$\alpha'\beta$ Elimination of Carbanions Derived from Thioethers†

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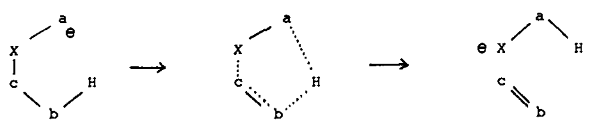
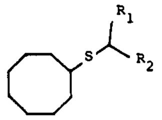
Abstract: The $\alpha'\beta$ elimination of the carbanions prepared with butyllithium from allyl, benzyl, and methyl cyclooctyl thioethers to *cis*-cyclooctene occurs in high yield. An explanation is presented for the production of *cis*-cyclooctene. Carbanions derived from alkyl benzyl thioethers undergo in high yield the $\alpha'\beta$ elimination to benzyl thiolate and to alkene. Carbanions bearing a long aliphatic chain C_{18} and C_{19} undergo the $\alpha'\beta$ elimination distinctly slower than those with a short chain. The 1-butene/2-butene ratio for the elimination on the carbanion of *sec*-butyl benzyl thioether is 5.3. Benzyl vinyl thioether may also be prepared from dibenzyl acetal by this elimination. A new method using carbanions as intermediate for the homologation $RCH_2X \rightarrow\rightarrow RCH{=}CH_2$ is proposed. The stereochemistry of this $\alpha'\beta$ elimination was shown to be syn using stereospecifically deuterated cyclooctyl derivatives and ^2H NMR spectroscopy. The high primary isotope effect is explained by a close to linear hydrogen transfer from the β carbon to the α' carbon.

The $\alpha'\beta$ elimination[1] occurs in a syn manner with a five-membered cyclic transition state.[2] The transition state involves the movement of six electrons and the reaction could be concerted according to the Woodward-Hoffmann rules.[3] The $\alpha'\beta$ elimination has been observed for amine oxide (Cope reaction),[4] amine-imide,[5] sulfoxide,[6] selenoxide,[7] derivatives of sulfimine,[8] and ylides derived from quaternary ammonium salts,[9] hydrazonium salts,[10] and sulfonium salts.[11] The $\alpha'\beta$ elimination is not restricted to ylides and has been observed beside the Wittig rearrangement of carbanions derived from ethers.[12,13] The Wittig rearrangement occurs very likely in a stepwise manner.[12b,c]



Carbanions derived from thioethers quite rapidly undergo concerted sigmatropic shifts: a [2,3] sigmatropic shift for diallyl thioether, for instance.[14] However, rearrangements which should be stepwise according to the Woodward-Hoffmann rules occur only when the migrating center is stabilized as in the cases of allyl benzyl thioether[15] and 5-phenyl-4-thiacyclohexene.[16] The reluctance of the carbanions derived from thioethers to undergo a Wittig-type rearrangement, which usually competes with the $\alpha'\beta$ elimination in the case of carbanions from ethers, may result in the predominance of the $\alpha'\beta$ elimination for the carbanions derived from thioethers bearing a β hydrogen.[17] With this hypothesis, we investigated the reactivity of the carbanion with a β hydrogen in such a position that an $\alpha'\beta$ elimination could occur. We report here the results of our investigations.

First we determined the nature of the carbanionic center which is the most convenient. The $\alpha'\beta$ elimination was tried with carbanions from methyl, allyl, and benzyl cyclooctyl thioethers (**1a, 1b,** and **1c**). The metalation using butyllithium occurred for all three compounds. We prepared at −78 °C the carbanions from the allyl and benzyl cyclooctyl thioethers (**1b** and **1c**). After the addition of methyl iodide, the expected C-methylated products **1d** and **1e** were isolated, showing that at this temperature the carbanion in tetrahydrofuran was stable. If, after the metalation at −78 °C, the temperature was raised to 0-25 °C, elimination occurred at a reasonable rate. For methyl cyclooctyl thioether (**1a**), the metalation and the elimination were done at 20 °C in hexane-tetramethylethylenediamine. Mainly *cis*-cyclooctene was isolated with a trace (< 1%) of *trans*-cyclooctene. The possibility that the *trans*-cyclooctene would eventually be isomerized to *cis*-cyclooctene in the reaction medium[18] was excluded by carrying out the elimination of benzylic carbanion in the presence of *trans*-cyclooctene. Only a trace of isomerization was detected. Thus *cis*-cyclooctene originates directly from $\alpha'\beta$ elimination.



