Polar Effects in Halogen Abstraction Reactions of Alkyl Radicals

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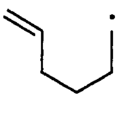
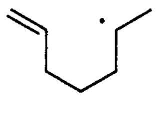
Key Words: Polar effects / Radical clock / Cobaloximes, alkyl / Radicals, alkyl / Chlorine abstraction

In a series of structurally similar alkyl radicals **1a**–**c** the tertiary 1,1-dimethyl-5-hexenyl radical **1c** reacts 30 times faster with carbon tetrachloride than the primary 5-hexenyl radical **1a**. The reactivity of the secondary 1-methyl-5-hexenyl radical **1b** aligns itself in between the primary and the tertiary radical **1a** and **1c**. The results indicate that the increasing nucleophilicity of the alkyl radicals is the major factor contributing to the reactivity.

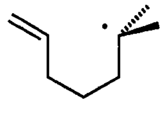
The last few years have witnessed a breakthrough in the application and understanding of alkyl radical chemistry in organic synthesis[1]. These achievements are largely based on mechanistic insights and the collection of kinetic data which gave useful reactivity and selectivity guidelines for the design of syntheses via alkyl radical intermediates[1,2]. Additions of alkyl radicals to activated olefins are largely governed by polar effects[3]. The reaction is exothermic, because one carbon–carbon single bond is formed at the expense of an olefinic π-bond. The rate constants of these processes are ca. $10^3 - 10^6$ l mol^{-1} s^{-1} at ambient temperatures[3]. According to Hammond's postulate early transition states are involved in these reactions which can be described by the frontier molecular orbital theory[3,4]. The major stabilizing factor during the approach of electron-poor olefins and electon-rich alkyl radicals arises from LUMO–SOMO interactions. In general, the increase of nucleophilicity of alkyl radicals, if a hydrogen atom at the radical center is replaced by an alkyl group, overrides stabilizing contributions of the substituents[3,4].



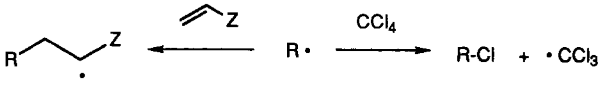
1a



1b



1c



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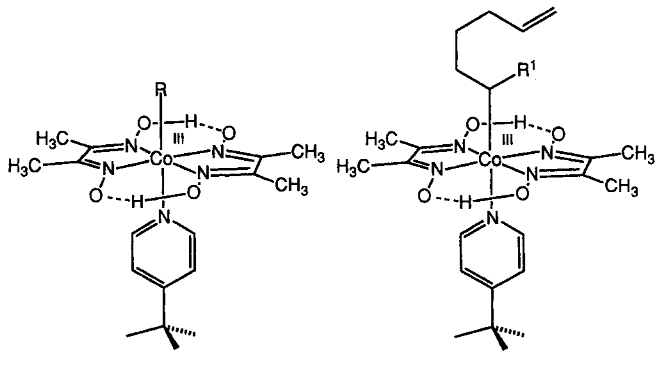
Z = e.g. CN, CHO, P(O)Et$_2$,
COOMe, C(O)Me, C$_6$H$_5$.

Similar polar effects were postulated for halogen atom abstractions by alkyl radicals from polyhalogenated methanes[5]. Due to the growing importance of halogen abstraction reactions[1,6] we set out to study the rate constants of chlorine abstraction reactions from carbon tetrachloride by primary 5-hexenyl, secondary 1-methyl-5-hexenyl, and tertiary 1,1-dimethyl-5-hexenyl radicals **1a**–**c**.

Alkyl radicals **1a** and **1b** were generated by photolysis of parent 5-hexenyl cobaloxime **3a** and 1-methyl-5-hexenyl cobaloxime **3b**. Alkyl cobaloximes have recently been successfully employed as sources of free alkyl radicals[7]. Alkyl cobaloximes **3a** and **3b** were prepared by the reaction of nucleophilic cobalt(I) complex **4** with 5-hexenyl bromide (**5a**) or 1-methyl-5-hexenyl bromide (**5b**), respectively[8].



