Chem. Ber. **119**, 3528 – 3535 (1986)

Experimental and Theoretical Studies on the Mechanism of 1,2-Migration of Vinyl and Formyl Substituents in Free Radicals

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Received July 14, 1986

Vinyl and formyl groups undergo rearrangements of the type $X{=}CH-CMe_2-\dot{C}H_2 \rightarrow \dot{C}Me_2-CH_2-CH{=}X$ ($X = CH_2$ or O) with comparable rates (10^6-10^7 l/mol · s, 20°C). This result is in line with high-level *ab initio* calculations performed on the basic systems, i.e. $X{=}CH-CH_2-\dot{C}H_2$, which give barriers of activation of 14.9 ($CH_2{=}CH-CH_2-\dot{C}H_2$) and 19.2 kcal/mol ($O{=}CH-CH_2-\dot{C}H_2$), respectively. The calculations suggest that the rearrangements proceed via cyclopropane-like intermediates.

Experimentelle und theoretische Untersuchungen zum Mechanismus der radikalischen 1,2-Umlagerung von Vinyl- und Formylgruppen

Die Umlagerungen von Vinyl- und Formylgruppen vom Typ $X{=}CH-CMe_2-\dot{C}H_2 \rightarrow \dot{C}Me_2-CH_2-CH{=}X$ ($X = CH_2$ oder O) erfolgen mit vergleichbaren Geschwindigkeiten (10^6-10^7 l/mol · s, 20°C). In Übereinstimmung mit diesen kinetischen Messungen stehen *ab-initio*-Rechnungen, nach denen für die Grundkörper Aktivierungsenergien von 14.9 ($CH_2{=}CH-CH_2-\dot{C}H_2$) und 19.2 kcal/mol ($O{=}CH-CH_2-\dot{C}H_2$) berechnet werden. Die Rechnungen sagen Cyclopropanderivate als Zwischenstufen der Umlagerung voraus.

Whereas 1,2-migrations in cations[1)] and in anions[2)] are thoroughly studied, less is known about the mechanism of 1,2-migrations in radicals, although radical rearrangements are discussed in various reactions, e.g. vitamin-B_{12}-catalyzed isomerizations[3)] or gas-phase reactions of radical cations[4)]. Experimental[5)] and theoretical[6)] studies show, that the 1,2-migration in radicals depends essentially upon the nature of the migration group. Three mechanisms have to be distinguished: (1) The rearrangement follows a dissociation/recombination mechanism, (2) the 1,2-migration is concerted, or (3) an intermediate is formed. All three cases have been discussed[6)] and it is known that H, alkyl, OH, and NH_2 groups migrate very slowly, whereas OH_2^+, NH_3^+, and $C(OH)_2^+$ substituents show a higher tendency for rearrangements. In the migration of vinyl and acyl groups (**1** → **3**) it was of interest for us, (1) whether a vinyl group ($X = CH_2$) migrates faster than a

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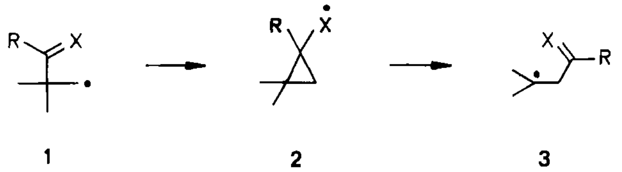
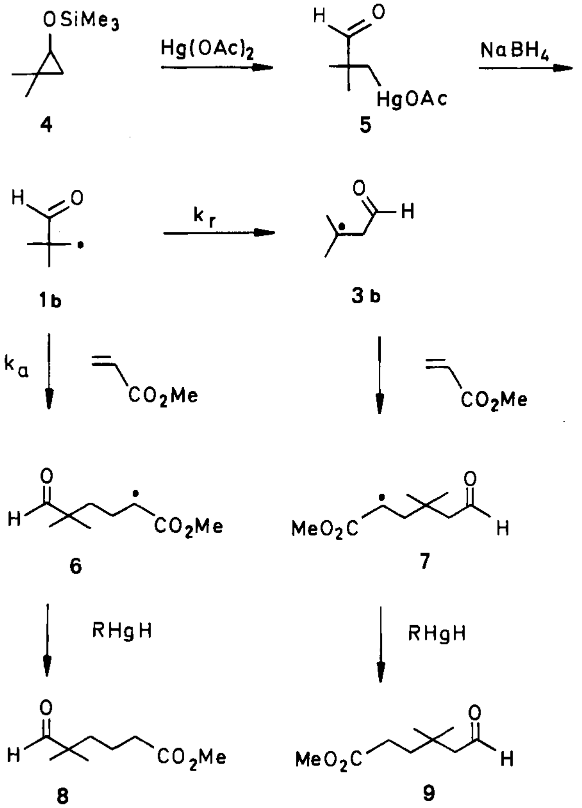
formyl group (X = O), because the C=C bond is weaker than a C=O bond, and (2) whether an intermediate **2** is formed during the rearrangements.