1a $R_1=R_2=H$
b $R_1=CH{=}CH_2$ $R_2=H$
c $R_1=C_6H_5$ $R_2=H$
d $R_1=CH{=}CH_2$ $R_2=CH_3$
e $R_1=C_6H_5$ $R_2=CH_3$

Initial work on the $\alpha'\beta$ elimination in cyclooctyl derivatives had led to the hypothesis that formation of *cis*-cyclooctene as a major olefin is characteristic of an $\alpha'\beta$ elimination.[9] However, for the ylides derived from ammonium salts the cis/trans ratio of cyclooctene originating from $\alpha'\beta$ elimination may be as low as 0.3[19] and could be influenced by the aggregation states of the ylides.[20] A thermodynamic control for the cis/trans ratio has also been proposed.[21] In Table I are presented the results of $\alpha'\beta$ elimination on cyclooctyl derivatives, with the isotope effect observed (for one case in a related system).

From these results, it is noticeable that a high isotope effect on the β hydrogen for the formation of *cis*-cyclooctene is observed for the cases where the *cis*-cyclooctene is the major olefin.[25] A high primary isotope effect implies that the hydrogen position is symmetrical in the transition state.[26] This may indicate that the transition state of the $\alpha'\beta$ elimination is planar. A planar transition state leading to the *trans*-cyclooctene is more strained than the planar transition state leading to *cis*-cyclooctene. Thus $\alpha'\beta$ elimination, which shows a high isotope effect, yields mostly *cis*-cyclooctene.

For further studies of this $\alpha'\beta$ elimination, we chose benzyl thioether. The $\alpha'\beta$ elimination was then performed on carbanions derived from *tert*-butyl, *sec*-butyl, *n*-butyl, octadecyl, and nonadecyl benzyl thioethers (**2a–e**). The carbanions were

$R - S - CH_2C_6H_5$ $R - S - CH(CH_3)C_6H_5$

2a R=t-butyl 3
b R=sec-butyl
c R=n-butyl
d R=octadecyl
e R=nonadecyl

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† This article is dedicated to Professor W. S. Johnson on the occasion of his 65th birthday.

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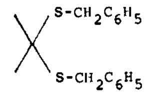
Table I. α'/β Elimination of Cyclooctyl Derivatives

cyclooctyl derivatives	product ratio *cis-trans*-cyclooctene	ref	k_{1H}/k_{2H} (temp, °C) for *cis*-cyclooctene	ref
N-butyl-*N*,*N*-dimethylammonium salt (ylide)	60/40 to 33/67	20	1.23-1.52	20
N-benzyl-*N*,*N*-dimethylammonium salt (ylide)	95/5	19	1.47	19
dimethylsulfonium salt (ylide)	100/0	22	3.5 (35)[a]	23
1-cyclooctyl-1,1-dimethylhydrazonium (ylide)	24/1	10		
N,*N*-dimethyl *N*-oxide	98/2	24	3.5 (100)	21
benzyl thioether (carbanion)	100/0		7.0–9.0 (0)	

[a] β-Arylethyldimethylsulfonium salt (ylide).

prepared at −78 °C by action of butyllithium and were stable at this temperature as shown by the reaction with methyl iodide to give the thioethers **3**. The $\alpha'\beta$ elimination proceeded at a reasonable rate at 20 °C and the olefins were isolated in high yield. It was remarkable that, in the case of octadecyl and nonadecyl benzyl thioethers (**2d** and **2e**), the $\alpha'\beta$ elimination took several hours in refluxing tetrahydrofuran. Two facts seemed surprising: first, that the carbanion did not attack the solvent; second, that there was such a rate difference between benzyl *n*-butyl thioether (**2c**), for instance, and these two thioethers **2d** and **2e**. This long chain containing carbanions may form an aggregate where the solvent is partially excluded and where the β hydrogens are at a distance from the carbanion center. The long aliphatic chains may stabilize this aggregate. A structural study of carbanions of this type could clarify this surprising long-chain effect. Are there other carbanionic reactions which are influenced by the long aliphatic chain, for example, polymerization?

Benzyl vinyl thioethers should also be accessible with this method. Acetone dibenzyl thioacetal (**4**) gave a 95% yield of benzyl propenyl thioether (**5**), butyllithium being used in a 1/1 molar ratio.



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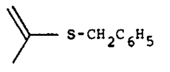

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The regioselectivity was studied for the carbanion from *sec*-butyl benzyl thioether (**2b**). The 1-butene/2-butenes ratio was determined after bromination. If the reaction was carried out at 20°C in tetrahydrofuran, the ratio was 5.2:1; if done in benzene the ratio was 4:1.[27] The ratio was the highest observed among $\alpha'\beta$ eliminations. Pyrolysis at 180 °C of ethyl *sec*-butyl sulfoxide gave a 1-butene/2-butenes ratio of 2.4.[28] This ratio depends on the experimental conditions for *sec*-butyl arenesulfonylsulfilimine: 2 at 115–120 °C, 1.7 at 160–170 °C, and 0.67 in benzene at 115–120 °C.[8a] The easy elimination in the case of 2-butyl phenyl selenoxide resulted in a ratio of 1.6.[7] For E2 elimination, the ratio varied from 18 for the pyrolysis of 2-butyltrimethylammonium hydroxide[29] to 0.5 for the acetolysis of 2-butyl tosylate.[30] For the E2 reaction of 2-butyl tosylate, it has been shown that there is a correlation between the base strength and the ratio 1-butene/2-butenes, the stronger base favoring 1-butene.[31] A similar trend could be seen for $\alpha'\beta$ elimination:[32] a more basic α' center favors the 1-butene.

