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Regioselectivity of Radical Addition of Thiols to 1-Alkenes

Ursula Biermann[a] and Jürgen O. Metzger*[a,b]

Abstract

The addition of dodecanethiol (**1**) to 1-alkenes H_2C=CHR having substituents R = Hex, $(CH_2)_8$COOMe, Ph, Bn, *c*Hex, CH_2*c*Hex, *t*Bu (**2a**-**g**) with different steric effect was studied. Some few percent of the branched Markownikow addition product **4** was formed in all cases with the exemption of styrene (**2c**) in addition to the linear anti-Markownikow product **3** as main product. The regioselectivities correlate well with the Taft steric parameter E_S of the R-substituent at the alkene. This gives evidence that the regioselective outcome of the radical addition of thiols to 1-alkenes is mainly steered by the steric effect of the R-substituent as it is well known for the addition of alkyl radicals to alkenes. In the case of thiol addition, however, the regioselectivity is strongly enhanced by the much faster fragmentation of the intermediate Markownikow than of the anti-Markownikow adduct radical.

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Introduction

The radical addition of thiols to alkenes is a long-known reaction and has been studied and applied intensively since more than hundred years.[1] The addition is initiated photochemically or thermally with and without radical initiators.[1, 2, 3] It is thoroughly used for the synthesis of low molecular [2] as well as polymeric thioethers,[3, 4 , 5] and is often named thiol-ene click reaction.[5a] There is a large number of review articles on most aspects of the radical chemistry of thiols including addition reactions.[6, 7] It is well-known that the addition to 1-alkenes occurs with high selectivity as anti-Markownikow orientation. The most recent review by Dénès et al. has been assessing that the thiyl radical adds to the less substituted end of the C=C bond to form a carbon centered radical via a reversible process. This regioselectivity was rationalized in terms of the heat of formation or by the enhanced stability of the intermediate carbon-centered radical.[7] The given references [8, 9] appeared some years before Giese´s seminal paper demonstrating the importance of steric effects on the addition of carbon radicals to alkenes.[10] Only some very few papers have been reporting on the detection of both regioisomers,[11, 12, 13, 14] also in polymeric thioether synthesis.[15] Cadogan and Sadler found a ratio of methyl thioglycollate addition to C(1) and C(2) of 1-octene and 1-heptene of about 98:2 at room temperature.[12] They attributed this selectivity to the greater stability of the secondary in comparison to the primary adduct radical. However, the small predominance of the attack at C(2) of 2-octene was rationalized with a greater steric effect of the pentyl substituent at C(3) than the methyl substituent at C(2). Oswald and Naegele reported on the UV-initiated addition of methanethiol, ethanethiol, benzenethiol at 16°C and thiolacetic acid at room temperature to diallyl maleate giving 2 – 5 % of the branched Markownikow beside the linear anti-Markownikow addition products. The regioselectivity was explained on the basis of the relative stability of the intermediate radicals involved.[11] Brace studied the radical addition of 2-(perfluorohexyl) ethanethiol to 1-hexene and observed 2.3 % of the branched Markownikow product.[14] Morgan et al. polymerized 1,4-butanediol-di-*N*-allyl carbamate with ethylene glycol di-β-mercaptopropionate and observed extremely minor formation of the Markownikow product (<10%) by ^{1}H-NMR spectroscopy.[15] Both latter papers didn´t give any explanation of this regioselective outcome. Finally, Crich stated that the addition of thiyl radicals to alkenes is much less susceptible to steric hindrance in the alkene than are the corresponding reactions of alkyl radicals, though no respective examples were

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given.[16] Most remarkably, there are no systematic investigations on this most important topic. We are reporting herein our studies on the radical addition of dodecanethiol (**1**) to 1-alkenes **2a**-**g** giving unambiguous evidence of the importance of steric effects on the regioselective outcome.

Results and Discussion

We studied the addition of thiol **1** to 1-alkenes **2** with alkyl groups R having different steric effects as given in Table 1 and measured by GC the ratio of the regioisomeric addition products **3** and **4**. In the case of alkene **2d** a further addition product **5d** was observed. We performed the reaction without any solvent and initiator added, taking advantage of the molecule assisted homolysis (MAH) of thiol and alkene.[17, 18] This radical chain initiation gives often cleaner, though slower reactions than other more often used initiations, because of the fact that only both substrates without any additional reagent are present in the reaction mixture and because of the very low steady state concentration of the chain carrying radical. For comparison, some examples were initiated with AIBN as well. The reaction temperature was mostly 80°C with some variation to obtain information on the temperature dependence of the regioselectivity. Alkenes **2e** and **2g** were also reacted at room temperature. The reaction time was about some hours to some days. The major isomers **3** were unambiguously identified by ^{1}H-NMR, ^{13}C-NMR and GC-MS, and the minor isomers **4** by GC-MS. All isomers **4** show the same characteristic α-scission of the molecular ion in EI-MS giving fragment peak m/z 229 (Scheme S1). The results are compiled in Table 1.

