Marked Effect of the Three-dimensional Shape of Solvent Molecules on Chemical Selectivity

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In the oxidation of a pair of associating thiols [(**1**) and (**2**)] with oxygen in propan-1-ol–water and propan-2-ol–water mixtures, the selectivity is controlled by the three-dimensional shape of the propanols.

There have been many studies of the effect of solvents on chemical reactivity[1—3] and selectivity,[2—4] almost all of which have concentrated on their polarity or other properties which arise from the *polar* atoms or groups in the solvent molecules. We have been studying the factors controlling chemical selectivity in aqueous binary solvent systems,[5—7] and report here the first example of the dependence of selectivity upon the three-dimensional shape of the *nonpolar* groups in solvent molecules.

Triethylamine-catalysed oxidation of a pair of associating thiols [(**1**) and (**2**)]† with oxygen gives one unsymmetrical (**4**) and two symmetrical disulphides [(**3**) and (**5**)].‡ The selectivity (r) is represented by the logarithmic ratio of the yield of (**4**) to twice that of (**3**): $r = \ln\{[(\mathbf{4})]/(2[(\mathbf{3})])\}$.

Table 1 shows the selectivity (r) in oxidation of (**1**) and (**2a**) for R = iso- and normal pentyl groups at 35.0 °C in a pair of aqueous binary solvent systems each containing a propanol (mole fraction of propanol = x_{PrOH}). The r values for R = iso-C_5H_{11} are larger in the propan-2-ol system than in the propan-1-ol system regardless of solvent composition exam-

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† Thiols (**1**) and (**2**) were readily prepared as described previously.[6] All new compounds had satisfactory spectroscopic data.

‡ Thiols (**1**) and (**2**) (0.50 mmol each) in 12.5 ml of solvent were treated with O_2 in the presence of Et_3N (0.05 mmol) at 35.0 °C until the oxidation was complete. The yields of (**3**) and (**4**) were determined as described previously.[6] The r values presented in Tables 1 and 2 were reproducible within ±0.05 in two or more experiments.

Table 1. Selectivity (r) and product ratio {[(**4**)]/[(**3**)]} in the oxidation of a pair of associating thiols [(**1**) and (**2a**) (R = iso- or n-C_5H_{11})] in propanol (PrOH)–water systems at 35.0 °C.

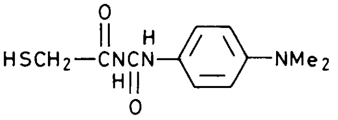
R	iso-C_5H_{11}				n-C_5H_{11}			
	$\mathrm{Pr^nOH}$		$\mathrm{Pr^iOH}$		$\mathrm{Pr^nOH}$		$\mathrm{Pr^iOH}$	
x_{PrOH}	[(**4**)]/[(**3**)]	r	[(**4**)]/[(**3**)]	r	[(**4**)]/[(**3**)]	r	[(**4**)]/[(**3**)]	r
0.36	7.0 ± 0.3[a]	1.3	12.3 ± 0.6	1.8	0.369 ± 0.009	−1.7	0.211 ± 0.008	−2.2
0.50	4.2 ± 0.1	0.75	10.3 ± 0.3	1.6[b]	0.35 ± 0.02	−1.7	0.172 ± 0.007	−2.5[b]
0.60	6.8 ± 0.3	1.2	10.5 ± 0.5	1.7	0.290 ± 0.003	−1.9	0.224 ± 0.009	−2.2
0.85	11.6 ± 0.4	1.8	13.7 ± 0.6	1.9	0.270 ± 0.007	−2.0	0.154 ± 0.007	−2.6
1.00	13.5 ± 0.6	1.9	20 ± 1	2.3	4.3 ± 0.2	0.77	2.28 ± 0.09	0.13

[a] Errors given are three times the standard deviations. [b] Values from T. Endo, H. Takei, K. Guro, M. Yamashita, S. Yonenaga, M. M. Ito, and K. Matsushita, *Chem. Lett.*, 1984, 1717.

Table 2. Selectivity (r) and product ratio {[(**4**)]/[(**3**)]} in the oxidation of a pair of associating thiols [(**1**) and (**2b**) (R = iso- or n-C_3H_7)] in PrOH–water systems at 35.0 °C.

