Communications to the Editor

Steric Effects in the Oxidation of Secondary Alcohols with Chromic Acid

Sir:

The rates of oxidation of secondary alcohols with chromic acid are traditionally interpreted with decrease or increase of steric strain during the conversion of the sp^3-hybridized alcohol to the sp^2-hybridized ketone.[1] This interpretation implies a product-like transition state. However, the hypothesis of a late transition state has been questioned for various reasons and alternatively a rather sp^3-hybridized transition state has also been postulated.[2] The difficulty of rationalizing oxidation rates lies mainly in the absence of quantitative correlations between oxidation rates and alcohol or ketone structures. It is the purpose of this communication to establish such a correlation.

A study of the activation parameters for the oxidation of 13 secondary alcohols showed that the alcohols represent an isoentropic series.[3] The alcohol reactivities are therefore proportional to the enthalpies of activation. Accordingly, their relative reactivities should be proportional to the strain difference between the alcohols and their respective transition states. The strain of the alcohols could in principle be derived from their enthalpies of formation. Unfortunately, the amount of reliable data in the literature is rather limited. It was therefore decided to generate ΔH_f° values by force-field calculations. The BIGSTRN program, which became available to us through the courtesy of Schleyer and Mislow,[4] is not parametrized for alcohols. For the calculations the OH groups were replaced by methyl; we assume that the strain of the alcohols reflects that of the corresponding methyl compounds.[5] Enthalpies of formation were calculated with the force-field of Allinger[6a] and by means of the "pattern search minimization",[4,7] both incorporated in the program. For some 20 compounds, calculations were also performed with the Engler force-field by Jemmis,[8] Princeton University. The average disagreement between the two methods was ca. 0.8 kcal in strain. The Allinger

Table I. Oxidation Rates of Alcohols and Strain in Their Methyl Analogues and Ketones

Alcohol	No.	Log k_{Ox}[a]	ΔH_f°[b] R_2CHCH_3	Strain energy[c] R_2CHCH_3	ΔH_f°[b] $R_2C{=}O$	Strain energy[c] $R_2C{=}O$	Δ strain[d]