3 ≡ R-Co^{III}(dmgH)$_2$Bupy

3a: R^1 = H

3b: R^1=CH$_3$

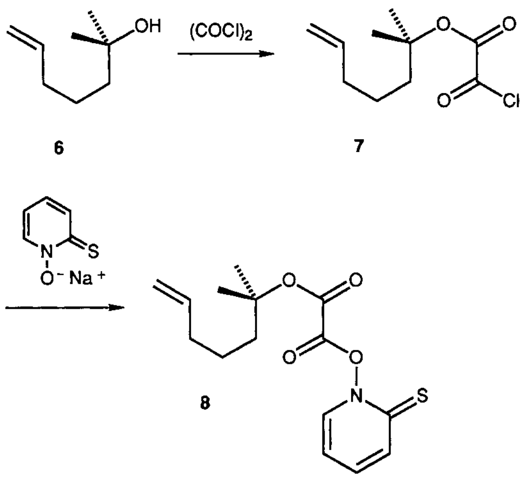
dmgH = 2,3-butanedione dioxime monoanion
Bupy = 4-tert-butylpyridine

$$\underset{\mathbf{4}}{\text{Na}\,[\text{Co}^{\text{I}}(\text{dmgH})_2\text{Bupy}]} \xrightarrow[\text{-NaX}]{\substack{+\text{R-X}\\ \mathbf{5}}} \underset{\mathbf{3}}{\text{R-Co}^{\text{III}}(\text{dmgH})_2\text{Bupy}}$$

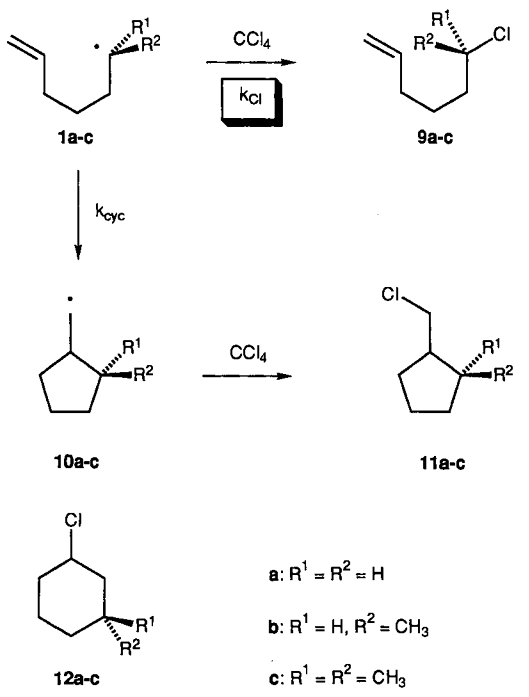
X = Br, OTos

Tertiary alkyl cobaloximes are not stable with respect to β-cleavage and decomposition to olefin and hydridocobaloxime[9]. However, 1,1-dimethyl-5-hexenyl radical **1c** can be generated from 1,1-

dimethyl-5-hexenol (**6**) via oxalate **8**[10]. The radical precursor **8** is thermally labile and has to be generated in situ.



Alkyl radicals **1a**–**c** were chosen for this study because of their well-known ability to cyclize irreversibly to cyclopentylmethyl radicals **10a**–**c**[11,12]. Bimolecular chlorine abstraction of **1a**–**c** from carbon tetrachloride in competition with unimolecular cyclization to **10a**–**c** (radical clock reaction)[13] can be used to measure the unknown rate constant k_{Cl}. A minor side reaction leads to the corresponding six-membered rings **12** by 6-*endo-trig* cyclization[11]. In order to trap the trichloromethyl radical (**2**) three equivalents of triphenylmethane were added to the cobaloxime reactions. Because the thiocarbonyl group of **8** is an efficient trap the addition of triphenylmethane is superfluous in this system.



To detect the rate constants k_{Cl} of the primary, secondary, and tertiary radicals **1a**–**c** the radical precursors **3a**, **b**, and **8** were photolyzed and thermolyzed, respectively, at 26°C in the presence of an at least tenfold excess of CCl_4. This led to alkyl halides **9a**, **c**, **11a**, **c**, and **12a**, **c**. From the ratios of products **9a**–**c**:**10a**–**c** and the known rates for cyclizations the rate constants k_{Cl} could be calculated according to pseudo first-order kinetics (Table 1)[14].

Table 1. Product ratios and rate constants for the reaction of radicals **1a**–**c** in the presence of CCl_4 at 26°C

Radical	Concentration of CCl_4 [M]	Products	Product ratio **9**:**11**	Rate constant [$M^{-1}\,s^{-1}$]
1a	2.66	**9a**, **11a**	0.084	$6.9 \cdot 10^3$
	5.28		0.155	
	6.56		0.215	
	7.83		0.230	
	9.90		0.300	
1b	2.53	**9b**, *cis*-**11b**	0.491	$2.1 \cdot 10^4$
	5.16		1.192	
	9.90		1.919	
1c	0.83	**9c**, **11c**	0.572	$2.1 \cdot 10^5$
	3.65		2.019	
	9.80		5.831	

It is interesting to note that the rate for the chlorine abstraction of the 5-hexenyl radical (**1a**) in Table 1 is nearly identical with the literature value. Warkentin et al.[15] generated **1a** from an azo compound and measured a rate of $7.3 \cdot 10^3$ at 25°C. The data of Table 1 are also in accord with rate constants for the chlorine abstraction by other alkyl radicals[16]. Our measurements show that the tertiary radical **1c** is 10 times more reactive against CCl_4 than the secondary radical **1b**, which reacts three times faster than the primary radical **1a**. Thus, reactivity increases with increase of the number of alkyl groups at the radical center.

