REFERENCES

[1] *C. A. Grob & P. W. Schiess*, Angew. Chem. internat. Edit. *6*, 1 (1967).
[2] *E. Vinkler & K. Autheried*, Acta phys. et chem. Szeged. *2*, 105 (1948).
[3] *R. L. Autrey & P. W. Scullard*, J. Amer. chem. Soc. *90*, 4924 (1968); *iidem*, ibid. *87*, 3284 (1965).
[4] *M. Ohno et al.*, J. Amer. chem. Soc. *88*, 3168, 5683 (1966).
[5] *R. K. Hill & D. A. Cullison*, J. Amer. chem. Soc. *95*, 2923 (1973).
[6] *L. G. Donaruma & W. Z. Heldt* in 'Organic Reactions', Vol. 11, p. 1, Wiley, New York 1960; *P. A. S. Smith* in 'Molecular Rearrangements', Part 1, p. 483, Interscience, New York 1963.
[7] *H. P. Fischer, C. A. Grob & E. Renk*, Helv. *45*, 2539 (1962); *C. A. Grob, H. P. Fischer, H. Link E. Renk, ibid. 46*, 1190 (1963); *C. A. Grob*, Angew. Chem., internat. Edit. *8*, 535 (1969).
[8] *C. A. Grob, H. P. Fischer, W. Raudenbusch & J. Zergenyi*, Helv. *47*, 1003 (1964).
[9] *C. A. Grob & J. Ide*, Helv. *57*, 2571 (1974).
[10] *K. D. Berlin & S. Rengaraju*, J. org. Chemistry *36*, 2912 (1971).
[11] *G. J. Karabatsos, R. A. Taller & F. M. Vane*, J. Amer. chem. Soc. *85*, 2326 (1963).
[12] *N. J. Leonard & J. Figueras*, J. Amer. chem. Soc. *74*, 917 (1952).
[13] *E. A. Fehnel*, J. Amer. chem. Soc. *70*, 1813 (1948); *R. F. Naylor*, J. chem. Soc. *1949*, 2749.
[14] *G. M. Bennett & L. V. D. Scorah*, J. chem. Soc. *1927*, 194; *C. Barkenbus et al.*, J. org. Chemistry *20*, 871 (1955).
[15] *W. Z. Heldt*, J. Amer. chem. Soc. *80*, 5880 (1958).
[16] *M. F. Shostakovskii et al.*, Žur. Obšč. Chim. *31*, 1453 (1961), cited from Chem. Abstr. *55*, 22177 (1961).
[17] *F. Jakob & P. Schlack*, Chem. Ber. *96*, 88 (1963).
[18] *K. Becker & C. A. Grob*, Helv. *56*, 2723 (1973).
[19] *H. C. Brown & R. S. Fletcher*, J. Amer. chem. Soc. *71*, 1845 (1949).

---

282. *Beckmann* Fragmentation and Rearrangement. Part VII. Fragmentation and Cyclization of α-Methylthio-Ketoximes

Fragmentation Reactions No. 27

by **Cyril A. Grob** and **Junya Ide**

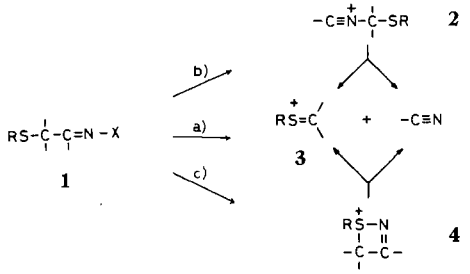
Institute of Organic Chemistry, University of Basle

(16. X. 74)

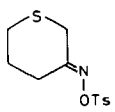
Summary. α-Methylthio-propiophenone *anti*-oxime *p*-toluenesulfonate (tosylate) (**12b**) fragments quantitatively in 80% ethanol yielding benzonitrile and a methylidenesulfonium ion **15**. The *syn*-isomer, however, undergoes a *Beckmann* rearrangement. The fragmentation of α-methylthio-isobutyrophenone *anti*-oxime tosylate (**13b**) is accompanied by cyclization to the 1,2-thiazetin-1-ium ion **27**, which is hydrolyzed *via* the sulfimine **29** to the keto sulfide **20** and the keto sulfoxide **30**. A comparison of the rates of the α-alkylthio *anti*-ketoxime tosylates **12b** and **13b** and of the homomorphous oxime tosylates **16b** and **17b** shows that fragmentation and cyclization are strongly assisted by the sulfur atom. Whereas both the *anti*- and *syn*-isomers of α-amino ketoxime derivatives fragment quantitatively, only the *anti*-isomers of α-alkylthio ketoxime derivatives undergo facile fragmentation.

In Part VI [1] three pathways were considered for the nitrile forming fragmentation [2] of α-alkylthio ketoxime derivatives **1** (*Scheme 1*, X = nucleofugal group), *i.e.* a) a concerted process; b) rearrangement to a nitrilium ion **2** followed by cleavage to a methylidenesulfonium ion **3** and a nitrile, and c) cyclization to a 1,2-thiazetin-1-ium ion **4** which also leads to fragmentation products.

