TABLE I

Run No.	Solvent	Base: Nature	Base: Concn., N	T, °C.	Yield, %	Net steric course
1	$(CH_3)_3COH$	$(CH_3)_3COK$	0.30	100	83	80% Ret.
2	n-C_4H_9OH	n-C_4H_9OK	0.30	100	72	68% Ret.
3	C_2H_5OH	C_2H_5OK	0.37	100	58	60% Ret.
4	CH_3OH	CH_3OK	0.30	100	73	44% Ret.
5	$HOCH_2CH_2OH$	$HOCH_2CH_2OK$	0.085–1.00	100	21–48	15–37% Ret.
6	H_2O	HOK	0.30–1.1–9.7	100	27–58	2% Inv.–10% Inv.–70% Ret.
7	$(CH_3)_3COH$[a]	$(CH_3)_3COK$	0.16	53	78	92% Ret.
8	$(CH_3)_3COH$[a]	$(CH_3)_4N^+OH^-$	0.16	53	59	60% Ret.
9	$HOCH_2CH_2OH$[b]	$HOCH_2CH_2OK$	0.34	25	52	48% Ret.
10	$HOCH_2CH_2OH$[b]	$(CH_3)_4N^+OH^-$	0.34	25	50	46% Ret.
11	$(CH_3)_2SO$	$HOCH_2CH_2OK$	0.088	53	51	37% Ret.
12	$(CH_3)_2SO$	$(CH_3)_4N^+OH^-$	0.11	53	42	34% Ret.

[a] Solutions 0.32 M in water. [b] Solutions 0.68 M in H_2O.

amide (+)-I, m.p. 112–112.2°, $[\alpha]^{25}_{546}$ +32.6° (c 9, dioxane), was prepared from (+)-II, $[\alpha]^{25}_{546}$ +12.8° (l = 1 dm., neat), by the usual method. Repeated recrystallization of grossly optically impure (−)-I from ether–pentane gave optically pure (−)-I, m.p. 112.5–113°, $[\alpha]^{25}_{546}$ −35.4° (c 9, dioxane). These data relate the configurations and maximum rotations of starting materials and products in reactions (1), (2) and (3).

Cleavage of sulfonamide (+)-I without base at 100° in water, t-butyl alcohol or dimethyl sulfoxide gave completely racemic III. Results obtained in the presence of base are summarized in Table I. Except in ethylene glycol and water, base concentrations were reached where an increase in base did not change stereospecificity. In ethylene glycol, retention increased regularly as base was increased (run 5). In water, as base concentration increased, the reaction occurred first with increasing net inversion and then with increasing net retention (run 6).

Oxidation of II with potassium periodate under conditions of runs 1, 3 and 4 gave results within experimental error of the corresponding cleavages of I. In water, oxidation of II without base at 100° gave 100% racemization, whereas at 0.012 to 0.30 M base, 30–32% inversion was observed (compare with run 6).

Treatment of (−)-2-phenyl-2-butylamine p-toluenesulfonate (95°, 3 M solution of sodium hydroxide in 90% water–10% ethanol) with hydroxylamine-O-sulfonic acid[6] gave III (10%) with 32% net retention. Cleavage of I under the *average conditions* of the above reaction gave III (83%) with 37% net retention. Oxidation of II under the same average conditions gave III (10%) with 26% net retention. The stereochemical results vary enough with concentrations of hydroxylamine, base and sodium sulfate to make the three results within experimental error of one another.

These data suggest several conclusions: (1) The same intermediate, probably RN_2H, is produced in all three of the reactions employed. (2) This intermediate partitions between a base-catalyzed anionic elimination reaction to give III somewhat stereospecifically, and a homolytic elimination to give racemic III. (3) Generation of a proton donor at the front of the carbanion in the base-catalyzed reaction of RN_2H provides for the retention mechanism, whereas a nitrogen molecule as a shield at the front of the carbanion provides for the inversion mechanism.[7] (4) In relatively non-polar solvents the homolytic cleavage of RN_2H can be eliminated, but not in water or ethylene glycol. (5) In water, different intermediates are involved in the anionic cleavage depending on whether I or II are starting materials.

(6) A. Nickon and A. Sinz, *J. Am. Chem. Soc.*, **82**, 753 (1960).