trans-4-Methylcyclohexanol	1	−0.12[e]	44.21	0.83	62.44	2.62	1.79
cis-4-Methylcyclohexanol	2	0.34[e]	42.56	2.48	62.44	2.62	0.14
cis-3,5,5-Trimethylcyclohexanol	3	0.13	58.14	1.96	77.07	3.05	1.09
trans-3,5,5-Trimethylcyclohexanol	4	1.57	54.18	5.92	77.07	3.05	−2.87
2-Propanol	5	−0.22	32.19	−0.08	52.13	0.00	0.08
di-*t*-Butylmethanol	6	0.58	60.33	12.28	83.52	9.11	−3.17
Cyclobutanol	7	0.19[f]	1.14	26.57	19.22	28.51	1.94
2,2,4,4-Tetramethylcyclobutanol	8	1.56	30.76	27.07	47.41	30.44	3.37
Cyclopentanol	9	0.18[f]	25.24	7.65	42.71	10.21	2.56
trans-2,4,4-Trimethylcyclopentanol	10	0.15	47.65	7.26	65.53	9.40	2.14
cis-2,4,4-Trimethylcyclopentanol	11	0.72	46.07	9.38	65.53	9.40	0.02
3-*exo*-Bicyclo[3.2.1]octanol	12	0.61	31.29	11.11	50.82	11.60	0.49
3-*endo*-Bicyclo[3.2.1]octanol	13	2.00	26.61	15.79	50.82	11.60	−4.19
8-*exo*-Bicyclo[3.2.1]octanol	14	−0.60	30.31	12.09	46.64	15.78	3.69
8-*endo*-Bicyclo[3.2.1]octanol	15	1.10	28.74	13.66	46.64	15.78	2.12
2-*endo*-Bicyclo[3.2.1]octanol	16	0.30	30.66	11.74	49.15	13.27	1.53
2-*exo*-Bicyclo[3.2.1]octanol	17	0.96	29.66	12.74	49.15	13.27	0.53
9-Bicyclo[3.3.1]nonanol	18	0.86	35.54	12.05	54.29	13.32	1.27
2-Adamantanol	19	0.83	39.00	7.71	57.34	9.39	1.68
2-*exo*-Norbornanol	20	0.18[g]	19.92	17.29	38.87	18.36	1.07
2-*endo*-Norbornanol	21	1.00[g]	19.09	18.12	38.87	18.36	0.24
7-Norbornanol	22	−0.85	18.77	18.44	33.14	29.09	5.65
endo-5,6-Trimethylene-*exo*-2-norbornanol	23	0.38	18.73	27.98	38.45	28.28	0.30
endo-5,6-Trimethylene-*endo*-2-norbornanol	24	2.71	13.62	33.09	38.45	28.28	−4.81
endo-5,6-Trimethylene-*exo*-8-norbornanol	25	0.27[g]	19.25	27.46	39.91	26.82	−0.64
endo-5,6-Trimethylene-*endo*-8-norbornanol	26	1.67[g]	17.95	28.76	39.91	26.82	−1.94
Isoborneol	27	1.69[h]	36.59	23.79	60.12	20.28	−3.51
Borneol	28	1.40[h]	38.54	21.84	60.12	20.28	−1.56
3-*endo*-*endo*-Tetracyclo[$4.4.0.1^{2,5}.1^{7,10}$]dodecanol	29	3.31[i]	−5.79	56.81	22.02	49.02	−7.79
α-Isonopinol	30	1.43	13.32	38.95	36.75	35.54	−3.41
β-Isonopinol	31	1.48	12.73	39.54	36.75	35.54	−4.00
β-Nopinol	32	1.07	13.49	38.78	34.16	38.13	−0.65
α-Nopinol	33	2.25	11.26	41.01	34.16	38.13	−2.88
Isopinocampheol	34	1.40	18.09	41.13	41.47	37.77	−3.36
neo-Isopinocampheol	35	2.32	15.29	43.93	41.47	37.77	−6.16
Pinocampheol	36	1.28	20.08	39.14	41.97	37.27	−1.87
Cyclohexanol	37	0.00	36.99[6a]	1.05[6a]	55.32[6b]	2.79[6b]	1.74