The alkylation of the carbanion derived from dimethyl thioether occurred in high yield by the addition of hexamethylphosphoramide (HMPA) to the reaction medium.[33] The reaction of the carbanion derived from dimethyl thioether with alkyl halogenide gave a high yield of the homologous alkyl methyl thioether. By action of butyllithium on this compound, the carbanion $RSCH_2^-$ was prepared and its $\alpha'\beta$ elimination produced the terminal olefin. The entire sequence proceeded at a high yield. The following is a completely carbanionic alternative reaction scheme for the sequence:

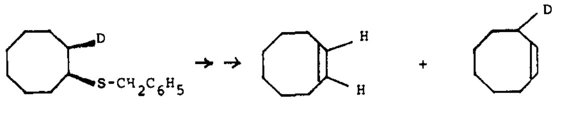
$$R-CH_2-X + CH_3-S-CH_2^{\ominus}Li^{\oplus} \longrightarrow R-CH_2-CH_2-S-CH_3$$

$$R-CH_2-CH_2-SCH_3 \rightarrow R-CH_2-CH_2-S-CH_2^{\ominus}Li^{\oplus} \rightarrow R-CH_2=CH_2$$

$$RCH_2X \rightarrow \rightarrow RCH{=}CH_2$$

Other solutions for such a transformation are the Wittig reaction and the alkylation of dimesylsodium followed by pyrolysis.[34]

In order to have a deeper understanding of the mechanism of this $\alpha'\beta$ elimination, we undertook a stereochemical study of the reaction course with deuterated benzyl cyclooctyl thioethers. The stereospecifically deuterated cyclooctanols were prepared according to the published procedures: the trans β-deuterated cyclooctanol from the epoxide of *cis*-cyclooctene with lithium aluminodeuteride[35] and the cis β-deuterated cyclooctanol by deuterioboration and oxidation of *cis*-cyclooctene.[36] The reaction of the corresponding mesylates with sodium benzylthiolate in hexamethylphosphoramide resulted in the labeled thioethers **6** and **7**. We assume that this last reaction proceeded with inversion. In the ^2H NMR spectra of the two epimers, a high-field shift for the signal attributed to the β deuteron in *cis*-**6** (δ 1.46 ppm) was observed with respect to that of *trans*-**7** (δ 1.96 ppm). The ^1H NMR spectrum of **6** and **7** showed the expected change in the δ 1.6–1.8-ppm region. The elimination on these compounds was conducted in the usual way. After 3 h, methyl iodide was added. The *cis*-cyclooctene and benzyl methyl thioether were separated and analyzed by coupled gas chromatography-mass spectrometry.



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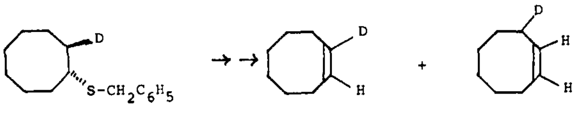

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A decrease of the deuterium content in the *cis*-cyclooctene was observed during its elution from the gas chromatography column. In order to obviate that variation, the deuterium content was determined throughout the elution by integration of the area for each peak. These values are presented in Table II. For the cis thioether **6**, deuterium was found in the benzyl methyl thioether and the ^2H content of *cis*-cyclooctene was decreased; for the trans thioether **7**, no deuterium transfer to the benzyl methyl thioether was detected. This agrees with a syn elimination. In order to ascertain this conclusion, the location of the deuterium atom in the *cis*-cyclooctene was determined by ^2H NMR.[37] The ^2H NMR spectrum of *trans*-cyclooctene at natural deuterium abundance (Figure 1A) was

Table II. Deuterium Content Determination by Mass Spectrometry[a]

	analyzed products deuterium content				resulting
	benzyl methyl thioether		*cis*-cyclooctene		isotope effects
starting product	$^2H_0$	$^2H_1$	$^2H_0$	$^2H_1$	$k_{^1H}/k_{^2H}$
tetrahydrofuran–TMEDA (0 °C)					
6	87.5	12.5	12.5	87.5	7.0
7	100	0	0	100	
tetrahydrofuran–HMPA (0 °C)					
6	89.5	10.5	10	90	8.5–9.0
7	100	0	0	100	
tetrahydrofuran–HMPA (40 ° C)					
6	88.5	11.5	11.5	88.5	7.7

[a] All data were the results of at least two experiments and were found to be reproducible within 0.5%. The deuterium contents are corrected for the isotopic purity of labeled benzyl cyclooctyl thioeter (at least 83% $^2H_1$ content). The conversion was complete as checked by the absence of C-methylated product. Determination was done by mass spectrometry with an ionization potential of 15 eV.