The isomerization of the primary homoallyl radical **1a** to give the tertiary homoallyl radical **3a** proceeds with rate coefficients of about 10^7 l/mol · s[5a)] and **2a** is discussed as an intermediate. But rearrangements of ketones (X = O, R = alkyl) and thioesters (X = O, R = SR′) occur 10^2 and 10^6 times slower, respectively[5d,e)].



	X	R
a	CH_2	H
b	O	H



We could now measure the rearrangement of the formyl group in **1b**. The radical **1b** was generated via mercuration of cyclopropane **4** and reduction of the organomercuric salt **5** by $NaBH_4$[7)]. Trapping of the radicals **1b** and **3b** with methyl acrylate yields adduct radicals **6** and **7** which abstract hydrogen atoms from the intermediate organomercury hydride[7)] to give products **8** and **9**, respectively.

Under the conditions of pseudo-first order (at least tenfold excess of methyl acrylate) the ratio of the rate of addition, k_a, to the rate of rearrangement, k_r, is given by equation (1)[8)] in which K is a constant, that is independent of the methyl acrylate concentrations.

$$\frac{[\mathbf{8}]}{[\mathbf{9}]} = \frac{k_a}{k_r}\,[H_2C{=}CHCO_2Me] + K \tag{1}$$

By plotting the ratio of the concentration [**8**]/[**9**] against the concentration of methyl acrylate a straight line with the slope $k_a/k_r = 2.18 \cdot 10^{-2}$ results.

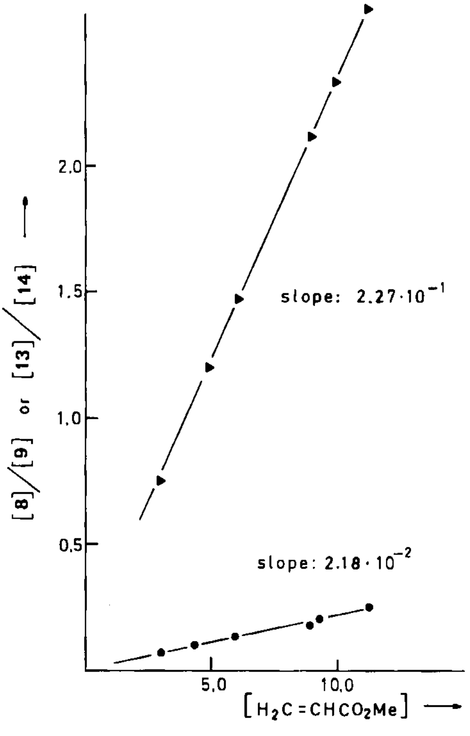
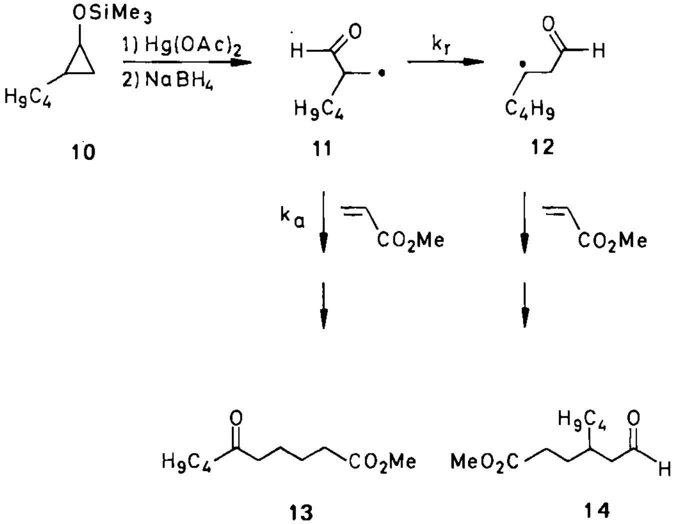


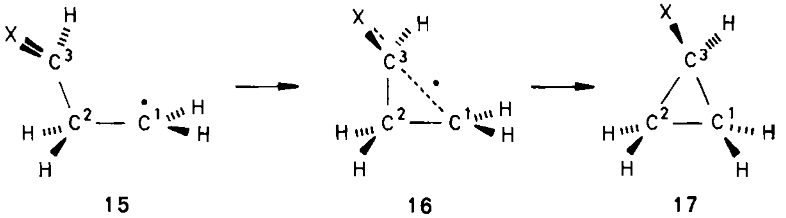
Figure 1. Plot of the ratio of products **8/9** (●) and **13/14** (▾), respectively, against the concentration of methyl acrylate

