successful synthesis of optically active brexane (2), we briefly discussed a probable stereochemistry of this Wagner–Meerwein rearrangement which had provided us with our synthetic starting material, the (+)-*exo*-lactone 8 from the (+)-*endo*-bicyclic carboxylic acid 4 with known absolute configuration.[6]

We have studied the steric course of this remarkable rearrangement using both optically active *endo*-bicyclic carboxylic acid 4 and *exo*-bicyclic carboxylic acid 14, and in the present paper we report the result of our recent investigation where special attention was paid to follow the configurational as well as optical purity relationship between the starting materials and the final products.[7]

Results

Absolute Configuration and Absolute Rotation of the

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