

ASYMMETRIC SYNTHESIS VI.
STEREOCHEMISTRY OF THE REDUCTION OF 2-SUBSTITUTED CYCLOPENTANONES

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The stereochemistry of the reduction of cyclic ketones has been investigated by many authors and generalizations concerning the steric course of the reactions have also been suggested¹.

It is a common feature of the interpretations published so far¹ that they require detailed information about the geometry of the transition state. Since appropriate data for this are not available, we believe that this kind of treatment fails to lead to reliable results. For this reason, regardless of the transition state, we consider the trivial relationship between the ratio of specific rate of formation of the cis and trans isomers (k_c and k_t , resp.) and some kind of characteristic parameters (λ_R) of the substituent R changed systematically:

$$\log \frac{k_c}{k_t} = \sum_{n=0}^m a_n \lambda_R^n \quad (1)$$

A set of coefficients, a_0, a_1, \dots, a_m , can always be selected so as to fit simultaneously any expected values provided that m is at least as large as the number of the different substituents considered. Since the scale of λ_R values can be fixed arbitrarily, we specify them as quantities identical with the "ligand constants" introduced by Ugi and Ruch². The utility of Eq. (1) depends on its reducibility to simpler form in which the number of coefficients to be estimated is essentially less than that of the substituents.

The results obtained from LAH reduction of 2-R-cyclopentanones in ether at 35° (Table) indicate that Eq. (1) can be reduced to a quadratic form ($a_0=0$ follows from the definition² $\lambda_H = 0$):

$$\log \frac{k_c}{k_t} = -a_1 \lambda_R + a_2 \lambda_R^2 \quad (2)$$

Although this quadratic form may also hold for the case of cyclohexanone derivatives, a five-membered model seems to be more adequate for a first test because only a much smaller conformational change has to be considered in the reactant state; the equatorial-axial transition in the cyclohexanone series involves a twist by 120° in contrast to that of about 23° in the cyclopentanone series³. Neglecting this oscillation of relatively small amplitude, we treated the five-membered skeleton as an approximately planar one.

TABLE: Reduction of 2-R-cyclopentanones with LAH

$$\lambda_S = 1.34; \quad \tau = 1.1; \quad a_1 = 1.95; \quad a_2 = 1.46$$

R	λ_R	cis isomer percent		lit.
		Δ_{found}	calcd.	
CH ₃	1.00	24	24	25 ^{1b, 4, 5}
C ₂ H ₅	1.05	27	26	
n-C ₃ H ₇	1.08	26	28	
c-C ₅ H ₉	1.21	39	37	38 ⁴
C ₆ H ₅	1.23	40	39	41 ⁶
iso-C ₃ H ₇	1.27	47	43	57 ⁷
+t-C ₄ H ₉	1.40	54	57	

^Δ Experimental data were obtained by vpc.

⁺ For preparation and configuration see: G. Bernath, L. Gruber and I. Tömösközi, Acta Szegediensis in press.

^{*} This value was selected in agreement with Prof. Ugi instead of 1.49².

The consistency of the treatment outlined above is reflected by the fact that Eq. (2) is identical with the Ugi-Ruch equation. If we consider formally the skeletal moiety, starting from C-3, as a substituent (λ_S) attached to the chiral centre C-2, the Ugi-Ruch equation gives

$$\log \frac{k_c}{k_t} = \tau (\lambda_R - \lambda_H) (\lambda_H - \lambda_S) (\lambda_S - \lambda_R) \quad (3)$$

which is identical with Eq. (2) if $a_1 = \tau \lambda_S^2$ and $a_2 = \tau \lambda_S$.

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