The generally accepted mechanism of the thiol radical chain addition reaction [2, 7] is given in Scheme 1, here initiated by MAH and assuming the competitive addition of the thiyl radical to C(1) and C(2) of alkene **2**. Because the addition of thiyl radicals with the rate constants $k_{a,I} > k_{a,II}$ is reversible, the ratio of the products **3** and **4** is not only influenced by the ratio of the addition rate constants $k_{a,I}$ and $k_{a,II}$, as can be assumed for carbon radicals at moderate temperature,[10] but also by the fragmentation rate constants $k_{f,I} << k_{f,II}$ of the adduct radicals I and II and by their trapping reaction having the rate constants $k_3 < k_4$, respectively (Eq. 1, Scheme 1).[12]

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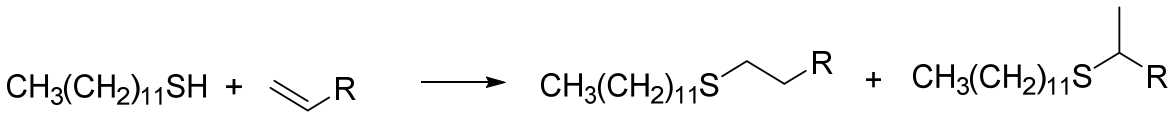
Table 1. Results of the addition of thiol **1** to 1-alkenes **2** to give the regioisomeric thioethers **3** and **4**.[a]



1 **2** **3** **4**

Entry	2	R	E_S	T [°C]	[**3**]:[**4**][b]	S=log([**3**]:[**4**])
1[c]	**a**	$(CH_2)_5Me$	-0.4	70	97.9:2.1	1,67
2[c]	**a**			80	97.8:2.2	1.65
3[c]	**a**			90	97.7:2.3	1.63
4[c]	**b**	$(CH_2)_8COOMe$	-0.4[d]	63	98.4:1.6	1.82
5[c]	**b**			80	98.1:1.9	1.71
6	**c**	Ph		80	100:1	-
7	**d** [e]	Bn	-0.38	80	96.9:2.8	1.54
8	**d** [e,f]			80	96.2:3.5	1.4
9	**d** [e,f]			60	97.0:2.8	1.54
10	**e**	*c*Hex	-0.79	80	98.1:1.9	1.71
11	**e**			r. t.	98.9:1.1	1.95
12	**f**	CH_2*c*Hex	-0.98	80	98.6:1.4	1.85
13	**f** [e]			80	97.8:2.2	1.64
14	**g**	*t*Bu	-1.54	r. t.	99.4:0.6	2.21

[a] [**1**]:[**2**] = 1.5:1, neat; [b] determined by GC; [c] [**1**]:[**2a, b**] = 1:1, neat; [d] E_s was assumed to be the same as of R=$(CH_2)_5Me$; [e] 0.3 % (entry 7,8) and 0.2 % (entry 9) of isomer **5d** was formed (see Scheme 2); [f] AIBN was added.

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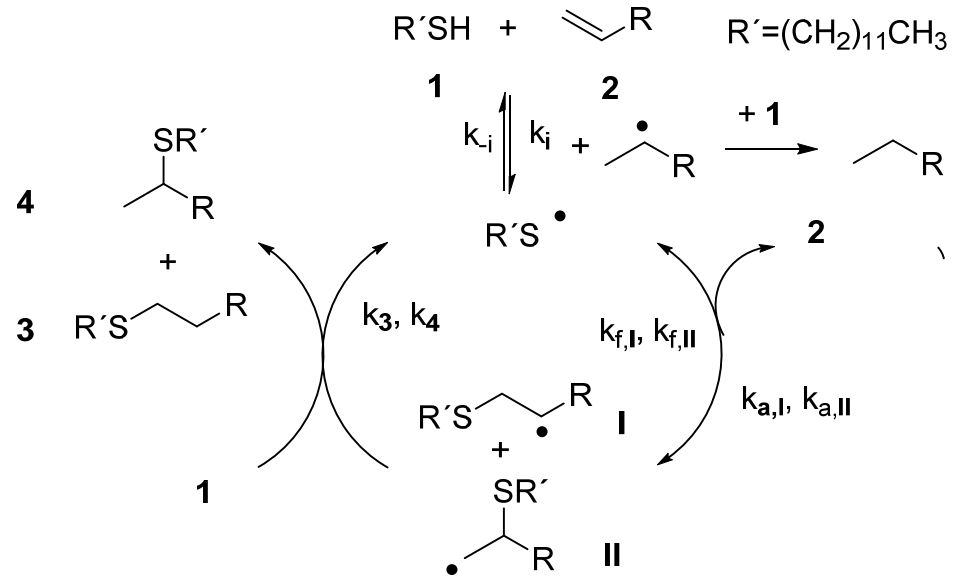

$$\frac{[\mathbf{3}]}{[\mathbf{4}]} = \frac{k_3\, k_{a,I}\,(k_{f,II} + k_4[R'SH])}{k_4\, k_{a,II}\,(k_{f,I} + k_3[R'SH])} \qquad (1)$$

