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Formation of Tertiary 3-Nitro Allylic Alcohol by Condensation of 2-Chloroisobutyrophenone with Nitromethanide Anion: Estimation of *Gibbs* Free Enthalpies of Reaction in Solution for the Reaction Mechanism [1]

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Summary. The reaction of 2-chloroisobutyrophenones and nitromethanide anion gives stereoselectively (*E*)-3-nitro allylic alcohols. The *Gibbs* free enthalpies of reaction in *DMSO* for carbanion addition, epoxide formation, and rearrangement to 3-nitro allylic alcohol, as elementary steps for the reaction, were estimated from corresponding neutral gas reactions and using a thermodynamical approach to the transfer of gaseous compounds to *DMSO*. A criterion for assigning the sign of affinity of liquid compounds to *DMSO* was developed on the basis of the *Gibbs* enthalpies of liquefaction. The information obtained on reaction rate and thermodynamic viability of the steps indicates that carbanion addition is the rate-determining step.

Keywords. 2-Chloro ketones; Hydrogen bonds; Reaction *Gibbs* enthalpies; Reaction mechanisms; Thermodynamics.

Introduction

The tautomerisation of 3-nitro 1,2-epoxides which have a 3-hydrogen represents an approach to 3-nitro allylic alcohols (Scheme 1). Compounds of the former kind, prepared by epoxidation of 2,3-unsaturated nitroalkenes, have been rearranged to 3-nitro allylic alcohols by mild basic treatment [2]. Analogously, 2,3-epoxy oximes have been converted to 3-nitro allylic alcohols by oxidation under basic conditions [3]. 2-Haloisobutyrophenones together with secondary 1-nitro carbanions give rise

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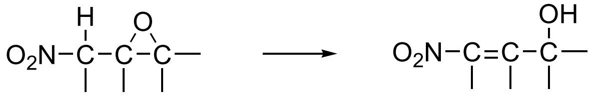
† In memory of Prof. Dr. *M. Ballester*, deceased on April 6, 2005



Scheme 1

to 3-nitro 1,2-epoxides [4], but the reaction cannot progress to 3-nitro allylic alcohols on account of the absence of a 3-hydrogen. Presently, we have proven that reaction of 2-chloroisobutyrophenone (**1a**) with nitromethanide anion actually goes on to the 3-nitro allylic alcohol **2a**, which represents a new and direct access to 3-nitro allylic alcohols.

Our interest in that reaction has been mainly about the mechanism, in particular, to find out the rate-determining step of the process. To this matter a dual approach was used. First, the reactions of 2-chloroisobutyrophenones, which bear selected substituents at the phenyl, were carried out with the nitromethanide anion to obtain experimental information on the electronic and steric effects of substituents on the rate of overall reaction. Then the *Gibbs* free enthalpies of reaction in solution (*DMSO*) for the elementary steps were estimated to disclose and compare the viabilities of these individual steps.

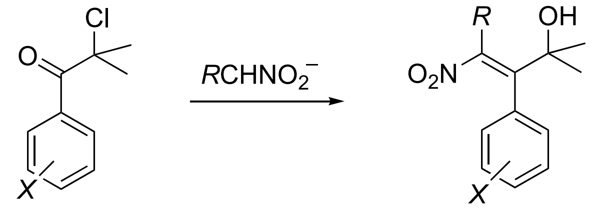
Such estimations of *Gibbs* enthalpies were undertaken realistically in respect of the elementary steps in solution, which, however, required the *Gibbs* energies of transfer of nonionised compounds in the gas state to solution as a difficult point. Facing the problem, we calculated approximate values of these *Gibbs* enthalpies of transfer to *DMSO* by a newly used thermodynamical method: by means of approximate values of *Henry*'s-law constants as constants that represent vapour pressures of liquids altered for the ideal solution state ($K \equiv p_{\mathrm{v}}^{\square} = p_{\mathrm{v}}/x, x \equiv$ mol fraction [5]); the unaltered vapour pressures for the undissolved compounds were estimated with standard methods.

The transfer of gaseous hydrogen chloride (leaving group in the reaction) has been approached dealing with hydrogen bonding in solution in an original way: the hydrogen-bonded compound of hydrogen chloride with Me_2SO ($Me_2SO\cdots HCl$) was treated as a liquid in *DMSO*. The additional *Gibbs* enthalpy for hydrogen bonding in the gas phase was estimated by the classic method of statistical thermodynamics. This simple model for the transfer of gaseous hydrogen chloride to *DMSO* proved to be adequate as pointed out by the calculated enthalpy of transfer.

Results and Discussion

Reaction of **1a**–**1f** with potassium nitromethanide in *HMPA* afforded **2a**–**2f**. The reactions were conducted to *ca*. 80% consumption of reactants, thus generally furnishing significant yields (Table 1). A test to *DMSO* as solvent instead of *HMPA* (using **1c**) resulted in a lower yield of alcohol, consistent with previous observations on the worse reactivity of 1-nitro carbanions and other types of carbanions in *DMSO* compared with *HMPA* [4b, 6].