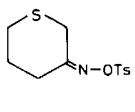
Scheme 1



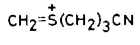
As a first step towards establishing the reaction course thian-3-one *anti*- and *syn*-oxime *p*-toluenesulfonate (tosylate) (**5**) were investigated. These compounds are unable to cyclize for structural reasons and should therefore react according to pathways a) or b) (*Scheme 1*). Rate and product studies in 70% aqueous dioxane showed that the *anti*-oxime tosylate **5** undergoes concerted fragmentation to the methylidenesulfonium ion **6**. With the *syn*-isomer **5**, *Beckmann* rearrangement to the lactam **7** competed with concerted fragmentation in the ratio 4:1. The rearrangement/fragmentation pathway b) (*Scheme 1*), however, was not observed [1].



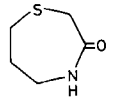
anti **5**



syn **5**

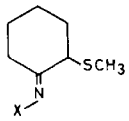


6

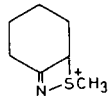


7

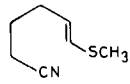
These results do not exclude the transient formation of 1,2-thiazetin-1-ium ions **4** in the case of cyclizable α-alkylthio ketoxime derivatives **1**. In fact such an ion **9** was proposed by *Autrey* & *Scullard* [3] as an intermediate in the reaction of α-methylthio *anti*-ketoxime derivatives of the type **8**, which led to moderate yields of the enethiol ether **10**.



8

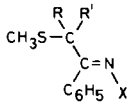


9



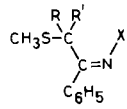
10

While there is no reason to reject *a priori* the cyclization step **8** → **9**, which involves nucleophilic displacement on the oxime nitrogen by sulfur, the postulated cleavage of the thiazetin-1-ium ion **9** presents some unusual features which warrant a detailed study[1][2].



anti

11 R = R′ = H
12 R = H, R′ = CH_3
13 R = R′ = CH_3

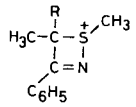


syn

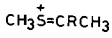
a) X = OH b) X = OTs

[1] We thank Prof. *R. L. Autrey* for calling our attention to this problem.
[2] This mechanism for fragmentation was considered unlikely by *Hill* & *Cullison* [4].

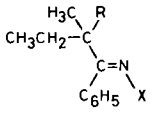
The *anti*- and *syn*-isomers[3]) of α-methylthio acetophenone oxime (**11a**) and their α-mono- and α-di-methyl derivatives **12a** und **13a** were chosen as models for the elucidation of the fragmentation pathway of open chain α-alkylthioketoximes. However, for steric reasons two of the desired oximes, namely *anti*-**11a** and *syn*-**13a**, were unstable relative to their isomers. The investigation was therefore confined to α-methylthio-propiophenone *syn*- and *anti*-oximes (**12a**) and to α-methylthio-isobutyrophenone *anti*-oxime (**13a**). The tosylates of both *anti*-oximes, *i.e.* *anti*-**12b** and *anti*-**13b**, should, on steric grounds, be able to undergo cyclization to a 1,2-thiazetin-1-ium ion **14** as well as fragmentation to benzonitrile and the methylidenesulfonium ion **15**. The *syn*-oxime tosylate **12b**, on the other hand, would be expected to rearrange predominantly [1] or exclusively.



14

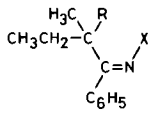


15



anti

a) X = OH



syn

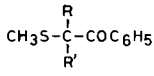
b) X = OTs

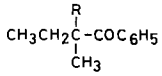
16 R = H

17 R = CH_3

Cyclization and fragmentation of the *anti*-oxime tosylates **12b** and **13b** could be concerted processes involving participation of the sulfur atom in the transition state. Both kinds of participation, *i.e.* by a neighbouring group (anchimeric effect) or through the intervening bonds (frangomeric effect [5]), should lead to an increased ionization rate relative to a homomorphous tosylate. Lack of participation should entail a decreased rate due to the -I-effect of sulfur [1]. The homomorphous oxime tosylates **16b** and **17b** were therefore also prepared and subjected to the reaction conditions of the α-alkylthio ketoxime tosylates **12b** and **13b**.

Results. – Treatment of α-methylthio-acetophenone (**18**) [6] with sodium hydride in tetrahydrofuran followed by methyl iodide gave the α-methylated ketone **19** accompanied by *ca.* 10% of the dimethylated product **20**. After purification by distillation the ketone **19** was converted to a 4:5 mixture of *syn*- and *anti*-oximes **12a**, which were separated by chromatography on silica gel. Further methylation of **19** gave **20**, which yielded only the *anti*-oxime **13a** under relatively drastic conditions.





18 R = R′ = H

19 R = H, R′ = CH_3

20 R = R′ = CH_3

21 R = H

22 R = CH_3

[3]) *anti* and *syn* with respect to the α-thio and the N—OH groups.