a complex pattern for the deuterons at positions 3, 4, and 5. This is due to the rigid structure of this medium ring.[38] The ^2H NMR spectrum of *cis*-cyclooctene at natural deuterium abundance (Figure 1B) showed three signals (δ) at 5.78, 2.3, and 1.69 ppm (relative to tetramethylsilane) with the relative areas 1:2:4 attributed to the deuterium at the vinylic, allylic, and other positions. The simplicity of the spectrum of *cis*-cyclooctene is due to the equivalence of the deuterons caused by a rapid conformational equilibrium.[39] The *cis*-cyclooctenes from the reaction of cis and trans thioethers **6** and **7** at 0 °C in the presence of tetramethylethylenediamine or hexamethylphosphoramide were analyzed by ^{2}NMR as above except that the number of scans was lower so that only the positions enriched in deuterium were revealed. The *cis*-cyclooctene originating from *cis*-**6** showed one intense signal at δ 2.3 ppm (Figure 1C) and the *cis*-cyclooctene from *trans*-**7** two signals: one at δ 5.78 ppm and another one at δ 2.3 ppm with an area ratio of 43/57 (Figure 1D). The presence of deuterium mainly at the allylic position in the cyclooctene arising from *cis*-**6** agrees with the syn mechanism as the major process. The presence of small peaks corresponding to the vinylic position for *cis*-cyclooctene from *cis*-**6** and to the positions at C-4 and C-5 for *cis*-cyclooctene from *trans*-**7** could be explained by the presence, to a small extent, of a nonstereospecific elimination or better to the incomplete stereochemical purity of the deuterated thioethers. It is known that the deuterioboration of cyclooctene introduces, because of the reversibility of the borane addition,[36] some deuterium at other positions than at β, and that beside the expected reductive ring opening of epoxide other processes introduce the label at positions different from the expected one.[35] However, this does not change the conclusion that the elimination of the carbanion of benzyl cyclooctyl thioether is essentially a syn elimination.

The secondary isotope effect was found to be 1.3 from the ^2H NMR of the cyclooctene from *trans*-**7**. From the mass spectrometric determinations, the primary isotope effect $k_{^1H}/k_{^2H}$ was 7.0 in tetrahydrofuran at 0 °C and 8.5–9.0 and 7.6–7.8 in tetrahydrofuran–HMPA at 0 and 40 °C.[40] The primary isotope effects are quite large, close to the maximum calculated on a semiclassical basis for the isotope effect involving a C–H bond.[41] The primary isotope effect $k_{^1H}/k_{^2H}$ has been found to be as low as 2–3 for the pyrolysis of amino oxide. This was attributed to a nonlinear transition state.[42]

The distances $H_\beta \cdots O$ for *N*-oxide and $H_\beta \cdots C^-$ for the carbanion are 1.7 and 2.2 Å, respectively, and the angles $C–H_\beta \cdots X$ are 114 and 122°, all the atoms concerned in the α'β elimination being coplanar, using published bond lengths and angles for *N*-oxides and thioethers.[43,44] The deformation of the C–S–C angle does not involve much energy (this angle is close to 84° in some cyclic structures[44]). Then a transition stage for α'β elimination, where the hydrogen transfer is almost linear, may be more easily achieved with the thioether carbanion than for the *N*-oxide.[45]

The isotope effect would then be larger for the thioether (linear transfer for H_β) than for the amine oxide (angular transfer for H_β). It would be surprising if the C–S bond were completely broken in the transition state, because thioethers are very poor leaving groups.[47] Some quantum mechanical tunneling in case of the carbanion may explain the large primary isotope effect. In order to ascertain this, the temperature dependence of the isotope effect should be studied. This was not undertaken here, because the nature of the ions present (dissociation and aggregation) may show a temperature dependence. This could then induce changes in the transition state and consequently in the isotope effect. The temperature dependence of the isotope effect would thus not be attributed to a single cause. The primary and secondary isotope effects determined in the present work result from the competition between two transition states: one involving a hydrogen and the second a deuterium. So the isotope effects are valid, even if the reaction steps from which they originate were not rate determining.[48] The secondary isotope effect was also high and agreed with a hybridization change at the β carbon. If the β proton is half transferred in the transition state, the carbon–carbon bond must already have some double-bond character.

The change of the primary isotope effect on going from tetrahydrofuran–tetramethylethylenediamine to tetrahydrofuran–hexamethylphosphoramide suggested that in the more cation solvating medium the transition state is more symmetrical with respect to the hydrogen transfer.