(7) Compare nitrogen as leaving group with carbon and hydrogen. (a) D. J. Cram, J. L. Mateos, F. Hauck, A. Langemann, K. R. Kopecky, W. D. Nielsen and J. Allinger, *ibid.*, **81**, 5774 (1959); (b) D. J. Cram, C. A. Kingsbury and B. Rickborn, *ibid.*, **83**, 3688 (1961).

(8) Eastman Kodak Fellow, 1961–1962.

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EVIDENCE FOR PARALLEL CONTROL OF REACTION RATE AND STEREOCHEMISTRY *via* THE ELECTROSTATIC INFLUENCE OF REMOTE SUBSTITUENT DIPOLES

Sir:

We wish to report evidence we have obtained in studies of sodium borohydride reduction of 4-substituted cyclohexanones indicating that, in systems where rate variations are strongly governed by remote substituent effects, parallel control of product stereochemistry also is exercised. Furthermore, the existence of a field effect of this nature appears to be unexpected in view of assumptions to the contrary applied in various interpretations of rate and stereochemical effects.[1-6]

The rates of reduction obtained by use of the kinetic method devised by Brown and co-workers[7] are presented in the accompanying data table. The existence of a linear free energy relationship

(1) W. G. Dauben, G. J. Fonken and D. S. Noyce, *J. Am. Chem. Soc.*, **78**, 2579 (1956).

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(5) S. Winstein and N. J. Holness, *ibid.*, **77**, 5562 (1955).

(6) E. L. Eliel, *J. Chem. Educ.*, **37**, 126 (1960).

(7) H. C. Brown, O. H. Wheeler and K. Ichikawa, *Tetrahedron*, Vol. 1, 214 (1957).

TABLE I

RATE AND PRODUCT DATA

4-Substituted cyclohexanone	I[a]	$NaBH_4$ Reduction[b] 10^2 (k) (l. mole^{-1} sec.$^{-1}$)	$NaBH_4$ Product[c] % (*cis*)	Al(oipr)$_3$ % *cis*
-H	0	1.62 (1.61)[7]	...	...
-CH_3	+0.03	1.90	22.4 (15[12], 25[3])	26.4
-di-CH_3	+0.09	2.40	...	
t-Bu	+0.016	2.47	24.1 (21)[6]	
-OCH_3	+0.25	5.72	41.4	49.1
-$COOC_2H_5$	+0.30	7.42	73.8	
-$OCOC_6H_5$	+0.469	19.9	67.0	49.2
-Cl	+0.47	21.9	66.0 (63)[12]	48.1

[a] Most of these values were obtained from R. W. Taft, *J. Am. Chem. Soc.*, **79**, 1045 (1957). The positive σ_I values of alkyl groups were inferred from the data given in ref. 8. [b] Rates were measured at 0° in isopropyl alcohol solution according to the procedure of ref. 7. [c] Determination of the *cis–trans* composition of the product was carried out by vapor phase chromatography on the quantitatively acetylated product mixture.

is established by the plot of log k *vs.* σ_I from which $\rho_I = +2.78$ was computed. For comparison purposes the corresponding rates of reduction of a series of *para* substituted acetophenones were measured, yielding a value $\rho_H = +2.6$. Once again[8] we note that the somewhat greater value of ρ_I *vs.* ρ_H correlates with the smaller distance of separation from the reaction center and the magnitude and orientation of the substituent dipole.

The question as to whether the polar substituent effect is transmitted predominantly through the carbon chain or through the dielectric medium surrounding these bonds is clearly answered by the stereochemistry of the cyclohexanol products (also listed in the table). Thus, although the number and types of bonds between the substituent and reaction centers are identical for the alternative transition states leading (respectively) to *cis* and *trans* product, it is quite apparent that the degree of preference for formation of the *cis* product is directly proportional to the electron withdrawing capacity of the substituent. Furthermore, when the σ_I values of the substituents are plotted against the log of the *cis* product fraction, the resulting linear relationship suggests that the identical electrostatic effects are at work deciding both rate and stereochemistry.

The preference for *cis* product formation induced by electronegative substituents is obviously the consequence of the shorter distance and (thereby) increased electrostatic interaction in the *cis* transition state. By means of a simple graphical computation[9] it is possible to dissect the **stereo**-ρ_I (as distinct from the **veloc.**-ρ_I) into two components: $\rho_{cis} = +3.78$ and $\rho_{trans} = +1.96$. This affords a quantitative measure of the greater probability of the *cis* transition state developing in the field of a remote electronegative center.