Chlorine atom abstraction by alkyl radicals from CCl_4 is exothermic by more than 10 kcal/mol[17]. So these reactions should proceed via early transition states that can be rationalized in terms of frontier orbital interactions between the SOMO of the alkyl radical and the LUMO of the C–Cl bond of CCl_4. Addition of methyl groups at the radical center increases the SOMO of the radical, and the SOMO–LUMO energy gap decreases. As the rate constants of Table 1 show this affects the reactivity of the radicals to a larger extent than the increase of their stability.

This work was supported by the *Volkswagen-Stiftung* and the *Swiss National Science Foundation.*

Experimental

NMR: Bruker WM 300, Bruker AC 300 (TMS as internal standard). – MS: Finnigan MAT 311 A. – UV/Vis: Beckman UV 5240 and DK 2A. – IR: Perkin-Elmer 325. – Gas-liquid chromatography: Carlo Erba GC 6000 (Vega Series); FID; connected to Spectra Physics Integrator 4290; nitrogen at a flow rate of 3 ml/min (equals 120 kPa pressure) was used as carrier gas; injector and detector temperature 250°C; OV 17/01 and SE 30 capillary columns from Macherey & Nagel. – Preparative column chromatography: Merck silica gel 60 (0.063–0.200 mm). – Purification of the solvents: benzene was distilled from sodium/benzophenone under nitrogen directly before use. *n*-Hexane was refluxed for several hours with calcium hydride, distilled under nitrogen, und stored over molecular sieves 4 Å. Carbon tetrachloride was refluxed for 4 hours with calcium oxide; the center cut of the distillation was collected, refluxed with potassium permanganate for 4 hours, distilled under nitrogen, and stored in dark bottles over molecular sieves 4 Å for periods not exceeding one week.

Syntheses of Alkyl(4-tert-butylpyridine)cobaloximes **3**: All cobaloximes containing the axial ligand 4-*tert*-butylpyridine are new compounds. 5-hexenyl and 1-methyl-5-hexenyl(pyridine)cobaloximes have been prepared previously[18]. In a typical procedure 1.0 g (4.2 mmol) of cobalt(II) chloride hexahydrate and 1.0 g (8.4 mmol) of 2,3-butanedione dioxime (dimethylglyoxime) were stirred in 25 ml of degassed methanol under nitrogen at −20°C. 1.0 ml of 50% aqueous degassed sodium hydroxide solution was added dropwise to the reaction mixture followed by addition of 0.6 ml (4.2 mmol) of 4-*tert*-butylpyridine and 0.2 g (5.3 mmol) $NaBH_4$ dissolved in 1−2 ml of methanol. The reaction mixture was allowed to warm to room temp. and stirred for 60 min. Alkyl bromides **5a, b** (8.0 mmol) were added dropwise to the black solution at −20°C, and the reaction mixture was stirred for 14 h at 20°C in the dark. The solvent was distilled off from the orange solution, 100 ml of water, containing 1 drop of 4-*tert*-butylpyridine, was added to the oily residue, and the precipitated orange crystals of alkyl cobaloximes **3a, b** were filtered, dried, and stored in amber-colored vials.

(4-tert-Butylpyridine)bis(dimethylglyoximato)(5-hexenyl)cobalt(III) (**3a**): Yield 1.53 g (71%), m.p. 169−170°C (methanol/water). − ^{1}H NMR ($CDCl_3$): δ = 18.25 (s, 2H, OH), 8.42 (dd, *J* = 1.5, 5.3 Hz, 2H, Bupy), 7.28 (dd, *J* = 1.5, 5.3 Hz, 2H, Bupy), 5.72 (ddt, *J* = 6.8, 10.2, 17.0 Hz, 1H, 5-H), 4.93−4.83 (m, 2H, 6-H, 6′-H), 2.13 (s, 12H, CH_3), 2.00−1.93 (m, 2H, 4-H), 1.61−1.55 (m, 2H, 1-H), 1.32−1.25 (m, 2H, 3-H), 1.28 (s, 9H, CH_3), 0.97−0.86 (m, 2H, 2-H). − ^{13}C NMR ($CDCl_3$): δ = 12.00, 29.70, 29.94, 30.25, 31.62, 33.57, 34.80, 113.74, 122.32, 139.42, 148.89, 149.36, 161.59. − MS (FD): *m/z* = 508/507 [M^+]. − UV/Vis (CH_2Cl_2): λ_{max} (ε) = 483 nm (180) sh, 419 (1485) sh, 370 (2680) sh, 293 (8810) sh, 230 (29300). − IR (KBr): $\tilde{\nu}$ = 3010 cm^{-1}, 2990, 2920, 2860, 1740, 1610, 1565, 1420, 1215, 1095.