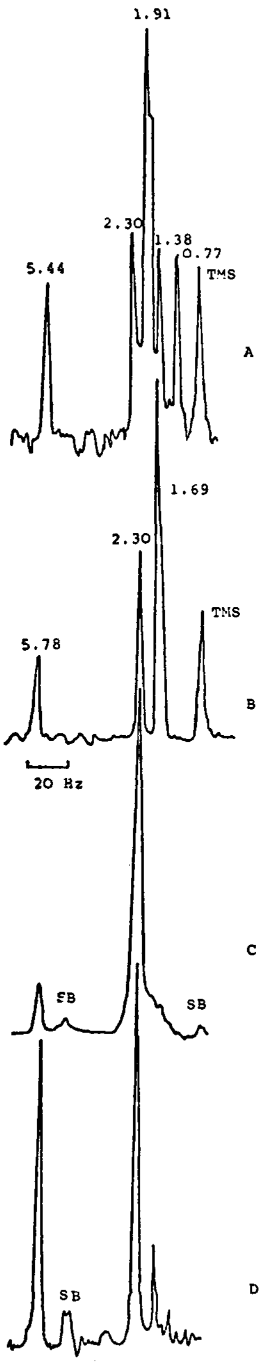
Taken as a whole, our results show that the carbanion derived from thioethers may undergo an α'β elimination. This elimination of thioethers, certainly of preparative value, is to be extended to other carbanions; for example, it would be surprising if the carbanion derived from selenoethers did not undergo such an α'β elimination.

The α'β elimination of the carbanion derived from thioether prepared by nucleophilic substitution with thiolates may complement the usual elimination methods.

Experimental Section

The *n*-butyllithium used here was the commercially available hexane solution which is approximately 2 M in butyllithium. TMEDA is tetramethylethylenediamine. Tetrahydrofuran (THF) was distilled from lithium aluminohydride or from benzophenone and sodium. The stationary phase for the gas chromatography (GC) was Triton X-305 (10%) on Chromosorb W-AW 80–100 DMCS and the mobile phase nitrogen.

Preparation of the Thioethers. The benzyl alkyl thioethers have been prepared from alkylthiol and benzyl chloride or from benzylthiol and alkyl bromide or tosylate. The reaction was run in the standard fashion. A solution of sodium thiolate (0.1 mol) in methanol (prepared



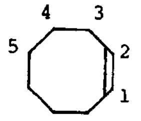


Figure 1. 13.8-MHz ^{2}H proton-decoupled NMR spectrum. (A) *trans*-Cyclooctene (natural abundance) in trichlorofluoromethane taken at 25 °C, tetramethylsilane as internal standard, numbers, chemical shift (ppm), concentration 0.5 g/mL, number of scans 50.000. (B) *cis*-Cyclooctene as for (A), number of scans 37.000. (C) *cis*-Cyclooctene obtained from elimination of *cis*-β-deuteriocyclooctyl benzyl thioether (**6**) (in tetrahydrofuran-tetramethylethylenediamine) in pentane-deuteriochloroform as internal standard, concentration 25 mg/mL, number of scans 2.000 (SB sideband). (D) *cis*-Cyclooctene obtained from elimination of *trans*-β-deuteriocyclooctyl benzyl thioether (**7**) (as for (C)).

from sodium methanolate: sodium (2.3 g) added to methanol (550 mL)) was added dropwise at 0 °C to the halogenide (0.1 mL). After 12 h, the methanol was removed and the thioether distilled. The yields were 80-97%.

Reaction of Benzyl *tert*-Butyl Thioether (2a) at −78 °C. A solution of **2a**[49] (3 mmol) and of TMEDA (4 mmol) in THF (30 mL) was treated at −78 or −10 °C with butyllithium (4 mmol). After 50 min, ICH_3 (0.5 mL) was added. Addition of water and the ethereal extraction resulted in *tert*-butyl (α-methylbenzyl) thioether (**3a**): ^{1}H NMR ($CDCl_3$) δ 1.2 (s, 9 H), 1.54 (d, J = 7.5 Hz, 3 H), 4.02 (q, J = 7.5 Hz, 1 H), 7.25 (m, 5 H).

Elimination on Benzyl *tert*-Butyl Thioether (2a). The reaction was carried out in an NMR tube at 20 °C. Butyllithium (0.5 mmol) was introduced into the tube and dried by a stream of nitrogen; thioether **2a** (0.3 mmol) in hexadeuteriobenzene (0.5 mL) was added. No metalation took place. After the addition of TMEDA (0.2 mmol) and heating at 60 °C for 5 min, the signals corresponding to isobutene (δ 1.60 and 4.70 ppm with complex pattern) were detected and the yield, as determined by area integration, was 95-100%. In a similar experiment on a larger scale (3 mmol of thioether, 4 mmol of TMEDA, 4 mmol of butyllithium) carried out at 20 °C (3 h), benzyl chloride (0.46 mL) was added and dibenzyl thioether was isolated in a yield of 97%.

Elimination on Benzyl *sec*-Butyl Thioether (2b). A. In Tetrahydrofuran. A solution of **2b** (5 mmol) and TMEDA (5 mmol) in THF (50 mL) was treated at 20 °C with butyllithium (5.5 mmol). During 7 h, the butenes formed were swept away with a nitrogen stream and bubbled through a bromine solution in carbon tetrachloride. The ratio of 1,2- and 2,3-dibromobutanes (total yield 80%) was found by NMR to be 5.3/1.

