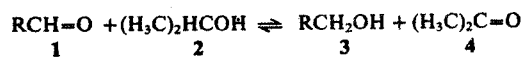


**Thermally Induced Redox Reaction of Carbonyl Compounds and Alcohols in a Radical Chain Reaction: Comproportionation to Two Hydroxyalkyl Radicals**

By Dietmar Malwitz and Jürgen O. Metzger\*

The reduction of carbonyl compounds to alcohols is a very important reaction in organic chemistry.<sup>[1]</sup> But reductions with alcohols also play an important role and, commencing with the Meerwein-Ponndorf-Verley reduction, numerous variants have been described in the literature.<sup>[2]</sup> Ponndorf<sup>[3]</sup> pointed out in his classical work more than half a century ago the possibility of a thermally-induced redox reaction, but so far no mechanism has been described for this reaction. Two routes are conceivable: a) a comproportionation of carbonyl compound and alcohol to two hydroxyalkyl radicals and their further reaction to give the products, or b) a pericyclic reaction in which two hydrogen atoms are transferred from the alcohol to the carbonyl group in one step.

We have found that aldehydes 1 are reduced by 2-propanol 2 in a thermal reaction to the alcohols 3, whereby 2 is oxidized to acetone 4.<sup>[4]</sup> Instead of 2, methanol, primary alkyl alcohols and benzyl alcohols can also be used, whereas tertiary alcohols are not reducing.



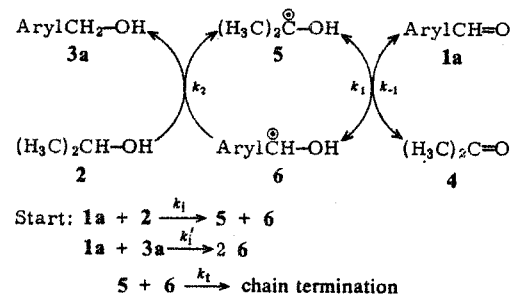
a, R = 4-*i*-Pr-C<sub>6</sub>H<sub>4</sub>; b, R = C<sub>6</sub>H<sub>5</sub>

To elucidate the reaction mechanism we investigated the kinetics of the reaction of 2 and 4-isopropylbenzaldehyde 1a. Preliminary experiments showed that the reaction proceeds as a radical chain reaction: active carbon as radical trapping agent completely inhibits it; radical formers such as di-*tert*-butyl peroxide<sup>[5]</sup> or atmospheric oxygen accelerate it; as soon as the radical formers are consumed, the rate is the same as for the reaction without radical former. Under the conditions used for the kinetic measurements,<sup>[6]</sup> no secondary reactions were observed. The rate law for the reaction is described by equation (1), and the Arrhenius equation is fulfilled quite well in the temperature range investigated (Eq. (2),  $\Theta = 2.303 [RT \text{ kJmol}^{-1}]$ ).

$$-\frac{d[1a]}{dt} = \frac{d[3a]}{dt} k_{exp}[1a][2] \quad (1)$$

$$\log k_{exp} = 7.56 \pm 0.05 - (125 \pm 1)/\Theta \quad (2)$$

With deuteriated 2, an almost temperature-independent kinetic isotope effect is obtained, both when 2 is *O*-deuteriated ( $k_H/k_D = 2.06$ ), as well as *C*-deuteriated ( $k_H/k_D = 2.61$ ). For perdeuteriated 2 one obtains  $k_H/k_D = 5.34$ .<sup>[7]</sup> A Hammet correlation gave a reaction constant  $\rho = -0.62$ .<sup>[8]</sup>



Aryl = 4-*i*-Pr-C<sub>6</sub>H<sub>4</sub>

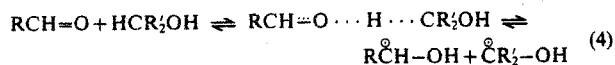
Scheme 1.

$$-\frac{d[1a]}{dt} = \frac{d[3a]}{dt} = (k_1/k_3)^{1/2} \cdot (k_1/k_{-1})^{1/2} \cdot k_2[1a][2] \quad (3)$$

All results are consistent with a radical chain reaction as shown in Scheme 1: Chain initiation starts with the formation of the hydroxyalkyl radicals 5 and 6 from 1a and 2. The radical 5 is converted by H-transfer to 1a into the oxidation product 4, a reaction which is already known from the analogous photochemical<sup>[10]</sup> and radical-induced<sup>[5]</sup> reactions, and which here is thermodynamically controlled; further reaction of the radical 6 to give the product 3a by H-abstraction from 2 is the rate-determining step in the radical chain reaction.

Reaction of the two chain-carrying radicals 5 and 6 with each other leads to chain termination. After a relatively small conversion of ca. 5%, the comproportionation of 3a and 1a dominates as initiation reaction, since this reaction requires an activation energy about 45 kJ mol<sup>-1</sup> less than the original initiation reaction because of the formation of two hydroxybenzyl radicals 6.<sup>[11]</sup>

With this mechanism the experimental rate law is easy to simulate [Eq. (3)], both regarding the reaction order [Eq. (1)] as well as the Arrhenius parameter [Eq. (2)].<sup>[13]</sup> The isotope effect<sup>[14]</sup> and the reaction constant<sup>[15]</sup> are also consistent with this mechanism, a mechanism which is remarkable in two ways: 1) It describes a radical chain reaction with a "kinetic chain length" of ca. 10<sup>7</sup> at 200 °C.<sup>[16]</sup> In contrast, the analogous photochemical<sup>[10]</sup> and the radical-induced<sup>[5]</sup> reduction are not chain reactions. 2) The initiation reaction is the back reaction of the known disproportionation of hydroxyalkyl radicals and thus is analogous to the comproportionation of alkanes and alkenes to alkyl radicals.<sup>[17]</sup> Decisive is the "molecule-induced" homolysis<sup>[18]</sup> of a C-H bond [Eq. (4)] with a markedly reduced activation energy in comparison to the monomolecular bond cleavage.