$C_{23}H_{38}CoN_5O_4$ (507.5) Calcd. C 54.43 H 7.55 N 13.80
Found C 54.32 H 7.51 N 13.73

(4-tert-Butylpyridine)bis(dimethylglyoximato)(1-methyl-5-hexen-2-yl)cobalt(III) (**3b**): Yield 1.64 g (75%), m.p. 116−119°C (dec.) (2-propanol). − ^{1}H NMR ($CDCl_3$): δ = 18.13 (s, 2H, OH), 8.41 (dd, *J* = 1.4, 5.2 Hz, 2H, Bupy), 7.23 (dd, *J* = 1.4, 5.2 Hz, 2H, Bupy), 5.76 (ddt, *J* = 6.4, 10.4, 17.0 Hz, 1H, 5-H), 4.98−4.76 (m, 2H, 6-H, 6′-H), 2.14 (s, 12H, CH_3), 2.03−1.85 (m, 3H, 1-H, 4-H), 1.85−1.60 (m, 1H, 2-H), 1.53−1.46 (m, 2H, 3-H), 1.26 (s, 9H, 3 CH_3), 0.93−0.81 (m, 1H, 2′-H), 0.43 (d, *J* = 6.9 Hz, 3H, CH_3). − ^{13}C NMR ($CDCl_3$): δ = 12.06, 21.96, 27.40, 30.25, 33.74, 34.78, 38.25, 43.45, 113.41, 122.19, 139.53, 149.17, 149.35, 161.36. − MS (FD): *m/z* = 522/521 [M^+]. − UV/Vis (CH_2Cl_2): λ_{max} (ε) = 428 nm (1340) sh, 329 (6970) sh, 291 (8690) sh, 245 (24150). − IR (KBr): $\tilde{\nu}$ = 3080 cm^{-1}, 2960, 2920, 2850, 1740, 1605, 1550, 1410, 1235, 1080

$C_{24}H_{40}CoN_5O_4$ (521.6) Calcd. C 55.27 H 7.73 N 13.43
Found C 54.82 H 7.74 N 12.96

Kinetic Experiments with Cobaloximes **3a, b** *and Carbon Tetrachloride:* Ca. 0.2 mmol of cobaloxime **3a** or **3b** and ca. 0.6 mmol of triphenylmethane were added to a definite amount of carbon tetrachloride (neat or diluted with a certain amount of benzene or hexane). At 26°C this solution was irradiated (250-W discharge lamp, Osram Power Star HQI) for 2 h. The brown reaction mixture was filtered through a short column (silica gel), and the alkyl chlorides were eluted with 50 ml of *n*-hexane. The colorless filtrate was carefully concentrated and analyzed by gas chromatography. The product ratios of acyclic versus cyclic chlorides for different concentrations of carbon tetrachloride are collected in Table 1. Control experiments were carried out which showed that the ratio of acyclic versus cyclic chloride did not change during irradiation and workup.

Kinetic Experiments with Oxalate **8** *in Carbon Tetrachloride:* A solution of 1.00 ml (10.0 mmol) of oxalyl chloride in 5 ml of benzene was added to 0.13 g (1.00 mmol) of 1,1-dimethyl-5-hexenol (**6**) in 5 ml of benzene at 25°C. The reaction mixture was stirred for 12 h, the solvent and excess starting material were distilled off in vacuo, leaving a colorless oil of **7** which was taken up in 1 ml of carbon tetrachloride. This solution of **7** was added at 26°C to a suspension of 0.16 (1.10 mmol) of sodium salt of 2-mercaptopyridine *N*-oxide in a definite amount of carbon tetrachloride (neat or diluted with a certain amount of *n*-hexane). After 15 min, the colorless precipitate was filtered off through a short column (silica gel), the alkyl chlorides were eluted with 50 ml of *n*-hexane and analyzed by gas chromatography. The product ratios of acyclic versus cyclic chlorides **9c**:**11c** for different concentrations of carbon tetrachloride are collected in Table 1.

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CAS Registry Numbers

1a: 16183-00-9 / **1b**: 38295-10-2 / **1c**: 38295-12-4 / **3a**: 118799-74-9 / **3b**: 118799-75-0 / **6**: 77437-98-0 / **7**: 141293-29-0 / **8**: 141293-30-3 / $(COCl)_2$: 79-37-8 / CCl_4: 56-23-5 / 2-Mercaptopyridine *N*-oxide, sodium salt: 3811-73-2