The (*E*) configuration of **2a**–**2f** was established by means of N*O*E ^{1}H-NMR spectrometry, which indicated a close spatial relationship between the vinylic hydrogens and the isopropylic methyls. The stereoselectivity of the reaction is



1a: X = H
1b: X = 4'-*Me*O
1c: X = 4'-*Me*
1d: X = 2'-*Me*
1e: X = 4'-F
1f: X = 4'-NO_2

2a: R = H, X = H
2b: R = H, X = 4'-*Me*O
2c: R = H, X = 4'-*Me*
2d: R = H, X = 2'-*Me*
2e: R = H, X = 4'-F
2f: R = H, X = 4'-NO_2
3a: R = *Me*, X = 4'-*Me*
3b (Z): R = *Me*, X = 4'-*Me*

Scheme 2

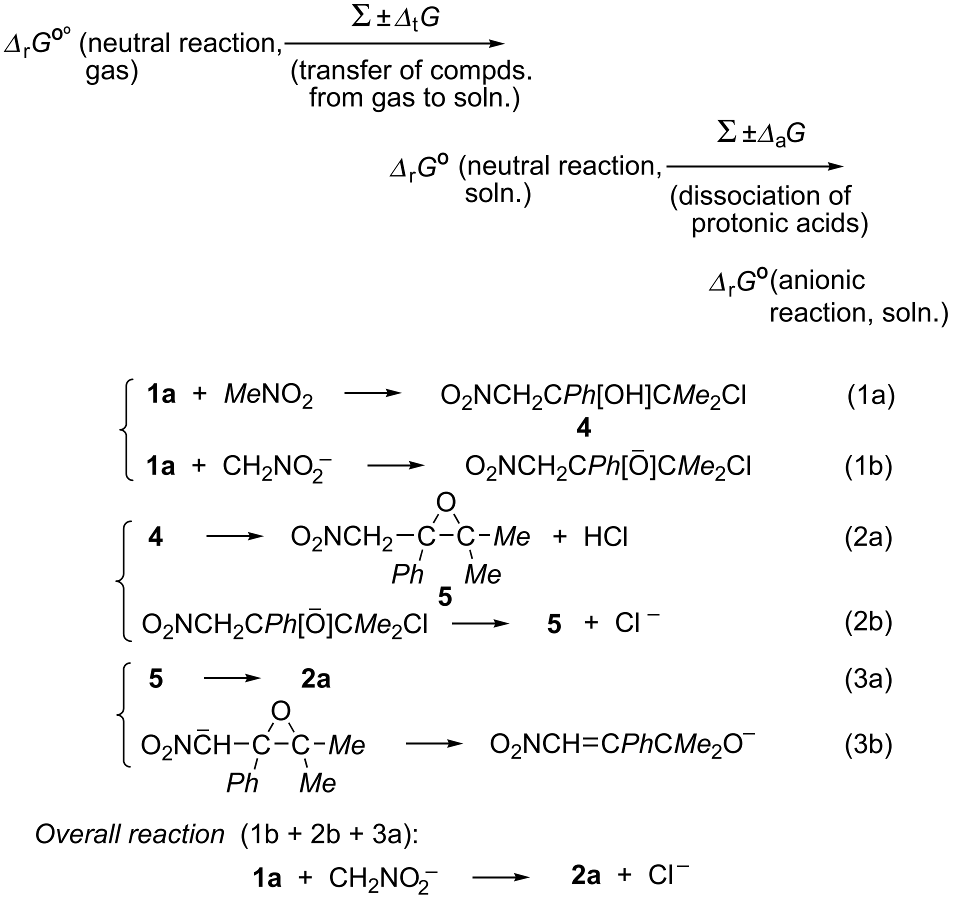
Table 1. Reaction of phenyl-substituted 2-chloroisobutyrophenones **1a–1f** with potassium nitromethanide in *HMPA* at room temperature

Substituent	t/h	Yield (%)
none	48	53
4′-*Me*O	93	44
4′-*Me*	48	51
2′-*Me*	72	28
4′-F	48	57
4′-NO_2	22	59

high: an (E):(Z) ratio of 97:3 was shown by a crude product by GLC-MS analysis. Stereoselectivity probably results from steric inhibition of resonance for the conjugated nitro group in the (Z)-isomer because of the neighbouring bulky 1-hydroxyisopropyl group, which renders the (E)-isomer. In support for this interpretation, reaction of **1c** with 1-nitroethanide anion resulted in the isomers **3a** and **3b** in a low stereoselectivity ((E):(Z) = 40:60) as the (Z)-isomer now cannot be circumvented on account of the substitution of methyl for the small hydrogen.

Compound **2d** provides a new example of restricted conformational mobility in branched-chain compounds [6c, 7]: **2d** is composed of the pair of enantiomers resulting from the noncoplanarity of the 2′-methylphenyl and vinylic moieties. Noncoplanarity occurs due to the sterically hindered rotation of the 2′-methylphenyl moiety; the existence of the enantiomers in solution was indicated by the NMR nonequivalence of the isopropylic methyls.