[a] Rate constants relative to cyclohexanol in 80% (by volume) acetic acid, 0.01 *N* sulfuric acid at 25°. Values quoted from the literature refer to somewhat different conditions. [b] Calculated standard enthalpies of formation at 25°, in kcal/mol. [c] Strainless values according to Allinger.[6] [d] Δ strain = strain energy ($R_2C{=}O$) − strain energy (R_2CHCH_3), in kcal/mol. [e] In 75% acetic acid.[9] [f] In 0.25 *M* perchloric acid.[10] [g] In 75% acetic acid.[11] [h] In 30% acetic acid.[12] [i] In 40% acetic acid.[13]

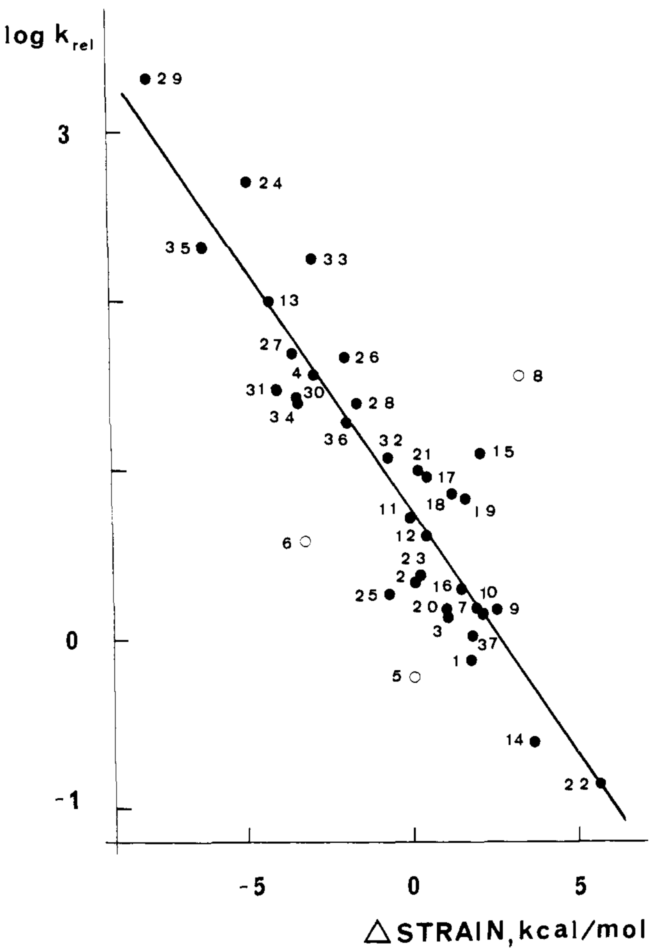

Figure 1. Plot of log k vs. Δ strain. Data from Table I. Slope: −0.3. Correlation coefficient 0.92. Points not included in the correlation are indicated with open circles.

parametrization was used in order to have a consistent set of parameters (see below). For the evaluation of the strain in the transition state we accept the hypothesis of a product-like transition state, and we assume that its energy should be related to that of the ketone. Calculations of ketone strain were made in the same way as the hydrocarbons with the Allinger force-field, which is also parametrized for carbonyl compounds.[6b] The calculations of 37 hydrocarbons and ketones, together with the oxidation rates of the respective alcohols are summarized in Table I. Figure 1 shows a plot of the oxidation rates (log k) against the strain difference ketone–alcohol (Δ strain). The straight line has a slope of −0.3 and a correlation coefficient of 0.92. The compounds **5**, **6**, and **8**, which deviate by more than 2 standard deviations (Sy = 0.37) from the straight line are not included in the correlation (see below).

The plot covers a rate range of 1 to 15000. The correlation coefficient of 0.92 is surprisingly high, and it seems to justify both our hypotheses, namely that alcohol strain reflects methyl strain, and that the properties of the ketone are reflected in the transition state. However, it is interesting to note that a difference of 15 kcal/mol in Δ strain corresponds only to a variation of 15000 in rates or ca. 5.7 kcal in enthalpies of activation. This could in part be due to a systematic overestimation of the alcohol strain by our use of the methyl analogues for the calculations. The more important part must, however, be due to the fact that either the strain of the alcohol has not fully disappeared or the strain of the ketone is not fully developed in the transition state.[12] There is good reason to believe that the nonbonded interactions of the alcohol are mostly, if not entirely, relieved.[9] The structure of the transition state must be such that this strain relief can occur, while the (angle-) strain in the ketone is only partially built up. Our approach does not allow more detailed conclusions concerning the structure of the transition state.

The exclusion of the compounds **5**, **6**, and **8** from the correlation can in part be justified. The entropies of activation for oxidation of tetramethylcyclobutanol (**8**) and di-*tert*-butylmethanol (**6**) differ considerably from the average value obtained for unhindered alcohols.[3] This indicates that other factors might contribute in these cases. Kwart suggested that sterically hindered alcohols such as **6** are oxidized by another mechanism than the unhindered ones.[15] Our calculations lead to a similar conclusion. In the case of isopropyl alcohol (**5**) it is likely that the ketone model does not sufficiently reflect the polar substituent effects operating in the reaction ($\rho^* = -1$[1]). If an appropriate correction for the different alkyl substitution is applied, isopropyl alcohol falls within the limits of 2 standard deviations.

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Formation of Ethyl Ketones through Sequential Insertion Reactions of Alkyl Tetracarbonylferrates

Sir:

We previously demonstrated the utility of $Na_2Fe(CO)_4$ in the preparation of anionic alkyl and acyl iron complexes.[1] These complexes have been shown to be useful intermediates for the preparation of aldehydes,[1] ketones,[2] and other carbonyl derivatives[3] from common alkylating agents. We now wish to describe a facile conversion of alkyl halides and tosylates to ethyl ketones through the alkylation of $Na_2Fe(CO)_4$ in the presence of ethylene (eq 1). Examples of this