B. In Benzene. A solution of **2b** (5 mmol) and TMEDA (5 mmol) in benzene (50 mL) was treated ato 20 °C with butyllithium (5.5 mmol). During 2.5 h, the butenes formed were trapped as above and the ratio of 1,2- and 2,3-dibromobutanes (total yield 75%) was found by NMR to be 4/1.

Elimination on Benzyl *n*-Butyl Thioether (2c). A solution of **2c** (5 mmol) and TMEDA (5 mmol) in hexane (150 mL) was treated at 20 °C with butyllithium (5. 5 mmol). The 1-butene formed was swept away by a nitrogen stream which was bubbled through a bromine solution in carbon tetrachloride. The dibromide (1.02 g) was identified by NMR.

Elimination on Cyclooctyl Methyl Thioether (1a). A solution of **1a**[22] (1 mmol) and TMEDA (1 mmol) in hexane (3 mL) was treated at 0 °C with butyllithium (1 mmol). After 4 h at 25 °C (a precipitate appeared), benzyl chloride (1. 4 mmol) was added; after 12 h, water was added and an extraction with pentane was performed. *cis*-Cyclooctene was obtained in a yield of 65% (GC) and the benzyl methyl thioether was characterized by its NMR spectrum.

Reaction of Allyl Cyclooctyl Thioether (1b) at −78 °C. A solution of **1b** (0.6 mmol) in THF (20 mL) with TMEDA (0.6 mmol) was treated at −78 °C with butyllithium (0.7 mmol). After 1.5 h, ICH_3 (1 mL) was added. After the addition of water and extraction with pentane, the product ratio was determined by GC and NMR: 32% of starting material and 68% of monomethylated product, ratio α/γ 5.

Elimination on Allyl Cyclooctyl Thioether (1b). A solution of **1b** (3 mmol) and TMEDA (3.3 mmol) in THF (50 mL) was treated at −78 °C with butyllithium (3 mmol). After 1.5 h at −78 °C, the temperature of the reaction medium was kept at 0 °C for 2.5 h. Benzyl chloride (3.9 mmol) was added. After 12 h at 20 °C, water was added and the extraction with pentane performed. Cyclooctene was determined by GC (yield 95%). The other products were separated by chromatography on silica gel (230-400 mesh, 35 g). Hexane eluted benzyl chloride; hexane-benzene (9:1) eluted first cyclooctyl propenyl thioether[50] (10 mg) and then allyl benzyl thioether (**1b**, 2.4 mmol). According to its ^{1}H NMR spectrum ($CDCl_3$), cyclooctyl propenyl thioether is the trans isomer: 1.53 (large), 1.75 (d, J = 6.5 Hz, 3 H), 3.03 (m, 1 H), 5.71 (m, J = 15, 6.5 Hz, 1 H), 5.96 ppm (d, J = 15 Hz, 1 H).

Reaction of Benzyl Cyclooctyl Thioether (1c) at −78 °C. A solution of **1c** (3 mmol) and TMEDA (3 mmol) in THF (20 mL) was treated at −78 °C with butyllithium (3.1 mmol). After 1 h, ICH_3 (0.5 mL) was added. After the addition of water and ethereal extraction, cyclooctyl (α-methylbenzyl) thioether (**1e**) was isolated in 95% yield: bp 64 °C (0.1 mmHg); ^{1}H NMR ($CDCl_3$) δ 1.20-2.0 (m, 17 H), 2.55 (m, 1 H), 3.95 (q, J = 7.5 Hz, 1 H), 7.28 (5 H). Anal. ($C_{16}H_{24}S$) C, H.

Elimination on Benzyl Cyclooctyl Thioether (1c). The carbanion was prepared at −78 °C as above. The solution was then brought to 0 °C. After 2 h at 0 °C, ICH_3 (0.5 mL) was added. After the addition of water and ethereal extraction, a mixture of benzyl methyl thioether and *cis*-cyclooctene was obtained. The yield in both compounds was determined by NMR and GC and found to be 85%. No *trans*-cyclooctene[51] was detected.

Reaction of Benzyl Octadecyl Thioether (2d) at −78 °C. A suspension of **2d** (4 mmol) in THF (40 mL) was treated at −20 °C in the presence of TMEDA (4 mmol) with butyllithium (4 mmol). After 2 h at 20 °C, ICH_3 (0.6 mL) was added. After addition of water, the extraction was performed with chloroform. The (α-methylbenzyl) octadecyl thioether (**3d**) (95%) was recrystallized in methanol: mp 35-36 °C; ^{1}H NMR ($CDCl_3$) δ 0.89 (t, 3 H), 1.25 (32 H), 1.56 (d, J = 7 Hz, 3 H), 2.28 (t, J = 6.5 Hz, 2 H), 3.92 (q, J = 7 Hz, 1 H), 7.22 (5 H); mass spectrum M^+ 390, m/e 375, 300, 285. Anal. ($C_{26}H_{46}S$) C, H.