The data in Table 1 indicates that reaction rate increases with the electron-withdrawing strength of phenyl substituents and decreases with steric hindrance at the carbonylic carbon, which suggests that initial nucleophilic addition of nitromethanide anion to the carbonyl of **1a** is the rate-determining step of the reaction. An improved insight of the relevance of this step to reaction rate was achieved by means of the *Gibbs* enthalpies of reaction for the different steps.



Scheme 3

Estimation of Gibbs Free Enthalpies of Reaction in Solution for the Elementary Steps

The *Gibbs* enthalpies of reaction ($\Delta_r G^\circ$) in *DMSO* for the elementary steps of the reaction of parent 2-chloroisobutyrophenone (**1a**) and nitromethanide anion were estimated by the method shown in Scheme 3 for evaluating the *Gibbs* enthalpy of reaction for an anionic reaction in solution from the corresponding neutral reaction in the gas phase. *DMSO* was preferred as the solvent since it is a polar aprotic one as the experimentally used *HMPA* is, and since pK_a values in *DMSO* are available (for $\Delta_a G$).

The $\Delta_r G^\circ$ values in the gas phase for Eqs. (1a), (2a), and (3a) were estimated with *Benson*'s method for the enthalpy of formation and the entropy of a compound [8]. As **4**, **5**, and **2a** are compactly branched, repulsive interactions in staggered conformations in **4** and **2a**, and between *cis* groups in **5** were specially accounted for ($\delta_f H^\circ \approx 4\,\mathrm{kJ\,mol^{-1}}$). The resulting $\Delta_r G^\circ$ values are collected in Table 2 ($\Delta_r G^\circ$ (gas)).

In order to estimate the *Gibbs* enthalpies of transfer of compounds ($\Delta_t G$) from the gas phase to ideal solution in *DMSO* the three-stage method shown in Scheme 4 was devised ($x \equiv$ mol fraction, $c \equiv$ volume concentration; HCl will be discussed

Table 2. Estimated *Gibbs* free enthalpies of reaction in the gas phase and in *DMSO* at 298 K about the elementary steps of the reaction of 2-chloroisobutyrophenone and nitromethanide anion

Step	$\Delta_r G^\circ/\mathrm{kJ\,mol^{-1}}$ (gas)[a]	$\Delta_r G^\circ/\mathrm{kJ\,mol^{-1}}$ (*DMSO*)[b,c]
(1a)	15.1	1.71 [0.502]
(1b)		57.5 [8.49×10^{-11}]
(2a)	86.2	92.1 [7.39×10^{-17}]
(2b)		−56.7 [8.53×10^{9}]
(3a)	−21.1	−35.5 [1.65×10^{6}]
(3b)		20.3 [2.78×10^{-4}]
overall reaction		−34.7 [1.20×10^{6}]

[a] Ideal gas state of each species at 1 atm; [b] ideal solution state of each species in *DMSO* at 1 mol dm^{-3}; [c] corresponding equilibrium constant in brackets

$$\begin{tikzcd}
R\mathrm{H}\ (\mathrm{gas},\ p_g) \arrow[r, "\Delta_l G"] & R\mathrm{H}\ (\mathrm{liq.},\ p_v) \arrow[dr, "\Delta_{\mathrm{soln}} G^\square"] \arrow[ddrr, dashed, swap, "\Delta_{\mathrm{soln}} G"] & & \\
 & & R\mathrm{H}\ (\mathrm{soln.},\ p_v^\square,\ x = 1) \arrow[dr, "\Delta_{\mathrm{diln}} G"] & \\
 & & & R\mathrm{H}\ (\mathrm{diluted\ soln.},\ x < 1,\ c)
\end{tikzcd}$$

$$\Delta_l G = RT \ln \frac{p_v}{p_g} \qquad (4)$$

$$\left.\begin{aligned}
\Delta_{\mathrm{soln}} G^\square &= RT \ln \frac{p_v^\square}{p_v} && (5)\\
\Delta_{\mathrm{diln}} G = -T\Delta_{\mathrm{diln}} S &= RT \ln \frac{x_2}{x_1} \approx RT \ln \frac{c\, M_{\mathrm{solv}}}{\rho_{\mathrm{solv}}} && (6)
\end{aligned}\right\}\ \Delta_{\mathrm{soln}} G = \Delta_{\mathrm{soln}} G^\square + \Delta_{\mathrm{diln}} G$$

$$\Delta_t G = \Delta_l G + \Delta_{\mathrm{soln}} G \approx RT \ln \frac{p_v^\square\, c\, M_{\mathrm{solv}}}{p_g\, \rho_{\mathrm{solv}}}$$

Scheme 4

apart). Firstly, the *Gibbs* enthalpies of liquefaction ($\Delta_l G$, from a 1-atm gas pressure in correspondence to the precedent $\Delta_r G^\circ$ values) were calculated by Eq. (4) using estimated vapour pressures for the compounds. Such p_v values (at 25°C) were obtained by p_v-T correlation using *Antoine*'s equation [9], for which the normal boiling points of the compounds were previously estimated with *Meissner*'s equation [9]. The p_v values and the resulting $\Delta_l G$ values are collected in Table 3. It is worth noting in relation to the next point that the *Gibbs* enthalpy of liquefaction is a gauge for the attractive interaction in the liquid state (the cohesion energy [10]) despite the variation of its value with the gas-phase pressure; this variation is a consequence of merely the spatial entropy of the gas-phase (not the internal energy