R	iso-C_3H_7				n-C_3H_7			
	$\mathrm{Pr^nOH}$		$\mathrm{Pr^iOH}$		$\mathrm{Pr^nOH}$		$\mathrm{Pr^iOH}$	
x_{PrOH}	[(**4**)]/[(**3**)]	r	[(**4**)]/[(**3**)]	r	[(**4**)]/[(**3**)]	r	[(**4**)]/[(**3**)]	r
0.20	8.9 ± 0.3[a]	1.5	9.5 ± 0.4	1.6	1.20 ± 0.07	−0.51	0.72 ± 0.03	−1.0
0.50	3.7 ± 0.2	0.62	5.6 ± 0.1	1.0	1.55 ± 0.05	−0.25	0.93 ± 0.05	−0.76
0.80	4.3 ± 0.2	0.77	6.5 ± 0.2	1.2	1.77 ± 0.04	−0.12	0.63 ± 0.03	−1.2
1.00	5.0 ± 0.2	0.91	12.6 ± 0.5	1.8	9.3 ± 0.4	1.5	7.3 ± 0.1	1.3

[a] Errors given are three times the standard deviations.



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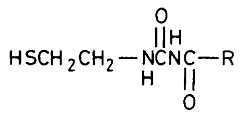


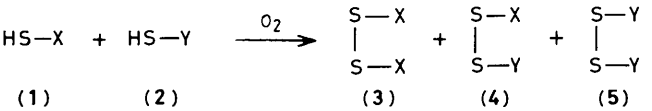
$HSCH_2CH_2-\underset{H}{N}C\underset{O}{\overset{}{N}}\overset{O}{C}-R$

iso-(**2a**) ; R = $[CH_2]_2CHMe_2$

n-(**2a**) ; R = $[CH_2]_4Me$

iso-(**2b**) ; R = $CHMe_2$

n-(**2b**) ; R = $[CH_2]_2Me$



ined. In contrast, for R = n-C_5H_{11}, r values are larger in the propan-1-ol system than in the propan-2-ol system. Thus, the thiol (**1**) reacts with iso-(**2a**) more preferentially, and with n-(**2a**) less preferentially, in the propan-2-ol system than in the propan-1-ol system.§

This 'solvent shape effect' was further investigated in the oxidation of (**1**) and (**2b**) (Table 2). The r values for R = iso-C_3H_7 were larger in the propan-2-ol system, whereas those for R = n-C_3H_7 were larger in the propan-1-ol system. The most unusual observation from the selectivity data is that, in pure propan-1-ol, the r value for R = n-C_3H_7 exceeds that for R = iso-C_3H_7, in contrast to the R–r relationship for lower mole fractions of propan-1-ol.

These two isomeric propanols have the same dipole moment (5.54×10^{-30} C m), and their dielectric constants are similar (20.33 for propan-1-ol and 19.92 for propan-2-ol at 25 °C).[2]¶ Consequently, the observed selectivity differences may best be attributed to the difference in the shape of the propyl group in the propanols.

We have thus demonstrated that higher selectivity is achieved when the nonpolar group of a propanol in a mixed solvent resembles a given nonpolar group of one of the reacting molecules in three-dimensional shape. Our work suggests that the three-dimensional shape of solvent molecules is one factor controlling selectivity.

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§ It has been shown that (i) the product ratio in this type of oxidation is kinetically controlled,[5,6] (ii) the oxidation proceeds through tetramers formed by dimerisation of dimers produced from (**1**) and (**2**) through two NH · · · O intermolecular hydrogen bonds between the inner -NHC(=O)- units in the -C(=O)NHC(=O)NH- group,[6] and (iii) the selectivity depends upon the relative concentration of the tetramers.[7]

¶ The dielectric constants of propanol–water mixtures (x_{PrOH} = 0.55) at 40 °C are 23.89 for propan-1-ol–water and 21.63 for propan-2-ol–water (J. B. Hasted, in 'Water—A Comprehensive Treatise,' ed. F. Franks, Plenum Press, New York, 1973, vol. 2, ch. 7).