$k_{a,I}$ [M^{-1} s^{-1}]	$k_{a,II}$ [M^{-1} s^{-1}]	$k_{f,I}$ [s^{-1}]	$k_{f,II}$ [s^{-1}]	k_3 [M^{-1} s^{-1}]	k_4 [M^{-1} s^{-1}]
1.9×10^6 [24]	2×10^5 [23]	3.4×10^5 [23]	1.6×10^8 [23]	1×10^7 [23]	1.9×10^7 [25]

Scheme 1. Radical chain addition of thiol **1** to 1-alkenes **2** initiated by molecule assisted homolysis (MAH) [17,18] giving regioselectively addition products **3** and **4**. The rate constants of addition $k_{a,I}$ and $k_{a,II}$, fragmentation $k_{f,I}$ and $k_{f,II}$ and hydrogen abstraction k_3 and k_4 assumed for the estimation of the regioselectivity of the addition of dodecanethiol **1** onto 1-octene **2a** using Eq.(1) are given.

All alkenes **2** showed preferential addition to the terminal carbon atom as expected, but also some addition to C-2 of the double bond with the exemption of styrene (**2c**) (Table 1, entry 6). We were not able to detect any addition product **4c** beside **3c**. The difference of the stability of the benzylic radical **Ic** and the primary radical **IIc** is about 65 kJ/mol.[19, 20] Thus with $k_{f,\mathbf{Ic}} << k_{f,\mathbf{IIc}}$, non-detectable amounts of product **4c** may be formed (Scheme 1). The observation of addition product **5d** that is formed via a secondary adduct radical (Scheme 2) having in comparison to the benzylic adduct radical a lower difference of stability of 53 kJ/mol gives evidence for this explanation.

The ratio of [**3a**]:[**4a**]=97.8:2.2 (Table 1, entry 1) is almost the same as given by Cadogan for the addition of thioglycollate to alkene **2a**,[12] by Brace for the addition of 2-(perfluorohexyl) ethanethiol to 1-hexene,[14] and similar to the additions of various thiols as reported by Oswald and Naegele.[11] This gives evidence that the polar as well as steric effect of R´ of the thiyl radical (Scheme1) has only minor influence on the regioselective outcome.

The selectivity increased slightly with decreasing temperature, for example **2a** (entry 1-3), **2b** (entry 4,5) and **2e** (entry 10,11), also with AIBN as initiator (entry 8,9). This slight temperature dependence is characteristic for systems showing reversibility of the radical addition, because of some compensation of the temperature effect of the involved rate constants of addition, β-fragmentation and hydrogen transfer (Eq. 1) and was reported also for radical alkane additions to alkenes at elevated temperature.[21, 22] It may be mentioned that the selectivity was found to be somewhat lower using AIBN as initiator in comparison to the MAH initiation (entries 7 and 8, 12 and 13).

Fortunately, the relevant absolute rate constants of the thiol radical chain addition reaction are known from literature and allow to estimate the regioselectivity of the addition of a primary alkane thiol *i.e.* **1** to alkene **2a** at room temperature. Chatgialialoglu et al. reported on the addition rate constant as k_a = 2.0 x 10^5 M^{-1} s^{-1} of 2-hydroxyethanethiyl radical ($HOC_2H_4S\cdot$) to an internal (*E*)-configured double bond of monounsaturated fatty compounds as well as on the fragmentation rate constant of the adduct radical as k_f = 1.6 x 10^8 s^{-1}.[23] McPhee et al. determined the addition rate constant of *t*-BuS· to 1-octene as k_a = 1.9 x 10^6 M^{-1} s^{-1}.[24] The reported kinetic data allowed Chatgialialoglu et al.[23] to calculate the rate constant of the reverse fragmentation reaction as k_f = 3.4 x 10^5 using the trapping rate constant of a secondary alkyl radical as k_{SH} = 1 x 10^7 M^{-1} s^{-1}. Eventually, Troche et al. measured the trapping rate constant of a primary alkyl radical by octadecanethiol as k_{SH} = 1.9 x 10^7.[25] Insertion of these rate constants as compiled in Scheme 1 with [R´SH] = 2.5 mol·L^{-1} in Eq. 1 gives a ratio [**3a**]:[**4a**] = 97.4:2.6, in good agreement with the results given in Table 1. Interestingly, the ratio of the addition of alkanethiyl radical R´S· to C(1) and C(2) amounts to $k_{a,I}$:$k_{A,II}$ = 90.5:9.5. Thus, the reason for the high selectivity of the addition of thiols to 1-alkenes is the fact that the moderate selectivity of the addition of thiyl radicals to 1-alkenes is strongly enhanced by the fragmentation of the adduct radicals **I** and **II** with $k_{f,I} << k_{f,II}$.