From the rates of addition of primary radicals to methyl acrylate of at least 10^5 l/mol · s (20°C)[8,9)] the rate of rearrangement for radical **1b** can be calculated to $10^6 - 10^7$ l/mol · s. *This means that formyl and vinyl groups migrate in radicals* **1** *with comparable rates.*

Radical **11**, generated from cyclopropane **10**, rearranges approximately 10 times slower than radical **1b** (Figure 1). This slower rate shows, that the rearrangement is facilitated by the dimethyl effect[10] in **1b** and, presumably, by the higher exothermicity of the formation of a tertiary radical **3b** compared to the formation of the secondary radical **12**.



In order to obtain further insight into the reaction mechanism, we have performed *ab initio* molecular orbital calculations on the basic system $X{=}CH{-}CH_2{-}\dot{C}H_2$ (X = CH_2; O).



	X
a	CH_2
b	O

All calculations were done using the GAUSSIAN 82 programme[11]. Complete geometry optimization, the calculation of harmonic frequencies (scaled by a factor of 0.9 in order to account for the overestimation of normal frequencies[12]) and the computation of zero-point vibrational energies (ZPVE) were executed using the 3-21 G basic set[13]. Improved energies were obtained by performing single-point calculations at the 6-31 G(d) basic set[14], and the effects of electron correlations were taken into account by *Møller-Plesset* perturbation theory up to the third order[15]. Our "best" level is designated as MP3/6-31 G(d)//3-21 G + ZPVE. Stationary points on the potential energy surface were located by using gradient techniques[16], and the analysis of the force constant matrix enabled us to characterize the stationary points as an equilibrium structure (no negative eigenvalue) or a transition state (one and only one negative eigenvalue). Bond lenghts are

Table 1. Calculated bond and dihedral angles [°] and bond lengths [Å] for educt radicals **15** (**15a**: X = CH_2; **15b**: X = O), transition states **16** (**16a**: X = CH_2; **16b**: X = O), and intermediates **17** (**17a**: X = CH_2; **17b**: X = O)

Structure	Bond lengths C_1-C_2	 C_2-C_3	 C_3-C_4	Bond angles $C_1C_2C_3$	Dihedral angles $C_1C_2C_3C_4$	 $C_1C_2C_3O$
15a	1.513	1.518	1.316	111.1	117.0	
16a	1.497	1.501	1.404	75.8	100.5	
17a	1.508	1.526	1.470	59.2	108.6	
15b	1.500	1.519		112.7		0.0
16b	1.490	1.507		75.2		95.7
17b	1.500	1.520		60.4		106.2

Table 2. Calculated total energies [Hartree] and relative energies [kcal/mol] for educts **15** (**15a**: X = CH_2; **15b**: X = O), transition states **16** (**16a**: X = CH_2; **16b**: X = O), and intermediates **17** (**17a**: X = CH_2; **17b**: X = O)

Structure	3-21G//3-21G	6-31G(d)//3-21G	MP2/6-31G(d)//3-21G	MP3/6-31G(d)//3-21G	$E_{rel.}$	ZPVE	$E_{rel.}$ + ZPVE	Number of negative eigen-values
15a (*cis*)[a]	−154.61142	−155.47264	−155.95776	−155.99781	1.1	56.3	0.8	0
15a (*trans*)[a]	−154.60898	−155.44980	−155.95277	−155.99326	3.5	55.8	2.7	1
15a (*gauche*)[a]	−154.61200	−155.47341	−155.95887	−155.99879	0.0	56.6	0.0	0
16a	−154.58320	−155.44774	−155.93604	−155.97424	15.4	56.1	14.9	1
17a	−154.59580	−155.46571	−155.96006	−155.99709	1.1	57.1	1.6	0
15b (*cis*)[a]	−190.24520	−191.31759	−191.85079	−191.87533	0.0	41.9	0.0	0
15b (*trans*)[a]	−190.24298	−191.31602	−191.84938	−191.87398	0.8	41.3	0.3	1
15b (*gauche*)[a]	−190.24404	−191.31738	−191.85073	−191.87518	0.1	41.8	0.0	1
16b	−190.21790	−191.28638	−191.81638	−191.84552	18.7	42.4	19.2	1
17b	−190.23088	−191.29757	−191.82185	−191.85405	13.3	44.2	15.6	0

[a] *cis, trans,* and *gauche* describes the orientation of the CH_2 and X substituents at the central $XHC-CH_2\dot{C}H_2$ bond.

given in Ångström, and bond angles in degrees (Table 1). Absolute energies are given in Hartrees, while relative energies (E) and ZPVE are given in kcal/mol (Table 2).