(8) H. Kwart and L. J. Miller, *J. Am. Chem. Soc.*, **83**, 4552 (1961).

(9) From various plots of the product composition data *vs.* ρ_I these equations can be deduced

(a) $2 + \log (k_c + k_t) = 2.78\ \sigma_I + 0.18$

(b) $2 + \log \left(\frac{k_c}{k_t + k_c}\right) = 1.0\ \sigma_I + 1.35$

(c) $2 + \log \left(\frac{k_c}{k_t + k_c}\right) = 0.82\ \sigma_I + 1.94$

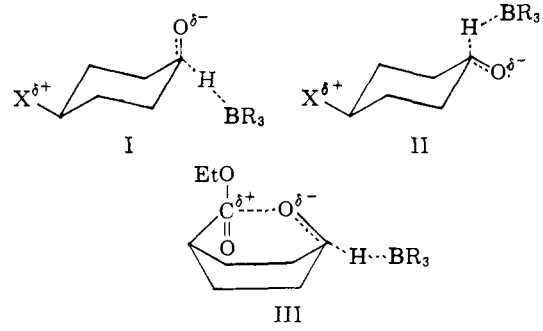
By simple transformations and substitutions we obtain

(d) $\log k_c = 3.78\ \sigma_I - 2.47$

(e) $\log k_t = 1.96\ \sigma_I - 1.88$

where k_c and k_t are the calculated rate constants corresponding to *cis* and *trans* alcohol formation.

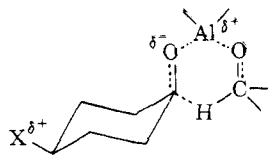
Since the transition state for borohydride reduction of ketones is known to resemble the structure of the products we have deduced that (I) and (II) depict the (respective) *cis* and *trans* charge–dipole interactions.[10] It will be seen that a single



point, that of the carbethoxyl group, stands above the **stereo**-ρ_I line, though the corresponding group value accords very well with the **veloc.** ρ_I line. The greater extent of *cis* product formation, than is predictable from the σ_I value, suggests the operation of a factor previously identified for the –COOEt group in our earlier studies on addition to cyclohexenes. Here the propensity for neighboring group participation by the –COOEt group can result in the reaction passing through the boat conformation in the transition state depicted by (III). This would effect a somewhat exalted amount of *cis* product without necessarily causing significant departure of the log k value predicted by the **veloc.**-ρ_I line. Clearly the additional energy expended in achieving the unfavorable boat is regained in the form of the resulting increased interaction energy.

It may be predicted, too, that a change in the character of the reducing agent from borohydride to aluminum isopropylate will alter the extent of electrostatic interaction and thereby stereochemical control by the remote substituent. This follows from the coördinating capacity of the aluminum tending to diminish the charge developing on oxygen in the transition state represented by IV. The limited number of data we have obtained thus far appear to bear out this conclusion since the plot of log % *cis* *vs.* σ_I is clearly non-linear, im-

(10) See also M. G. Combe and H. G. Henbest, *Tetrahedron Letters*, 404 (1961), where the authors have suggested entirely similar representations of these transition states.



IV

plying that product formation is controlled by other factors than the field effect of the remote substituent.

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RECEIVED MAY 24, 1962

STUDIES OF CHLOROBIUM CHLOROPHYLLS. V. CHLOROBIUM CHLOROPHYLLS (660)[1]

Sir:

The evidence presented below suggests that Chlorobium chlorophylls (660) are derivatives of δ - methyl - 2 - desvinyl - 2 - α - hydroxyethyl-pyropheophorbide *a*.[2,3]

Hydrolysis of crude "pheophytin" (660) in dilute hot methanolic KOH and partition chromatography between aqueous HCl and ether on Celite columns[4] gave seven fractions which were designated 1–7. All fractions possessed a conjugated carbonyl group[5]; all possessed a hydroxyalkyl group which could be oxidized to a conjugated carbonyl group[6] or dehydrated to an alkenyl group[7]; all gave a negative Molisch phase test.[8] Comparison of their visible absorption spectra revealed no significant differences among them.