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Most importantly, the regioselectivities correlate with Taft E_s parameters of substituent R of alkene **2** [26] (Figure 1) giving clear evidence that the regioselectivity of the radical addition of thiols to 1-alkenes is mainly controlled by the steric effect of substituent R because of an unsymmetrical transition state of the thiyl radical addition as was shown by Giese for alkyl radicals.[10] Northrup et al. expected, as a first approximation, that thiyl radicals will follow similar trends as carbon-centered radicals. [27]

The slope of the correlation line is δ = -0.80. This value can be compared with the addition of the cyclohexyl radical to alkenes at room temperature (δ = -1.19)[10] and at 400°C (δ = -0.84).[21] This gives evidence that the steric effect of substituent R on the thiyl radical addition is in the order of magnitude of the addition of the cyclohexyl radical.

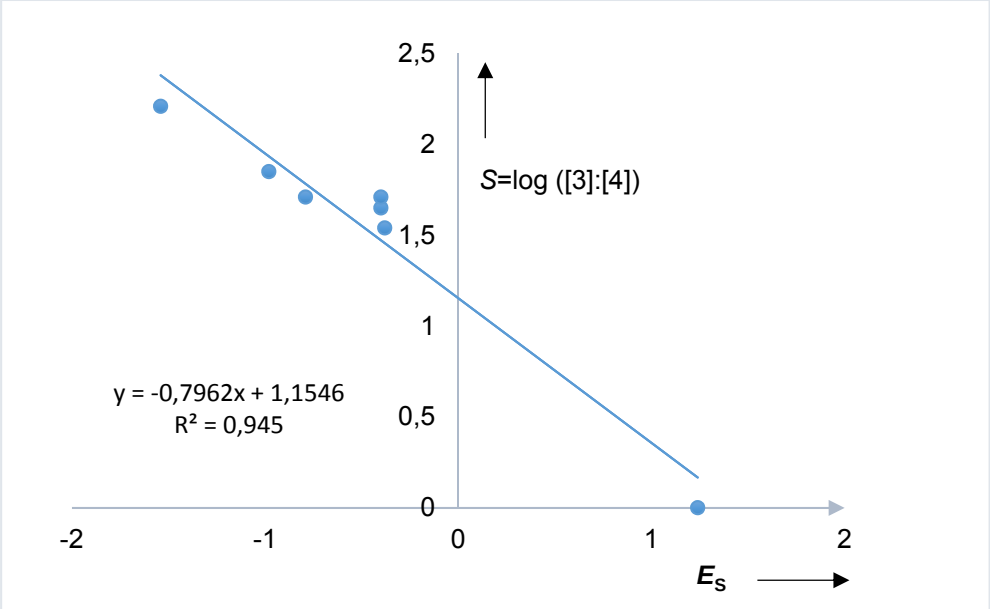

Figure 1. Correlation between the selectivity S = log ([**3**]:[**4**]) of the addition of thiol **1** to 1-alkenes **2a-f** at 80°C and **2g** at r.t. (see Table 1) and Taft E_S parameters including R=H (E_s +1.24).

It is known that thiyl radicals can abstract hydrogen from bisallylic C-H bonds,[28] and especially form allylic C-H bonds of allyl ethers,[29] -amines and -thioethers, giving an allylic radical, which by retransfer of hydrogen from thiol would result in isomerization of 1- to 2-alkene.[30] Addition of the thiyl radical to C(2) of the 2-alkene, though much

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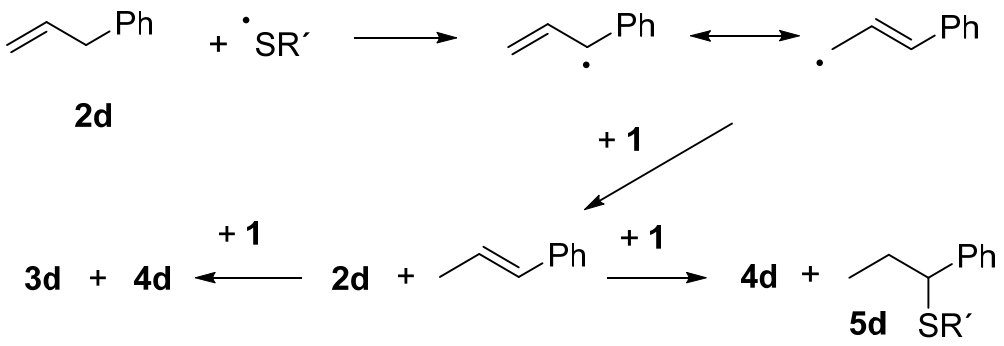
slower than to C(1) of the 1-alkene, could be another way to the minor regioisomer **4**, though also addition to C(3) giving a further isomer **5** should be observed (Scheme 2). Cadogan didn´t observe any addition to C(3) in the studied reaction of 1-octene and thioglycolic acid and concluded thereof that allylic hydrogen abstraction by thiyl radicals does not occur in the studied reaction.[12] We could confirm this result. We could not observe any third addition product beside the main product **3** and the minor isomer **4** with the exemption of alkene **2d** having allylic-benzylic C-H bonds. 0.3 % of isomer **5d** was formed at 80°C after 3 days reaction time (Table 1, entry 15), increasing to 0.6% after 6 days and 1.6 % after 8 days reaction time (see Experimental). 0.3 % and 0.2 % of isomer **5d** was formed at 80°C and 60°C, respectively, using AIBN as initiator after 100 min. reaction time (entry 8, 9). These results give clear evidence of the double bond isomerization followed by thiol addition. The observation of the formation of isomer **5d** via a secondary adduct radical seems to be remarkable because in the case of styrene **2c** via a primary adduct radical no respective isomer **4c** could be detected.



