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Influence of H-Donor and Temperature on the Stereoselectivity of Radical Reactions[**]

By *Bernd Giese,* Juan Antonio González-Gómez, Stephen Lachhein, and Jürgen O. Metzger*

Radical reactions are finding increasing use in organic synthesis, whereby a knowledge of the reactivities and selectivities is of decisive importance. Stereoselectivity plays a crucial role, for it is dependent not so much on the product stability but rather on the shielding of the radical center because of the early transition states of rapid radical reactions. This is important in the case of H-abstraction reactions because the transfer of the small H-atoms from the less shielded side leads to the thermodynamically less stable product. Thus the addition of alkyl radicals to methylmaleic anhydride 1 and to phenylacetylene 3 in the subsequent H-abstraction step by cyclohexylmercury hydride preferentially affords the isomers (Z)-2 and (Z)-4, respectively, whereby the selectivity increases with increasing size of the substituent R.[2]
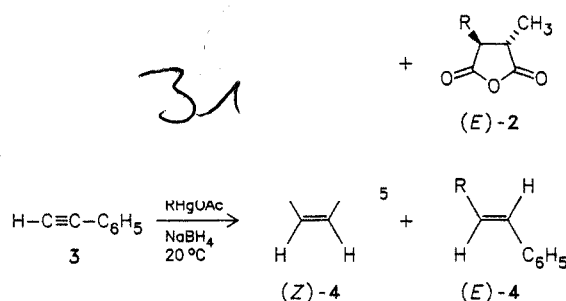
R	a $n\text{-}C_6H_{13}$	b $c\text{-}C_6H_{11}$	c $t\text{-}C_4H_9$
(Z)-2 : (E)-2	62 : 38	89 : 11	94 : 6
(Z)-4 : (E)-4		74 : 26	97 : 3

In the case of the π-vinyl radical 5b,[3] formed by addition of cyclohexyl radicals to phenylacetylene, we have now observed that the (Z)/(E) ratio can also be influenced, and even reversed, by variation of the H-donor and the reaction temperature. Measurements between −20°C and 260°C show that (Z)-4b is formed with less activation enthalpy then (E)-4b (Table 1).

The approach of the H-donor from the *anti* side of the vinyl radical 5b (away from the cyclohexyl group), for instance, requires less activation enthalpy than the attack from the *syn* side. The energy difference $\Delta H^+((E)\text{-}4b) - \Delta H^+((Z)\text{-}4b)$ thereby increases with decreasing

[*] Prof. Dr. B. Giese, Dr. J. A. González-Gómez, Dr. S. Lachhein
Institut für Organische Chemie und Biochemie
der Technischen Hochschule
Petersenstrasse 22, D-6100 Darmstadt (FRG)

Priv.-Doz. Dr. J. O. Metzger
Fachbereich Chemie der Universität
Carl-von-Ossietzky-Strasse 9-11, D-2900 Oldenburg (FRG)

Table I. Activation parameters for the stereoselectivity of H-transfer to the vinyl radical **5b**.

H-Donor	$\Delta H^{\neq}((E)\text{-}4b)-$ $\Delta H^{\neq}((Z)\text{-}4b)$ [kJ/mol]	$\Delta S^{\neq}((E)\text{-}4b)-$ $\Delta S^{\neq}((Z)\text{-}4b)$ [J mol^{-1} K^{-1}]	Temperature [°C]
c-C$_6$H$_{11}$HgH	2.5±0.2	1.2±0.5	−20–80
Bu$_3$SnH	4.6±1.5	7 ±5	0–84
c-C$_6$H$_{12}$	11.7±1.0	28 ±1.3	120–260