Table 3. Estimated vapour pressures and *Gibbs* free enthalpies of liquefaction, solution in *DMSO*, and overall transfer from the gas phase to *DMSO* at 298 K

Compound	p_{v}/atm	$\Delta_{\mathrm{l}}G$/kJ mol$^{-1\,\mathrm{a}}$	$\Delta_{\mathrm{soln}}G$/kJ mol$^{-1\,\mathrm{b}}$	$\Delta_{\mathrm{t}}G$/kJ mol$^{-1\,\mathrm{c}}$
1a	$1.07 \times 10^{-5\,\mathrm{d}}$	−28.4	−0.839	−29.2
*Me*NO$_2$	$4.73 \times 10^{-2\,\mathrm{e}}$	−7.57	−0.839	−8.41
4	1.67×10^{-7}	−38.7	−12.3	−51.0
5	8.39×10^{-7}	−34.7	−0.839	−35.5
2a	2.58×10^{-7}	−37.6	−12.3	−49.9
Me$_2$SO	$7.90 \times 10^{-4\,\mathrm{e}}$	−17.7		
Me$_2$SO · HCl	1.58×10^{-3}	−16.0	−6.55	−22.6

[a] From the ideal gas state at 1 atm; [b] from the liquid state to the ideal 1 mol dm^{-3} solution; [c] from the ideal gas state at 1 atm to the ideal 1 mol dm^{-3} solution; [d] Ref. [14a]; [e] Ref. [17]

or the enthalpy) and if this interference is removed by compressing the gas phase to the same volume that the liquid has the value becomes even more negative.

Secondly, and as a difficult point, an estimate of the *Gibbs* enthalpies of solution for the compounds as liquids in *DMSO* was made in respect of the ideal solution state at unity mol fraction ($\Delta_{\mathrm{soln}}G^{\square}$). This special kind of values stand for *Gibbs* enthalpies for the interaction between solute and solvent (both enthalpy and entropy) but excluding the spatial entropy of solution, which represents a materially unattainable solution state. However, corresponding $p_{\mathrm{v}}^{\square}$ values may experimentally be obtained by limit *Henry*'s law for infinite dilution [5]. With $p_{\mathrm{v}}^{\square}$ values $\Delta_{\mathrm{soln}}G^{\square}$ values can be calculated by Eq. (5). Stabilisation of a liquid upon solution implies a decrease in its vapour pressure ($p_{\mathrm{v}}^{\square} < p_{\mathrm{v}}$) and conversely for unstabilisation; else, differential interaction may not occur (null enthalpy and entropy of interaction) and the vapour pressure does not change ($p_{\mathrm{v}}^{\square} = p_{\mathrm{v}}$, *i.e.*, *Raoult*'s law instead of *Henry*'s law).

For ascribing the directions of such changes for the present compounds the following empirical criterion based on the *Gibbs* enthalpies of liquefaction for the compounds and *DMSO* was employed. Thus, the component of the solution that would be prevalent as to *Gibbs* enthalpy of cross-interaction would be that whose $\Delta_{\mathrm{l}}G$ value lies closer to the *geometric mean* of the values for the two components; then the prevalent component would determine either stabilisation or unstabilisation for itself and the subordinate component (shared affinity or incompatibility to the mutual solution, attraction or repulsion regarding the solution) *according as its* $\Delta_{\mathrm{l}}G$ *value lies underneath or exceeds that for the subordinate component.*

Application of the criterion gives unstabilisation for ketone **1a**, nitromethane, and epoxide **5**, and stabilisation for the alcohols **4** and **2a**. These assignments resulting from general energy considerations may be considered consistent with specific characteristics for the compounds and *DMSO* such as lipophilicity and hydrogen bonding.

As to the magnitudes of the changes a variation of one order of magnitude in the vapour pressure was assumed in a general way ($p_{\mathrm{v}}^{\square}/p_{\mathrm{v}}$ 0.1 or 10). This represents a moderately large alteration as judged from the classical behaviour of liquid mixtures [5] and results in a $\Delta_{\mathrm{soln}}G^{\square}$ value of ± 5.71 kJ mol^{-1}. This outcome value is generally smaller than the $\Delta_{\mathrm{l}}G$ values (see Table 3) and thus may be taken to justify the precedent criterion based on primordial *Gibbs* enthalpies of liquefaction. The cohesion energy of the compounds as liquids, as appraised by their *Gibbs* enthalpies of liquefaction, appears to be a primary factor for the affinity in their mixtures.