The data of Table 2 show that the activation energies for the migration of the vinyl group (14.9 kcal/mol) and the formyl group (19.2 kcal/mol) are of the same order. The calculated value is only slightly larger than the activation energy of 9.1 kcal/mol measured by *Ingold*[17] for the rearrangement **15a** ⟶ **17a**.

The *ab initio* calculations further predict, that not only during the vinyl migration but also during the formyl migration, cyclopropyl systems are intermediates of the rearrangements. The cyclopropylcarbinyl radical **17a** is nearly as stable as the homoallyl radical **15a** ($\Delta\Delta H^\circ = 1.6$ kcal/mol). It should be therefore possible to trap the intermediate **17a** under suitable reaction conditions. But the intermediate of the formyl rearrangement **17b** is 15.6 kcal/mol less stable than the alkyl radical **15b**. Thus, trapping of the cyclopropyloxy radical seems less probable.

We have also addressed the question, why the oxygen-containing intermediate **17b** is substantially less stable than the carbon analogue **17a**, relative to their acyclic isomers **15b, a**, and the answer is provided by the calculated heat of reaction of formaldehyde with ethyl radicals giving methoxy radicals and ethylene. At the MP3/6-31G(d)//3-21G level of theory we obtain a heat of reaction of 13.4 kcal/mol (absolute energies are given in equation (2) and are taken from ref.[18]).

$$\begin{array}{lccccccc} & CH_2 & + & C_2H_5^{\bullet} & \longrightarrow & CH_3O^{\bullet} & + & C_2H_4 \\ E_{tot} & (-114.17248) & & (-78.86156) & & (-114.70754) & & (-78.30512) \\ \multicolumn{3}{l}{\Delta H_r^\circ = 13.4 \text{ kcal/mol}} & & & & & \end{array} \qquad (2)$$

The formation of alkoxy radicals from carbonyl groups is much less favoured energetically than the formation of alkyl radicals from the corresponding alkenes. This difference in reaction energies can be explained by two effects. (1) The π bond in carbonyl groups is considerably stronger than in olefinic groups, and (2) alkoxy radicals are presumably less stable than alkyl radicals[19].

We thank the *Fonds der Chemischen Industrie* and the *Rechenzentrum of the TU Berlin* for support.

Experimental

Kinetic Experiments

3.00 mmol of the (trimethylsiloxy)cyclopropanes **4** and **10**[20], respectively, were treated with 956 mg (3.00 mol) of mercuric acetate in 10 ml of a 20:1 acetone/water mixture. After 1 h the solution was evaporated, treated with 10 ml of methylene chloride and again concentrated. The residue was filled up to 10.0 ml with an at least tenfold excess of an n-molar solution of methyl acrylate (see Table 3). At 20.0°C 280 mg (6.6 mmol) of $NaBH_4$ was added under stirring. After 15 min the mixture was filtered over $MgSO_4$, concentrated, and distilled under vacuum in a Kugelrohr. The mixture of the products (**8/9** and **13/14**, respectively)[7] was analyzed by NMR using the aldehyde singlets. The molarity of the methyl acrylate solution and the ratios of the unrearranged and the rearranged products are given in Table 3.

Table 3. Methyl acrylate concentration, ratio of products **8**/**9** and **13**/**14**, respectively, and rate ratio k_a/k_r of the kinetic experiments at 20°C

Cyclopropane	$H_2C=CHCO_2Me$	**8**/**9**	**13**/**14**	k_a/k_r [a]
4	3.00	0.070		$2.18 \cdot 10^{-2}$
	6.00	0.133		
	9.00	0.183		
	11.2	0.255		
10	3.00		0.754	$2.27 \cdot 10^{-1}$
	6.00		1.50	
	9.00		2.13	
	11.2		2.64	

[a] Mean error ±5%.

CAS Registry Numbers

1a: 87110-24-5 / **1b**: 104291-33-0 / **4**: 50338-45-9 / **8**: 74001-62-0 / **9**: 4007-81-2 / **10**: 87921-65-1 / **13**: 61820-00-6 / **14**: 87921-77-5 / **15a**: 2154-62-3 / **15b**: 68219-61-4 / **17a**: 2154-76-9 / **17b**: 104291-34-1 / CH_2O: 50-00-0 / $C_2H_5^{\bullet}$: 2025-56-1

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