Scheme 2: Abstraction of an allylic-benzylic hydrogen giving an allylic-benzylic radical and in addition to products **3d** and **4d** the regioisomeric product **5d** via propenyl benzene.

Conclusions

In conclusion, we could show unambiguously that the radical addition of thiyl radicals to 1-alkenes is mainly steered by the steric effect of substituent R at the alkene. However, the regiochemical outcome of the thiol addition is strongly enhanced by the much faster fragmentation of the intermediate Markownikow adduct radical **II** in

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comparison to the anti-Markownikow adduct radical **I** giving with high selectivity the major product by addition to C(1), and the minor product to C(2). This result is of utmost importance considering the wide applications of this reaction in synthesis and especially in macromolecular synthesis.

Experimental section

1. Materials and methods

1.1 General information

Dodecanethiol (**1**), 1-octene (**2a**), allyl benzene (**2d**), vinylcyclohexane (**2e**), allylcyclohexane (**2f**) were purchased from Sigma-Aldrich, Germany, and 3,3-dimethyl-1-butene (**2g**) (min. 96 %) from TCI Deutschland GmbH and used as received. Styrene (**2c**), Sigma-Aldrich, Germany, was freshly distilled. Methyl 10-undecenoate (**2b**) was obtained from elf atochem, France, and was dried over molecular sieve.
Analytical equipment: Analytical GC was performed on a Carlo Erba GC series 4160 with a FID detector and fused silica capillary column DB1, 29 m, 0.25 mm. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker AM 300 or Bruker DRX 500 spectrometer at 300 K using residual non-deuterated solvent (^{1}H NMR) or $CDCl_3$ (^{13}C NMR) as internal standards. GC/MS (EI) using Thermo DSQII with GC Focus, fused silica capillary column DB5, 25m x 0.25 mm
All reactions were performed under nitrogen using standard Schlenk techniques.

1.2 General Procedure of addition of thiol 1 to alkenes 2

1.5 eq. of **1** was stirred in a 2-necked round-bottomed flask under nitrogen. 1 eq. of alkene **2** was added. The mixture was reacted for the time and at the temperature given. The reaction was followed by GC. Non-reacted **1** and **2** was removed and product **3** with **4** obtained by Kugelrohr distillation.

1.2.1 **Dodecyl(octyl)sulfane** (**3a**) and **dodecyl(octan-2-yl)sulfane** (**4a**): 0.56 g (5 mmol) of 1-Octene (**2a**) was reacted with 1.03 g (5 mmol) of thiol **1** at 90°C, 6 h. Kugelrohr distillation (125°C, $5x10^{-3}$ mbar) yielded 0.92 g (58 %) of product. [**3a**]:[**4a**]= 97.7:2.3,
During the complete reaction time [**3a**]:[**4a**]=97.7:2.3. The reaction was performed analogously at 80°C: [**3a**]:[**4a**]=97.8:2.2, and at 70°C: [**3a**]:[**4a**]=97.9:2.1.

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3a: ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.50 (t, J = 7.7 Hz, 4 H, SCH_2), 1.54 (m, 4 H, SCH_2CH_2), 1.35 (m, 4 H, $SCH_2CH_2CH_2$), 1.22 (m, 24 H, CH_2), 0.84 (2 x t, J = 7.2 Hz, 6 H, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 32.2, 31.9, 31.8, 29.7-29.0, 22.7, 22.6, 2 x 14.1 ppm. EI-MS (70 eV): *m/z* (%): 314 (3) [M^+], 201 (26), 145 (68), 111 (12), 97 (30), 83 (42), 69 (100). **4a**: EI-MS (70 eV): *m/z* (%): 314 (3) [M^+], 229 (34), 201 (40), 145 (25), 112 (30), 97 (16), 83 (44), 69 (100).