In comparison, a pericyclic transfer of two H-atoms would be considerably slower<sup>[19]</sup> and, in view of the observed kinetics, highly unlikely, since according to equation (4) a radical chain reaction can be initiated. Our results are consistent with equation (4) most likely being the initiation reaction of the radical chain reaction.

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- [1] Houben-Weyl-Müller: *Methoden der organischen Chemie*, Vol. VI, 1b, Thieme, Stuttgart 1984.
- [2] a) K. Krohn in [1], p. 289; b) P. Margarethe, *ibid.* p. 432.
- [3] W. Ponndorf, *Angew. Chem.* 39 (1926) 138.
- [4] Typical reaction conditions: 2:1 = 100:1; 200 °C; 24–72 h; yields of 3 ca. 90%; increasing the temperature accelerated the reactions. Practically no secondary reactions occur up to 350 °C.
- [5] E. S. Huyser, D. C. Neckers, *J. Am. Chem. Soc.* 85 (1963) 3641.
- [6] Duran glass ampules; exclusion of atmospheric oxygen; analysis: GC with on-column injection, mass balance referred to 1a > 98%. a) Determination of reaction order at 200 °C; in the case of 1a: 0.02–0.24 mol/L 1a with 8.74 mol/L 2; in the case of 2: 8.74–1.7 mol/L 2 (variation by addition of *t*BuOH) with 0.02–0.05 mol/L 1a. Evaluation according to pseudo 1st-order gave  $k_{exp}/[2] = k_{exp}$ ; b) temperature dependence: 2/1a = 250:1; 175–230 °C (5 °C steps).
- [7] The kinetics of the reactions of 1a with (H<sub>3</sub>C)<sub>2</sub>HCOD, (D<sub>3</sub>C)<sub>2</sub>DCOH, and (D<sub>3</sub>C)<sub>2</sub>DCOD were investigated in the temperature range 175–225 °C as described in [6].
- [8] The following substituted benzaldehydes X-C<sub>6</sub>H<sub>4</sub>-CHO (X-1b) were measured for the Hammett correlation [9] in a competition reaction with 1b at 160 °C: X = *p*-CN, *p*-Cl, *p*-Ph, *p*-iPr, *p*-CH<sub>3</sub>O. Conversions < 5 mol %;  $\log([X-3b]/[3b]) = -0.62\sigma$  ( $r = 0.999$ ).
- [9] L. P. Hammett: *Physikalische Organische Chemie*, Verlag Chemie, Weinheim 1973, p. 352.
- [10] D. I. Schuster, P. B. Karp, *J. Photochem.* 12 (1980) 333.
- [11]  $\log(k_1/k_2) = \pm 0.217/\Theta$ ;  $\log(k_1/k_{-1}) = -0.7-172/\Theta$ ;  $\log(k_1/k_{-1}) = -1.4 + 52/\Theta$ . Calculated for 1b from thermochemical data according to Benson [12]. Substitution in equation (3) gives  $\log k_2 \approx 8.6-65/\Theta$ . The values of the A factor and of the activation energy are of the expected order of magnitude.
- [12] S. W. Benson: *Thermochemical Kinetics*, Wiley, New York 1976.
- [13] Other conceivable reaction sequences are not concomitantly consistent with both the observed rate law [Eq. (1)] and the experimental Arrhenius parameters [Eq. (2)].
- [14] The results evidence two different H-transfers: a) the cleavage of the O-H bond affects only  $k_1/k_{-1}$ ; b) the cleavage of the C-H bond affects only  $k_2$ .
- [15] In the competition reaction, the competition constant
- $$k = \frac{k_1^X}{k_{-1}^X} \cdot k_2^X \left/ \left( \frac{k_1}{k_{-1}} \cdot k_2 \right) \right.$$
- is measured. A value of  $\rho_1 > 0$  is to be expected for  $k_1/k_{-1}$  and  $\rho_2 < 0$  for  $k_2$ , since electron-withdrawing substituents X in the aryl moiety stabilize the radical 6. Since  $\rho_{exp} < 0$  it follows that  $|\rho_1| < |\rho_2|$ .
- [16] Kinetic chain lengths =  $v_{exp}/v_1 = k_{exp}[2]/k[3a]$ ;  $\log k_1 \approx 8.3-172/\Theta$ ; estimated from data in [11] with  $\log k_1 \approx 9.0 \pm 0/\Theta$  [12].
- [17] a) J. O. Metzger, *Angew. Chem.* 95 (1983) 914; *Angew. Chem. Int. Ed. Engl.* 22 (1983) 889; *Angew. Chem. Suppl.* 1983, 1256; b) J. Hartmanns, K. Klenke, J. O. Metzger, *Chem. Ber.* 119 (1986) 488.
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