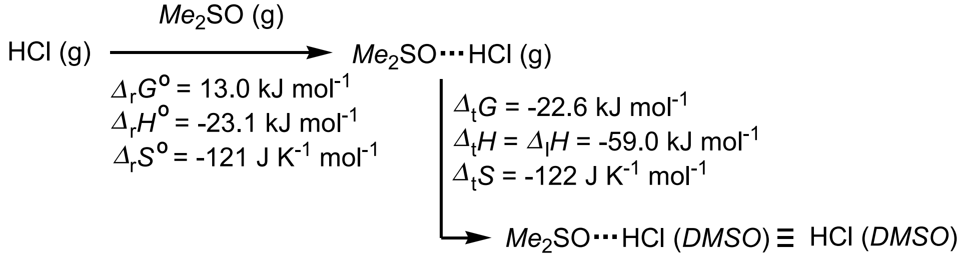
Finally and for suitability to pK_a values in the molarity scale, the $\Delta_{soln}G^{\square}$ values were corrected for unity molarity (to $\Delta_{soln}G$ values) adding the *Gibbs* enthalpy of dilution ($\Delta_{diln}G$, a term derived only from the spatial entropy since ideal solutions are being dealt with; Eq. (6)). The conversion of mol fraction to molarity cannot be made in an exact way since the molar volumes of the compounds in the states determined by the $p_v^{\square}$ values are not known. However, the assumption of taking the molar volume of *DMSO* for those of the compounds (as implied in Eq. (6)) should not result in a too large error for unity molarity ($x \approx 0.07$). Thus the $\Delta_{diln}G$ value is $-6.55\,kJ\,mol^{-1}$. The added-up $\Delta_{soln}G$ values and the final Δ_tG values are shown in Table 3. These data show that the main term for the *Gibbs* enthalpy of transfer of the compounds is the *Gibbs* enthalpy of liquefaction, not that of solution. That is, the cohesion energy of the compounds as liquids overrides their solution energy.

Transfer of Hydrogen Chloride to DMSO

The remaining transfer concerning HCl was approached in the stepwise and more detailed manner shown in Scheme 5, now referring to hydrogen bonding. Our approximation supposes that HCl is present in *DMSO* as just the simple hydrogen-bonded solvate. The *Gibbs* enthalpy of reaction for hydrogen bonding in the gas phase was estimated by the standard statistical-thermodynamics method for the internal energy and the entropy [11] (ideal gas state at 1 atm and 298 K, the details of the calculation are given under *Methods of Calculation*). As expected, $Me_2SO \cdot HCl$ does not actually exist as a gas under normal conditions ($K = 5.28 \times 10^{-3}$).

For the transfer of $Me_2SO \cdot HCl$ to solution the normal boiling point for the compound was obtained considering it an ordinary covalent compound for the usual *Meissner* equation (bp 176°C *vs.* 189°C for *DMSO*). Then the solution of $Me_2SO \cdot HCl$ as a liquid in *DMSO* was assigned to obey *Raoult*'s law ($p_v^{\square} = p_v$) inasmuch as the two liquids are almost equivalent in terms of the criterion referred to above (see the implicated Δ_lG values in Table 3). The *Gibbs* enthalpy of transfer for HCl amounts to $-9.60\,kJ\,mol^{-1}$.

As a test for this approach we additionally calculated the enthalpy of transfer of HCl, which simply equals the enthalpy of hydrogen bonding (Δ_rH°) plus the



Scheme 5

enthalpy of liquefaction of $Me_2SO\cdot HCl$ ($\Delta_l H$) since the enthalpy of solution of $Me_2SO\cdot HCl$ as a liquid in *DMSO* is zero recalling *Raoult*'s law. The enthalpy of liquefaction of $Me_2SO\cdot HCl$, being as it is the reverse of the enthalpy of vapourisation, was obtained by means of the entropy of vapourisation ($\Delta_v H = T\Delta_v S$); this was estimated with recently reported Eq. (7) [10] (using ρ_{DMSO} as a substitute for $\rho_{Me_2SO\cdot HCl}$, $\Delta_v S = 198\,\mathrm{J\,K^{-1}\,mol^{-1}}$ (298 K)). The requested enthalpy of transfer for HCl, *i.e.* $-82.1\,\mathrm{kJ\,mol^{-1}}$, is comparable to an experimental heat of solution of HCl in *DMSO* of $-72.7\,\mathrm{kJ\,mol^{-1}}$ [12].

$$\Delta_v S \approx 2R\ln\frac{\rho_l RT}{Mp_v} \qquad (7)$$

Applying the *Gibbs* enthalpy of transfer for HCl in addition to those for the previous compounds, the *Gibbs* enthalpies of reaction in *DMSO* for neutral Eqs. (1a), (2a), and (3a) were obtained (they are collected in Table 2). To obtain the final $\Delta_r G^\circ$ values in *DMSO* for anionic Eqs. (1b), (2b), and (3b), literature *pK*a values in *DMSO* for $MeNO_2$, benzyl alcohol, and HBr [12, 13] were used for $MeNO_2$ and nitro compound **5**, the alcohols **4** and **2a**, and HCl; the final $\Delta_r G^\circ$ values are shown in Table 2.

Significance of the Data to Reactivity

Comparison of the $\Delta_r G^\circ$ values in the Table for neutral Eqs. (1a), (2a), and (3a) in the gas phase with these values in *DMSO* shows that *DMSO* as solvent is not determinant for viability of the reactions (the sign of the *Gibbs* enthalpy is not changed in solution). However, Eq. (1a) becomes reversible in solution on account of the affinity of *DMSO* to the product alcohol, reversibility which is consistent with aldol additions.