1.2.2 **Methyl 11-(dodecylthio)-undecanoate** (**3b**) and **methyl 10-(dodecylthio)-undecanoate** (**4b**): 1.98 g (10 mmol) of **2b** was reacted with 2.02 g (10 mmol) of thiol **1** at 80°C, 24 h. Non-reacted substrates were removed by Kugelrohr distillation (75°C, 6x10^{-3} mbar), 3.3 g of residue, [**3b**]:[**4b**]=98.1:1.9. Recrystallisation from ethanol yielded 2.71 g (68 %) of pure **3b**. The reaction was performed analogously at 63°C giving [**3b**]:[**4b**]=98.4:1.6. M. p. 46-47°C; ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 3.65 (s, 3 H, OCH_3), 2.51 (t, J = 7.7 Hz, 4 H, SCH_2), 2.32 (t, J = 7.5 Hz, 2 H, $COCH_2$), 1.60 (m, bs, 6 H, SCH_2CH_2 and $COCH_2CH_2$), 1.38 (m, 4 H, $SCH_2CH_2CH_2$), 1.35-1.26 (m, 28 H, CH_2), 0.90 (t, J = 7.2 Hz, 3 H, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 174.2, 51.4, 34.0, 32.1, 31.9, 29.7-28.9, 24.9, 22.6, 14.1 ppm. EI-MS (70 eV): *m/z* (%): 400 (0.5) [M^+], 231 (2), 201 (38), 199 (36), 87 (38), 74 (40), 69 (100). **4b**: EI-MS (70 eV): *m/z* (%): 400 (0.5) [M^+], 231 (4), 229 (8), 201 (16), 199 (10), 97 (26), 83 (46), 74 (24), 100 (53).

1.2.3 **Dodecyl(2-phenylethyl)sulfane** (**3c**): 1.04 g (10 mmol) of **2c** was reacted with 3.03 g (15 mmol) thiol **1** at 80°C, 4.5 h. Kugelrohr distillation (170°C, 1x10^{-3} mbar). Isolated yield of **3c** 2,4 g (80 %). ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 7.28 (m, 2 H, H-Ph), 7.20 (m, 3 H, H-Ph), 2.88 (dd, J = 7.6, 9.0 Hz, 2 H, CH_2-Ph), 2.76 (dd, J = 7.6, 9.0 Hz, 2 H, CH_2CH_2-Ph), 2.52 (t, J = 7.7 Hz, 2 H, SCH_2),1.58 (m, 2 H, SCH_2CH_2), 1.37 (m, 2 H, $SCH_2CH_2CH_2$), 1.36-1.20 (m, 16 H, CH_2), 0.88 (t, J = 7.2 Hz, 3 H, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 140.7, 128.4, 128.3, 126.2, 36.5, 33.7, 32.4, 31.8, 29.7-28.5, 22.6, 14.0 ppm. EI-MS (70 eV): *m/z* (%): 306 (2) [M^+], 215 (24), 201 (4), 151 (1), 138 (4), 105 (52), 104 (100).

1.2.4 **Dodecyl(3-phenylpropyl)sulfane** (**3d**), **Dodecyl(2-phenylpropyl)sulfane** (**4d) and Dodecyl(1-phenylpropyl)sulfane** (**4d)**: a) 1.18 g (10 mmol) of **2d** was reacted

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with 3.03 g (15 mmol) thiol **1** at 80°C, 8d. The reaction was followed by GC. Yield 80 % (GC), [**3d**]:[**4d**]:[**5d**]=96.9:2.8:0.3 (t=3d); 96.7:2.7:0.6 (t=6d); 95.3:3.1:1.6 (t=8d).
b) 0.59 g (5 mmol) of **2d,** 1.52 g (7.5 mmol) of thiol **1** and 100 mg AIBN was reacted at 80°C, 100 min. Kugelrohr distillation yielded 1.5 g (94 %) product, [**3d**]:[**4d**]:[**5d]=** 96.2:3.5:0.3. The reaction was performed analogously at 60°C. [**3d**]:[**4d**]:[**5d]=**97.0:2.8:0.2.
3d: ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 7.32 (m, 2 H, H-Ph), 7.24 (m, 3 H, H-Ph), 2.77 (t, *J* = 7.6 Hz, 2 H, CH_2-Ph), 2.56 (t, *J* = 7.5, 7.4 Hz, 4 H, SCH_2),1.95 (tt, *J* = 7.6, 7.7 Hz, 2 H, CH_2CH_2C), 1.62 (m, 2 H, SCH_2CH_2), 1.41 (m, 2 H, $SCH_2CH_2CH_2$), 1.38-1.25 (m, 16 H, CH_2), 0.94 (t, *J* = 7.0 Hz, 3 H, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 141.6, 129.2, 128.5, 128.3, 125.9, 34.9, 34.8, 32.1, 31.9, 31.5, 31.4, 31.0-29.0, 22.7, 14.1 ppm. EI-MS (70 eV): *m/z* (%): 320 (1) [M^+], 229 (0.5), 201 (0.5), 118 (100), 117 (35), 91 (24). **4d**: EI-MS (70 eV): *m/z* (%): 320 (0.5) [M^+], 229 (46), 207 (26), 201 (0.5), 117 (16), 91 (100). **5d**: EI-MS (70 eV): *m/z* (%): 320 (2) [M^+], 207 (60), 201 (10), 118 (100), 117 (40), 117 (16), 91 (54).