reactivity of the H-donor. It increases from 2.5 (cyclohexylmercury hydride) to 4.6 (tributyltin hydride) to 11.7 kJ/mol (cyclohexane). At the same time, the rate of H-transfer in this series decreases by about a factor of 10^7.[4]
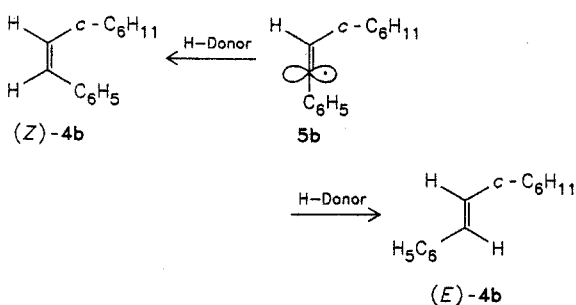
Apparently, the differences in the steric shielding have greater influence on the activation enthalpies the less reactive the H-donor is, because the distance between the reactants is smaller in the later transition states.[5] Since the difference in the activation entropies in the same series also increases from 1.2 to 7 to 28 J/mol^{-1} K^{-1}, the compensation of the activation enthalpies and activation entropies leads to an isoselective temperature,[6] which lies between 60 and 80°C (Fig. 1). In this temperature range the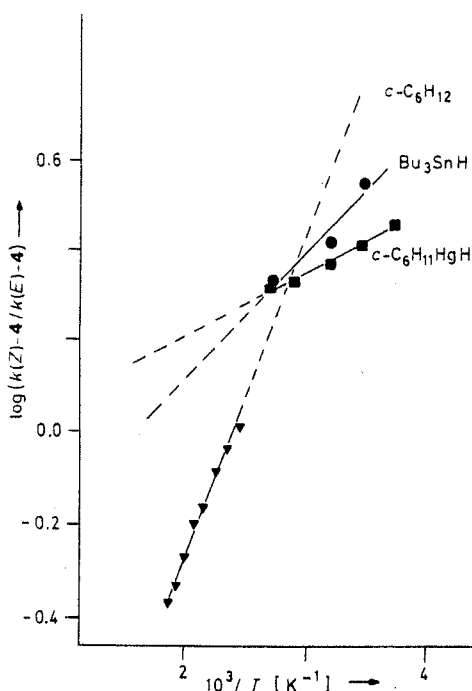 H-donors mentioned here react with the same selectivity. In the case of cyclohexane the entropy effects are so large that above 140°C the isomer (E)-**4b** is the major product. Thus, at 0°C the ratio (Z)-**4b** :(E)-**4b** is 78:22 with Bu$_3$SnH as donor, whereas at 260°C with cyclohexane as H-donor the selectivity (29:71) is reversed.[7]

These investigations on the vinyl radical **5b** show how the stereoselectivities of radical reactions can be steered by varying the H-donors (radical trapping agents) and the reaction temperature.

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[3] The phenyl substituent enforces sp hybridization at the radical center: R. M. Kochik, J. A. Kampmeier, J. Am. Chem. Soc. 90 (1968) 6733; J. E. Bennett, J. A. Howard, Chem. Phys. Lett. 9 (1971) 460; L. Bonazzola, S. Fenistein, R. Marx, Mol. Phys. 22 (1971) 689.
[4] The rate coefficients for H-transfer to alkyl radicals for cyclohexylmercury hydride, tributyltin hydride, and cyclohexane have been reported to be about 10^7, 10^6 and 1 L mol^{-1} s^{-1}, respectively at 20°C: B. Giese, G. Kretzschmar, Chem. Ber. 117 (1984) 3160; C. Chatgilialoglu, K. U. Ingold, J. C. Scaiano, J. Am. Chem. Soc. 103 (1981) 7739; D. J. Boddy, E. W. R. Steacie, Can. J. Chem. 39 (1961) 13.
[5] Later transition states are required by the Hammond postulate for slower reactions: G. S. Hammond, J. Am. Chem. Soc. 77 (1955) 334.
[6] B. Giese, Angew. Chem. 89 (1977) 162; Angew. Chem. Int. Ed. Engl. 16 (1977) 125; Acc. Chem. Res. 17 (1984) 438.
[7] For the experimental procedure with cyclohexane see J. Hartmanns, K. Klenke, J. O. Metzger, Chem. Ber. 119 (1986) 488. Control experiments show that an isomerization (Z)-**4b**→(E)-**4b** is not apparent up to 260°C.

Fig. 1. Temperature dependence of the stereoselectivity for H-transfer to the vinyl radical **5b** by c-C$_6$H$_{12}$, Bu$_3$SnH, and c-C$_6$H$_{11}$HgH as H-donors.