The actual addition of nitromethanide anion to **1a** (Eq. (1b)) is in itself unfavourable because of a low basicity of the anion with respect to the resulting alkoxide anion (compare the $\Delta_r G^\circ$ value with that for Eq. (1a)). On the contrary, the ring closure of alkoxide anion to epoxide (Eq. (2b)) is made viable by a lower basicity of released chloride ion, similarly to the alkylation of carbanions by alkyl halides [6c].

The force for overall reaction is neatly afforded by the rearrangement of 3-nitro 1,2-epoxide to 3-nitro allylic alcohol (Eq. (3a)) since the energy of Eq. (2b) is canceled by Eq. (1b). The $\Delta_r G^\circ$ value for rearrangement of epoxy-nitroalkane anion (Eq. (3b)), which is the actually operative rearrangement, serves to disclose that is however an unlikely reaction, by reason again of the weaker basicity of nitroalkane anion with respect to alkoxide ion. To-and-fro proton transfers yield the energy to the overall rearrangement.

The Rate-determining Step

The addition of nitromethanide anion and the rearrangement of epoxy-nitroalkane anion (Eqs. (1b) and (3b)) were considered to the rate-determining step as they lack force according to the $\Delta_r G^\circ$ values. It was considered unlikely that energetically disposed Eq. (2b) would control reaction rate and, moreover, the above-mentioned proton transfers should be fast.

The previously referred-to observation of an increase in reaction rate with the electrophilicity of the carbon attached to the phenyl is in agreement with Eq. (1b). However, it is not so for Eq. (3b) since in this case an electrophilic carbon arises instead of being destroyed; the consequent increment of electron density indicated by the rate data for the reactive centre is not to Eq. (3b) but to Eq. (1b). These arguments support an ascription of the rate-determining step to initial addition of nitromethanide anion to **1a.**

Experimental

HMPA was distilled from CaH_2 under reduced pressure and was stored over 3 Å molecular sieves under N_2. *Me*NO_2 and *Et*NO_2 were distilled under reduced pressure. The 2-chloroisobutyrophenones **1a** [14a], **1b** [14b], **1e** [14c], and **1f** [4b] were prepared by literature procedures. All new compounds gave satisfactory elemental analyses.

2-Chloro-4′-methylisobutyrophenone (**1c**, $C_{11}H_{13}ClO$)
A mixture of 5.0 g 4′-methylisobutyrophenone [15] (31 mmol) and 6.2 g SO_2Cl_2 (46 mmol) was allowed to react for 48 h. Unreacted SO_2Cl_2 was then evaporated under reduced pressure and the residue was purified by *Kugelrohr* distillation (oven temp. 50°C, 0.1 Torr) to give 4.0 g (65%) **1c** as a liquid; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 1.88$ (s, 6H), 2.41 (s, 3H), 7.24 (d, $J = 8.1$ Hz, 2H), 8.08 (d, $J = 8.1$ Hz, 2H) ppm.

2-Chloro-2′-methylisobutyrophenone (**1d**, $C_{11}H_{13}ClO$)
It was prepared similarly to **1c** using 2′-methylisobutyrophenone [16] (reaction temp. 70°C, reaction time 17 h); yield 56%; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 1.82$ (s, 6H), 2.29 (s, 3H), 7.26 (m, 3H), 7.53 (d, $J = 7.9$ Hz, 1H) ppm.

*Representative Procedure for **2a–2f**: (E)-2-Methyl-4-nitro-3-phenyl-3-buten-2-ol*
(**2a**, $C_{11}H_{13}NO_3$)
To a stirred solution of 130 mg *t-Bu*OK (1.16 mmol) in 1 cm^3 *HMPA* under N_2 was slowly added 66 mg *Me*NO_2 (1.1 mmol) in 1 cm^3 *HMPA*, followed by 197 mg **1a** (1.08 mmol) in 1 cm^3 *HMPA*. After 48 h, H_2O was added and the mixture was extracted with *Et*$_2$O. The ethereal extract was carefully washed with H_2O, dried (Na_2SO_4), and evaporated under reduced pressure. The crude product obtained was purified by TLC (silica gel, benzene/*AcOEt* 18/1, *Et*$_2$O as eluent) to give 119 mg (53%) **2a** as an oil; IR (film): $\bar{\nu} = 3450$ (OH), 1635 (w, C=C), 1525 (NO_2 asym. stret.), 1350 (NO_2 sym. stret.) cm^{-1}; UV-Vis (*Et*OH): $\lambda_{max}(\varepsilon) = 213$ (10800, conjd. *Ph*), 237 (7660, conjd. NO_2) nm (dm^3 mol^{-1} cm^{-1}); ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.42$ (s, 6H, C*Me*$_2$), 1.81 (br s, 1H, OH), 7.13 (m, 2H; 2′-, 6′-H), 7.38 (m, 3H; 3′-, 4′-, 5′-H), 7.47 (s, 1H, 4-H) ppm; ^{13}C NMR ($CDCl_3$, 50 MHz): $\delta = 28.8$, 76.4, 127.5, 128.25, 128.30, 133.0, 136.0, 156.4 (3-C) ppm; MS (70 eV): m/z (%) = 207 (2, M$^+$), 190 (21, M$^+$–OH), 160 (4, M$^+$–HNO_2).