1.2.5 **2-(Cyclohexylethyl)(dodecyl)sulfane** (**3e**) and **1-(Cyclohexylethyl) (dodecyl) sulfane** (**4e**): a) 1.37 mL (1.1 g, 10 mmol) of **2e** was reacted with 3.03 g (15 mmol) of **1** at 80°C for 3 h. Kugelrohr distillation yielded 2.87 g (92 %) of product, [**3e**]:[**4e**]= 98.2:1.8.
b) The reaction was also performed at r.t. After 24 h of reaction time **2e** was completely converted. [**3e**]:[**4e**]=98.9:1.1
3e: ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.51 (m, 4 H, SCH_2), 1.74 (m, 5 H, CH and *c*$CHCH_2$), 1.60 (dt, *J* = 8.1, 7.3, Hz, 2 H, SCH_2CH_2CH), 1.51 (m, 2 H, SCH_2CH_2), 1.38 (m, 2 H, $SCH_2CH_2CH_2$), 1.28 (m, 22 H, CH_2), 0.91 (t, *J* = 7.2 Hz, 3 H, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 37.3, 37.0, 33.1, 32.1, 31.9, 29.7-28.5, 26.6, 26.2, 22.7, 14.1 ppm. EI-MS (70 eV): *m/z* (%): 312 (1) [M^+], 201 (4), 143 (16), 110 (46), 96 (16), 81 (100). **4e**: EI-MS (70 eV): *m/z* (%): 312 (1) [M^+], 229 (16), 201 (6), 143 (6), 110 (56), 69 (100).

1.2.6 **3-(Cyclohexylpropyl)(dodecyl)sulfane** (**3f**) and **2-(Cyclohexylpropyl) (dodecyl)sulfane** (**4f)**: a) 1,24 g (10 mmol) of **2f** was reacted with 3.03 g (15 mmol) of **1** at 80°C for 22 h and followed by GC. Kugelrohr distillation (170-180°C, $3x10^{-3}$ mbar) yielded 2.25 g (70%) of product. During the complete reaction time [**3f**]:[**4f**]= 98.2:1.8.

b) The reaction was also performed in the presence of 100 mg of AIBN. [**3f**]:[**4f**]= 97.8:2.2.

3f: ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.52 (t, J = 7.6 Hz, 4 H, SCH_2), 1.71 (m, 4 H, *c*$CHCH_2$), 1.62 (m, 5 H, CH and SCH_2CH_2CH), 1.42 (m, 2 H, $SCH_2CH_2CH_2$), 1.28 (m, 24 H, CH_2), 0.91 (t, J = 7.2 Hz, 3 H, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 37.4, 36.7, 33.3, 32.5, 32.2, 31.9, 29.6-29.3, 27.1, 26.7, 26.3, 22.7, 14.1 ppm. EI-MS (70 eV): m/z (%): 326 (1) [M^+], 201 (8), 157 (100), 123 (10), 81 (74). **4f**: EI-MS (70 eV): m/z (%): 326 (1) [M^+], 229 (2), 201 (2), 157 (6), 124 (100), 82 (96).

1.2.7 **(3,3-dimethylbutyl)(dodecyl)sulfane** (**3g**) and **(3,3-dimethylbutan-2-yl)(dodecyl)sulfane** (**4g**): 1.29 mL (0.84 g, 10 mmol) of **2g** was reacted 14 d with 3.03 g (15 mmol) thiol **1** at r.t. Non-reacted substrates were removed by Kugelrohr distillation. Yield: n.d.; [**3g**]:[**4g**]= 99.4:0.6.

3g: ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 2.49 (m, 4 H, SCH_2), 1.61 (tt, J = 7.5, 6.7 Hz, 2 H, SCH_2CH_2), 1.50 (m, 2 H, CH_2C), 1.32-1.23 (m, 18 H, CH_2), 0.92 (s, 9 H, $C(CH_3)_3$), 0.88 (t, J = 7.0 Hz, 3 H, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 44.1, 32.1, 31.9, 30.7, 29.7-29.0, 27.6, 22.7, 14.1 ppm. EI-MS (70 eV): m/z (%): 286 (12) [M^+], 229 (100), 215 (16), 201 (82). **4g**: EI-MS (70 eV): m/z (%): 286 (1) [M^+], 229 (100), 201 (4).

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Keywords: Radical reactions • Regioselectivity • Steric hindrance• Substituent effect • Molecule Assisted Homolysis

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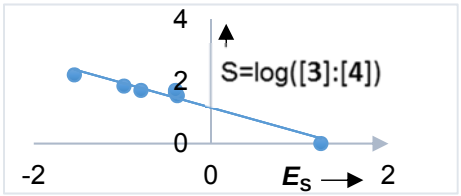
Steric effect

Ursula Biermann, Jürgen O. Metzger*

Regioselectivity of Radical Addition of Thiols to 1-Alkenes



The regioselectivities of the radical addition of thiol **1** to 1-alkenes **2** correlate with Taft E_s parameters of substituent R of **2** giving clear evidence that it is mainly controlled by the steric effect of substituent R because of an unsymmetrical transition state of the thiyl radical addition as is well known for alkyl radicals.