Elimination on Benzyl Octadecyl Thioether (2d) in THF. The carbanion was prepared as above. After 14 h of reflux, ICH_3 (0.6 mL) was added. After the addition of water, the extraction was performed with chloroform. The products were separated by chromatography on silica gel. Hexane eluted 1-octadecene (91%). A gradient hexane–benzene eluted the starting material (4%), benzyl methyl thioether (80%), and 1,2-di(methylthio)-1,2-diphenylethane (1%). 1-Octadecene was identified on the basis of its spectral properties: IR ($CHCl_3$) 1640 and 910 cm^{-1} ^{1}H NMR ($CDCl_3$) δ 0.85 (t, 3 H), 1.0-1.6 (28 H), 1.7-2.2 (2 H), 4.7-6.1 (3 H); mass spectrum M^+ 252, m/e 236, 224. The 1,2-di(methylthio)-1,2-diphenylethane was identified by comparing it with authentic samples. It was found to be an 8/1 *dl*/meso mixture.[52] The elimination of benzyl nonadecyl thioether (**2e**) gave similar results.

Elimination on Octadecyl Methyl Thioether in Hexane. A solution of octadecyl methyl thioether (2 mmol) and TMEDA (3 mmol) in hexane (50 mL) was treated with butyllithium (3 mmol). After refluxing for 20 h, ICH_3 (0.5 mL) was added. After the addition of water and extraction with chloroform, the compounds were separated by column chromatography on silica gel: hexane eluted 1-octadecene (90%) and benzene starting material (10%). 1-Octadecene was identified as above.

Preparation of Methyl Nonadecyl Thioether. A solution (10 mL) of CH_3SCH_2Li (in a total volume of 21 mL) prepared from dimethyl thioether (2.2 mL) with butyllithium (30 mmol) in the presence of TMEDA (30 mmol) was slowly added to a soltuion of octadecyl bromide (14.2 mmol) in THF (10 mL) and HMPA (10 mL) in the presence of a trace of triphenylmethane. The addition was stopped when the red color was stable. After 12 h, water was added and ethereal extraction performed. The product (95%) was recrystallized from methanol: mp 33.5-34 °C; ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 3 H), 1.25 (34 H), 2.07 (s, 3 H), 2.46 (t, 2 H, J = 7 Hz). Anal. ($C_{20}H_{42}S$) C, H.

Elimination on Methyl Nonadecyl Thioether. A solution of methyl nonadecyl thioether (2.9 mmol) and TMEDA (0.5 mL) in hexane (50 mL) was treated with butyllithium (3 mmol). After refluxing for 17 h, ICH_3 (0.5 mL) was added. After the addition of water and extraction with chloroform, the products were separated by chromatography on silica gel: hexane eluted 1-nonadecene (725 mg, 97%) and starting material (40 mg). 1-Nonadecene was identified on the basis of its spectral data: IR ($CHCl_3$) 1640 and 910 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.85, 1.0-1.6, 1.7-2.2 (2 H), 4.8-6.1 (3 H); mass spectrum M^+ 266, m/e 252, 238.

Elimination on the Dibenzyl Thioketal of Acetone 4. A solution of 4^{53} (3.8 mmol) and TMEDA (4 mmol) in THF (45 mL) was treated at 20 °C with butyllithium (4 mmol). After 12 h, water was added and the extraction with hexane was performed. The thiol was removed with an alkaline solution. The benzyl isopropenyl thioether (**5**) was distilled at 58-59 °C (0.1 mmHg), with a yield of 95%: ^{1}N NMR ($CDCl_3$) δ 1.98 (m, 3 H), 3.95 (s, 2 H), 4.79 (m, 1 H), 5.03 (m, 1 H), 7.32 (5 H); mass spectrum M^+ 164, m/e 149, 131, 118, 91. Anal. ($C_{10}H_{12}S$) C, H.

Preparation of *cis*- and *trans*-β-Deuteriocyclooctyl Benzyl Thioether. The cyclooctanols deuterated at β carbon were prepared by deuterioboration of *cis*-cyclooctene[36] and by reduction of the epoxide of *cis*-cyclooctene with $LiAlD_4$.[35] The corresponding methanesulfonates were prepared from cyclooctanols (50 mmol) with mesyl chloride (55 mmol) in methylene chloride (50 mL) in the presence of triethylamine (75 mmol). The methanesulfonates were converted to the thioethers by reaction with sodium benzylthiolate in dimethoxyethane and HMPA.

cis-β-Deuteriocyclooctyl benzyl thioether (**6**) had, according to the intensity of the parent peak, a content of $^2H_1$ 88% and *trans*-β-deuteriocyclooctyl benzyl thioether (**7**) a content of $^2H_1$ 83%.