(E)-3-(4′-Methoxyphenyl)-2-methyl-4-nitro-3-buten-2-ol (**2b**, $C_{12}H_{15}NO_4$)
Reaction time 93 h; purification by column chromatography (silica gel, petroleum-ether/*AcOEt* 9/1); yield 44%; mp 47–49°C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.42$ (s, 6H), 1.75 (s, 1H), 3.83 (s, 3H), 6.92 (d, $J = 8.9$ Hz, 2H), 7.05 (d, $J = 8.9$ Hz, 2H), 7.47 (s, 1H) ppm.

(E)-2-Methyl-3-(4′-methylphenyl)-4-nitro-3-buten-2-ol (**2c**, $C_{12}H_{15}NO_3$)
Reaction time 48 h; purification by column chromatography (silica gel, petroleum-ether/*AcOEt* 9/1); yield 51%; mp 72–73°C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.43$ (s, 6H, C*Me*$_2$), 1.87 (s, 1H), 2.40 (s, 3H), 7.03 (d, $J = 7.7$ Hz, 2H), 7.22 (d, $J = 7.7$ Hz, 2H), 7.50 (s, 1H, 3-H, N*O*E by C*Me*$_2$) ppm.

(E)-2-Methyl-3-(2′-methylphenyl)-4-nitro-3-buten-2-ol (**2d**, $C_{12}H_{15}NO_3$)
Reaction time 72 h; purification by column chromatography (silica gel, petroleum-ether/*Ac*O*Et* 9/1); yield 28%; mp 49–50°C; ^{1}H NMR (CDCl$_3$, 300 MHz): $\delta = 1.39$ (s, 3H, C(CH$_3$)C*H*$_3$), 1.52 (s, 3H, C(CH$_3$)C*H*$_3$), 1.75 (s, 1H), 2.26 (s, 3H), 7.00 (d, $J = 7.5$ Hz, 1H), 7.25 (m, 3H), 7.51 (s, 1H) ppm; ^{13}C NMR (CDCl$_3$, 50 MHz): $\delta = 20.2$, 28.9 (C(CH$_3$)*C*H$_3$), 29.4 (C(CH$_3$)*C*H$_3$), 73.6, 125.4, 127.0, 128.4, 130.4, 133.1, 136.0, 136.4, 156.1 ppm.

(E)-3-(4′-Fluorophenyl)-2-methyl-4-nitro-3-buten-2-ol (**2e**, $C_{11}H_{12}FNO_3$)
Reaction time 48 h; purification by recrystallisation (petroleum-ether/CH$_2$Cl$_2$); yield 57%; mp 86–87°C; ^{1}H NMR (CDCl$_3$, 300 MHz): $\delta = 1.42$ (s, 6H), 1.72 (s, 1H), 7.10 (d, $J = 1.0$ Hz, 2H), 7.12 (s, 2H), 7.49 (s, 1H) ppm.

(E)-2-Methyl-4-nitro-3-(4′-nitrophenyl)-3-buten-2-ol (**2f**, $C_{11}H_{12}N_2O_5$)
Reaction time 22 h; purification by recrystallisation (petroleum-ether/CH$_2$Cl$_2$); yield 59%; mp 143–146°C; ^{1}H NMR ((CD$_3$)$_2$SO, 300 MHz): $\delta = 1.26$ (s, 6H), 5.66 (s, 1H), 7.49 (d, $J = 8.8$ Hz, 2H), 7.54 (s, 1H), 8.25 (d, $J = 8.8$ Hz, 2H) ppm.

(E)-, (Z)-2-Methyl-3-(4′-methylphenyl)-4-nitro-3-penten-2-ols (**3a**, **3b**, $C_{13}H_{17}NO_3$)
The geometrical isomers were obtained from reaction of **1b** with *Et*NO$_2$ working similarly to the procedure for **2a**–**2f**; reaction time 72 h; the isomers were separated from each other by TLC (silica gel, petroleum-ether/*Ac*O*Et* 9/1, *Et*$_2$O as eluent, **3a** at higher R_f).

Isomer **3a**: yield 7%; mp 114–123°C; ^{1}H NMR (CDCl$_3$, 500 MHz): $\delta = 1.36$ (s, 6H, C*Me*$_2$), 1.83 (s, 3H, C=C*Me*), 1.86 (s, 1H, OH), 2.37 (s, 3H, 4′-*Me*), 7.04 (d, $J = 7.9$ Hz, 2H, 2′-, 6′-H), 7.20 (d, $J = 7.9$ Hz, 2H, 3′-, 5′-H) ppm; ^{13}C NMR (CDCl$_3$, 125 MHz): $\delta = 19.4$, 21.2, 29.5, 73.7, 128.3, 129.3, 133.6, 137.9, 140.7, 144.2 ppm.