[1] T. Posner, *Chem. Ber. Dtsch. Chem. Ges*. **1905**, *38*, 646 – 657.
[2] K. Griesbaum, *Angew. Chem. Int. Ed. Engl.* **1970**, *9*, 273 – 287; *Angew. Chem.* **1970**, *82*, 276 – 290.
[3] O. Türünc, M. A. R. Meier, *Eur. J. Lipid Sci. Technol.* **2013,** *115*, 41–54.
[4] A. Dondoni, Angew. Chem,. Int. Ed. 2008, 47, 8995-8997; *Angew. Chem*. **2008**, *120*, 9133–9135.
[5] a) A. B. Lowe, *Polym. Chem*., **2010**, *1*, 17–36. b) C. E. Hoyle, T. Y. Lee, T. Roper, *J. Polym. Sci., Part A: Polym. Chem***. 2004**, *42*, 5301–5338.
[6] Most reviews until 1969 are referenced in Ref. [2], from then to 2014 in Ref. [7].
[7] F. Dénès, M. Pichowicz, G. Povie, P. Renaud, *Chem. Rev*. **2014**, *114*, 2587−2693.
[8] F. R. Mayo, C. Walling, *Chem. Rev.* **1940**, *27*, 351–412.
[9]J. M. Tedder, J. C. Walton, *Acc. Chem. Res*. **1976**, *9*, 183–191.
[10] B. Giese, *Angew. Chem. Int. Ed. Engl.* **1983,** *22,* 753-764; Angew. Chem. **1983**, *95*, 771–782.
[11] A. A. Oswald, W . Naegele, J. Org. Chem. **1966**, *31*, 830–835.
[12] J. I. G. Cadogan, I. H. Sadler, J. Chem. Soc. (B), **1966**, 1191–1205.
[13] D. W. Grattan, J. M. Locke, S. R. Wallis, J. Chem. Soc. Perkin I, **1973**, 2264-2267.
[14] N. O. Brace, *J. Fluorine Chem*. **1993**, *62*, 217 – 241.
[15] C. R. Morgan, F. Magnotta, A. D. Ketley, J. Polym. Sci. Polym. Chem. Ed. **1977***, 15***,** 627-645.
[16] D. Crich, in Organosulfur Chemistry, P. Page (Ed.), London [u.a.] : Acad. Press, **1995**, p. . 49-84.
[17] a) O. Nuyken, G. Reuschel, F. Siebzehnrübl, *Makromol. Chem. Macromol. Symp*. **1989**, *26*, 313 –331; b) G. Reuschel, Ph.D. Thesis, Technical University of Munich, Munich, **1986**.
[18] U. Biermann, W. Butte, R. Koch, P. A. Fokou, O. Türünc, M. A. R. Meier,J. O. Metzger, *Chem. Eur. J.* **2012**, *18*, 8201 – 8207.
[19] C-H BDE: Ph$C\mathbf{H}_2CH_3$ 357 kJ/mol; $CH_3CH_2C\mathbf{H}_3$ 422 kJ/mol; $CH_3C\mathbf{H}_2CH_3$ 410 kJ/mol; Data taken from Ref. [20].
[20] Y.-R. Luo, Bond Dissociation Energies in Organic Chemistry, CRC Press, Boca Raton, **2003**.
[21] J. O. Metzger, K. Klenke, J. Hartmanns, D. Eisermann, Chem. Ber. **1986**, *119*, 508 – 513.
[22] J. O. Metzger, *J. Prakt. Chem.*, **1990**, *332*, 767–781.
[23] C. Chatgilialoglu, A. Altieri, H. Fischer, *J. Am. Chem. Soc.* **2002**, *124*, 12816-12823.
[24] McPhee, D. J.; Campredon, M.; Lesage, M.; Griller, D. *J. Am. Chem. Soc.* **1989**, *111*, 7563-7567.

10.1002/ejoc.201701692

[25] C. Troche, F. N. Martinez, J. H. Horner, M. Newcomb, M. Senn, B. Giese, *Tetrahedron Lett.* **1996**, *37*, 5845-5848.
[26] R. W. Taft, in *Steric Effects in Organic Chemistry*, M. S. Newman, Ed., Wiley, New York, **1956**, Chapter 13, p. 598.
[27] B. H. Northrop, R. N. Coffey, *J. Am. Chem. Soc***. 2012**, *134*, 13804−13817.
[28] J. Guin, C. Mück-Lichtenfeld, S. Grimme, A. Studer, *J. Am. Chem. Soc*. **2007**, *129*, 4498–4503.
[29] G. Povie, A.-T. Tran, D. Bonnaff, J. Habegger, Z. Hu,C. Le Narvor, P. Renaud, *Angew. Chem*. **2014**, *126*, 3975 –3979*; Angew. Chem. Int. Ed.* **2014**, *53*, 3894–3898.
[30] Hydrogen abstractions by thiyl radicals were reviewed in ref. [7], p. 2668-2675.