The neutral imides obtained from the fractions by oxidative degradation were examined by gas–liquid partition chromatography.[4,9] Fractions 1 and 2 yielded an unidentified product; fractions 3 and 4 yielded methyl-*n*-propylmaleimide; and fractions 5, 6 and 7 yielded methylethylmaleimide. After conversion of the hydroxyalkyl group to an alkyl group, fractions 3 and 4 yielded methylethylmaleimide in addition to methyl-*n*-propylmaleimide. Dihydrohematinic acid imide was shown earlier to occur in the acid fraction from partially purified pheophorbide (660).[5,9] These results indicate the nature of the substituents on Rings I, II and IV.

Fraction 5 (I) (*Anal.* Calcd. for $C_{35}H_{40}O_4N_4$: C, 72.39; H, 6.94; N, 9.65. Found: C, 72.45; H, 7.43; N, 9.39) was used for the following studies: Dehydration of (I) in phosphoric acid (100%, 65°, 30 min.) yielded the alkenyl derivative (II). *Anal.* Calcd. for $C_{35}H_{38}O_3N_4$: C, 74.70; H, 6.81; N, 9.96. Found: C, 75.09; H, 6.83; N, 10.00. Hydrogenation[10] of (II) yielded the alkyl derivative (III). *Anal.* Calcd. for $C_{35}H_{40}O_3N_4$: C, 74.44; H, 7.14; N, 9.92. Found: C, 73.86; H, 7.17; N, 9.94. Oxidative degradation of (III) yielded only methylethylmaleimide in the neutral fraction.

Oxidation of (I) by oxygen in alkaline dimethylformamide yielded a dicarbonyl derivative (IV). *Anal.* Calcd. for $C_{35}H_{38}O_5N_4$: C, 70.68; H, 6.44; N, 9.42. Found: C, 70.31; H, 6.32; N, 9.46. Under the same conditions mesopyropheophorbide *a* (V) yielded the C_9–C_{10} ring diketone.[11] (III) was likewise oxidized to its dicarbonyl derivative (VI). Further oxidation of (VI) by H_2O_2 in alkaline dimethylformamide yielded a tricarboxylic acid (VII). A portion was methylated and converted to its zinc complex. *Anal.* Calcd. for Zn-$C_{35}H_{35}O_3N_4(OCH_3)_3$: OCH_3, 13.0. Found: OCH_3, 12.9. The remainder was dried at 100° to yield a product (VIII) whose visible absorption spectrum resembled that of purpurin 18.[12] It was methylated and converted to its zinc complex. *Anal.* Calcd. for $ZnC_{35}H_{33}O_4N_4(OCH_3)$: OCH_3, 4.62. Found: OCH_3, 5.05. Dilute methanolic KOH converted (VIII) back to (VII). Treatment of the trimethyl ester of (VII) with methanolic KOH in pyridine did not generate the Molisch phase test intermediate as it does when chlorine$_6$-trimethyl ester is treated likewise.[13] This result excluded the possibility of a cyclohexanone ring in (I).

HI in acetic acid converted (I) into a porphyrin containing a conjugated carbonyl group and an ethyl in place of a hydroxyethyl group.[3] *Anal.* Calcd. for $C_{35}H_{38}O_3N_4$: C, 74.70; H, 6.81; N, 9.96. Found: C, 74.32; H, 7.03; N, 10.02. The visible absorption spectrum was of the "etio" type.[12] (VII) was heated in HCl (1%) in a sealed tube at 185° for three hours. The wave lengths of the absorption maxima of the resulting porphyrin and of phylloporphyrin[14] were identical. However, bands II and III of the Chlorobium product absorbed with equal intensities.

The above result suggested that (I) possessed an alkyl group attached to one of the methine bridge carbon atoms. It was shown to be at C_δ by the following: (V) exposed to somewhat aged, ethanol-free, dry chloroform was converted to a chlorine-containing product (IX) whose visible absorption spectrum was almost superposable upon that of (I).[15] *Anal.* Calcd. for $C_{33}H_{35}O_3N_4Cl$: C, 69.40; H, 6.18; N, 9.81; Cl, 6.20. Found: C, 69.14; H, 5.97; N, 9.75; Cl, 6.10. The same product was obtained using the method described by Woodward and Skarić.[16] The proton magnetic resonance spectra of (III), (V) and (IX) were measured in $CDCl_3$. The signal assigned to the C_δ-proton[16] was absent from the spectra of (III) and (IX) but present in that of (V). In

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