Reaction Conditions for the Elimination. The deuterated benzyl cyclooctyl thioethers (0.5-1.0 mmol) in THF (50 mL) with TMEDA (1 equiv) or HMPA (5 mL) were converted to the corresponding carbanion at −78 °C by the addition of butyllithium (0.8 equiv). After 1.5 h at −78 °C, the temperature was brought to the value indicated in Table I. ICH_3 (1 mL) was added after 4 h. The workup using pentane and washing of the organic layer with water (in order to remove all THF) was applied. The pentane was distilled after drying over sodium sulfate. The reaction mixtures were analyzed by gas chromatography (Triton X-305 on Chromosorb W AW-DMCS): temperature gradient 60°-200 °C, coupled to an LKB mass spectrometer. Product identification was done by use of an authentic sample. The peak areas were integrated.

For the ^{2}H NMR, the cyclooctene was separated by chromatography on silica gel using pentane as an eluant. After concentration by distillation of pentane, the sample was analyzed with an NMR spectrometer, Bruker WH 90.

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Supplementary Material Available: Spectroscopic data on thioethers **1a**, **1b**, **1c**, **2a**, **2b**, **2c**, **2d**, and **2e** (1 page). Ordering information is given on any current masthead page.

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Separation of Polar and Resonance Substituent Effects in the Reactions of Acetophenones with Bisulfite and of Benzyl Halides with Nucleophiles[1]

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Abstract: Application of the modified Yukawa-Tsuno equation log $(k/k_0) = \rho\sigma^n + \rho^r(\sigma^+ - \sigma^n)$ to the reversible reaction of bisulfite with substituted acetophenones gives $\rho = 0.6$ and $\rho^r = -0.45$ for the hydroxide ion catalyzed cleavage reaction, $\rho = 1.8$ and $\rho^r = 0.45$ for attack of sulfite dianion, and $\rho = 1.2$ and $\rho^r = 0.95$ for K_{eq} for bisulfite addition. Rate constants for the cleavage reaction exhibit a U-shaped Hammett plot and require a negative value of the r^+ parameter, although the reaction is facilitated by electron donation by resonance. Furthermore, the values of ρ and ρ^r for the equilibrium and rate constants in the two directions are additive, but the r^+ values are not. The same treatment accounts for most of the curvature in Hammett plots for the S$_N$2 reactions of nucleophiles with benzyl halides without invoking changes in mechanism or transition-state structure. The changes in transition-state structure that do occur in some of these reactions are discussed and it is suggested that the "reactivity-selectivity principle" represents an oversimplification that should be abandoned for all but the simplest reactions.

Hammett σ values are based on the ionization constants of benzoic acids, and $\rho\sigma$ correlations are successful when the balance between resonance and polar effects of substituents on a reaction center is the same as for the ionization of benzoic acids. Other σ scales have been developed to describe reactions with a different balance of resonance and polar effects, including the σ^+ scale for reactions in which the relative contributions of resonance and polar effects are the same as in the solvolysis of cumyl chlorides, and the σ^n and σ^o scales for reactions with no direct resonance contribution.[3-6] The simplest of the several[3,5-11] correlations that have been proposed to allow for varying relative amounts of electron donation by resonance in different reactions is the Yukawa-Tsuno equation[9,10]

$$\log (k/k_0) = \rho(\sigma^n + r^+(\sigma^+ - \sigma^n)) \qquad (1)$$

in which $\sigma^+ - \sigma^n$ is an empirical measure of the ability of a particular substituent to donate electrons by resonance and r^+ varies in some manner with varying contributions of resonance effects in different reactions.

We have advocated the use of a slight modification[12] of the Yukawa-Tsuno equation

$$\log (k/k_0) = \rho\sigma^n + \rho^r(\sigma^+ - \sigma^n) \qquad (2)$$

This equation is based on the use of separate ρ and ρ^r parameters for polar and resonance effects, respectively, as suggested earlier by Taft and others,[3,5,6,8,11] but preserves the simplicity of the Yukawa-Tsuno approach.[13] The principal advantage in the use of eq 2 is that ρ^r is a direct measure of the contribution of resonance effects to a particular reaction, in the same sense that ρ is a measure of polar effects, whereas r^+, which is equal to the ratio ρ^r/ρ, is a measure of the *relative* contributions of polar and resonance effects. The value of r^+, therefore, can vary in magnitude, and even in sign, for a series of reactions with a constant resonance contribution if ρ varies independently of ρ^r; such variation is known to occur.[8] Furthermore, the values of ρ and ρ^r (in contrast to values of r^+) are additive for the equilibrium and rate constants of a reaction in the forward and reverse directions according to

$$\rho_{eq} = \rho_{fwd} - \rho_{rev}$$

and

$$\rho^r{}_{eq} = \rho^r{}_{fwd} - \rho^r{}_{rev}$$

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