Isomer **3b**: yield 11%; mp 97–100°C; ^{1}H NMR (CDCl$_3$, 500 MHz): $\delta = 1.37$ (s, 6H), 1.61 (s, 1H), 2.31 (s, 3H), 2.54 (s, 3H, C=C*Me*, N*O*E by 2′-, 6′-H), 6.98 (d, $J = 7.9$ Hz, 2H, 2′-, 6′-H), 7.10 (d, $J = 7.9$ Hz, 2H) ppm; ^{13}C NMR (CDCl$_3$, 50 MHz): $\delta = 17.5$, 21.2, 30.3, 73.0, 128.4, 128.8, 133.0, 137.8, 141.7, 149.4 ppm.

Methods of Calculation

For the $\Delta_r G^\circ$ values in the gas phase (Table 2) the enthalpies of formation and the entropies of *Me*NO$_2$ and HCl were available and those of the other compounds were obtained by summation of *Benson* contributions of atomic groups [8]; involved symmetry numbers: $n = 18$ (**1a**), 36 (**4**, **5**, **2a**). The enthalpic contribution ($\delta_f H^\circ$) for O$_2$NCH= was found out subtracting the contribution of H$_2$C= from an approximate enthalpy of formation of H$_2$C=CHNO$_2$ (54 kJ mol^{-1}, obtained from the enthalpies of formation of H$_2$C=CH$^\bullet$ and NO$_2$, and the enthalpy of dissociation for the C–NO$_2$ bond in H$_2$C=C*Me*NO$_2$ [17], this increased by 8 kJ mol^{-1} to offset the substitution of *Me* for H): $\delta_f H^\circ = 28$ kJ mol^{-1} (O$_2$NCH=). Steric corrections: $\delta_f H^\circ = 2.5$ (**5**, *cis* interact.), 4.2 (**2a**, stagg. conform.), 6.7 (**4**, stagg. conform.) kJ mol^{-1}; $\delta S^\circ = 6.7$ J K^{-1} mol^{-1} (**5**, *cis* interact.). The entropy of mixing of enantiomers (*R*ln2) was included for **4** and **5**.

For the estimation of p_v values (Table 3) by p_v-T correlation the following normal boiling points were estimated with *Meissner*'s equation [9]: bp = 176 (*Me*$_2$SO · HCl, treated as an ordinary covalent compound), 310 (**5**), 335 (**2a**), 343°C (**4**).

For the potential energy of hydrogen bonding ($\delta_r U_{pot}$) for *Me*$_2$SO · HCl (concerning the $\Delta_r H^\circ$ value in Scheme 5) a literature value for H$_3$PO · HCl was adopted (-27.7 kJ mol^{-1}) [18]. The vibrational energy of bonding ($\delta_r U_{vib}{}^\circ$) was attributed entirely to the five vibrational degrees of freedom rised by bonding, to each of which a frequency of 6×10^{12} Hz was assigned (representing *ca.* 2/5 of the zero-point vibrational energy of hydrogen bonding for H$_3$PO · HCl, $\varepsilon_{vib}{}^0 = h\gamma/2$); the $\delta_r U_{vib}{}^\circ$ value was obtained from this frequency together with the formula of statistical thermodynamics for the energy of a harmonic oscillator [11] at 298 K: $\delta_r U_{vib}{}^\circ = 13.3\,\mathrm{kJ\,mol^{-1}}$. The rotational and translational energies of bonding, corresponding to a decrease of two and three degrees of freedom, respectively, were summed up in respect of the principle of equipartion of the energy as usual and for 298 K: $\delta_r U_{rot}{}^\circ = -2.48\,\mathrm{kJ\,mol^{-1}}$; $\delta_r U_{tr}{}^\circ = -3.72\,\mathrm{kJ\,mol^{-1}}$.

The values of the vibrational, rotational, and translational entropies of hydrogen bonding ($\delta_r S_{vib}{}^\circ$, $\delta_r S_{rot}{}^\circ$, $\delta_r S_{tr}{}^\circ$) were obtained from the above frequency, the moments of inertia of the molecules (HCl, Me_2SO, Me_2SO · HCl), and the molecular masses and a 1-atm pressure together with the usual formula of statistical thermodynamics for the entropy of a harmonic oscillator, a rigid rotator or a monoatomic gas [11] at 298 K; the moments of inertia of Me_2SO and Me_2SO · HCl were estimated by *Hirschfelder-Wilson* algorithm [11a, 19]: $I_B = 2.69 \times 10^{-47}\,\mathrm{kg\,m^2}$ (HCl); $I_A I_B I_C = 3.25 \times 10^{-135}$ (Me_2SO), 1.58×10^{-133} (Me_2SO · HCl) $\mathrm{kg^3\,m^6}$; $\delta_r S_{vib}{}^\circ = 44.6\,\mathrm{J\,K^{-1}\,mol^{-1}}$; $\delta_r S_{rot}{}^\circ = -17.0\,\mathrm{J\,K^{-1}\,mol^{-1}}$; $\delta_r S_{tr}{}^\circ = -149\,\mathrm{J\,K^{-1}\,mol^{-1}}$.

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