2-Butyl phenyl ketone (**21**) was prepared as described [7]. It yielded a 9:10 mixture of *anti*- and *syn*-oximes **16a**. Methylation of the ketone **21** with sodium amide and methyl iodide in refluxing 1,2-dimethoxyethane yielded *t*-amyl phenyl ketone (**22**). Treatment of the latter with hydroxylamine and potassium hydroxide in boiling methanol afforded only the *anti*-isomer of *t*-amyl phenyl ketoxime (**17a**).

The configurations of the above oximes were assigned on the basis of their UV. and NMR. spectra, and on the ability of α-alkylthio *anti*-ketoximes to chelate with cupric ions [3][4]. As shown in Table 1, the *anti*-oximes **12a**, **13a**, **16a** and **17a** absorb at shorter wave lengths or show only end absorption in the UV. region due to steric hindrance of conjugation. Furthermore, the α-methine protons in the *syn*-oximes **12a** and **16a** are deshielded relative to those in the corresponding *anti*-oximes because of the proximity of the oxygen atom [9] (Table 1). Finally, the α-alkylthio

Table 1. *UV. absorption and NMR. chemical shift δ of α-CH and =N—OH protons*

	λ_{max}^{EtOH} (nm)	log ε	δ (ppm) [a]	
			α-CH	=N—OH
syn-**11a**	250	4.04	3.84	11.44
anti-**12a**	221	3.84 [b]	3.36	10.76
syn-**12a**	236.5	3.89	4.74	11.36
anti-**13a**	–	–	–	10.66
anti-**16a**	223	3.71 [b]	2.58	10.42
syn-**16a**	232	3.88	3.30	10.94
anti-**17a**	–	–	–	10.32

[a] In $(CD_3)_2SO$.
[b] Shoulder.

ketoximes **12a** and **13a**, which were assigned the *anti* configuration by the above criteria, developed an immediate deep green color upon addition of ethanolic cupric sulfate, in contrast to the *syn*-isomers.

The oximes were converted to the corresponding crystalline tosylates by reaction of their lithium derivatives with *p*-toluenesulfonyl chloride. The *syn*-oxime tosylate **12b** was too unstable to permit isolation and was therefore prepared *in situ*.

$C_6H_5NHCOCH(CH_3)SCH_3$ **23**

$C_6H_5NHCOCH(CH_3)C_2H_5$ **24**

$C_6H_5CONHCH(CH_3)C_2H_5$ **25**

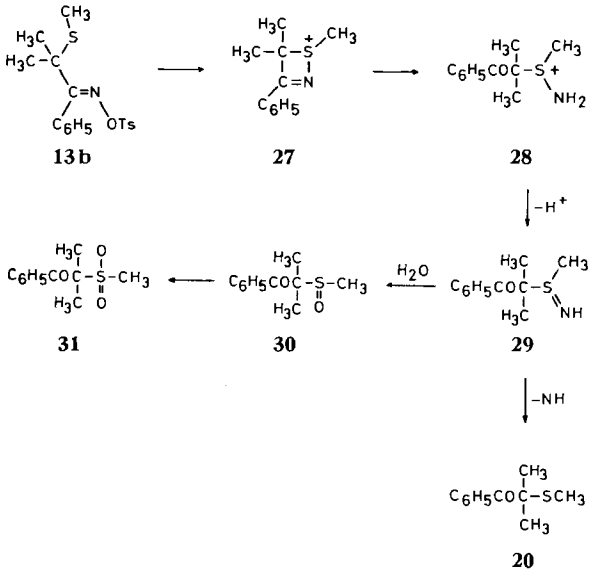
$C_6H_5C(OC_2H_5)=NCH(CH_3)C_2H_5$ **26**

In 80% aqueous ethanol α-methylthio-propiophenone *anti*-oxime tosylate (**12b**) underwent quantitative fragmentation with the formation of benzonitrile beside methanethiol and acetaldehyde, the hydrolysis products of the electrofugal fragment **15** (R = H). By contrast, the *syn*-isomer **12b** underwent *Beckmann* rearrangement

[4] Chelation was previously demonstrated with α-amino *anti*-ketoximes [8].

to the amide **23** in practically quantitative yield[5]). The UV. absorption in ethanol at 244 nm (log ε 4.14) was in good agreement with that of the homomorphous amide **24** ($\lambda_{(max)}$ 242 nm, log ε 4.18), which is obtained by rearrangement of the *syn*-oxime tosylate **16b**. Reaction of the corresponding *anti*-oxime tosylate **16b** led to rearranged products, *i.e.* 87% of the isomeric amide **25** ($\lambda_{(max)}$ 224 nm, log ε 4.04) beside 13% ethyl benzoate, the hydrolysis product of the imino ether **26**[6]). The structures of these amides are consistent with the established stereochemical course of the *Beckmann* rearrangement [12].

Scheme 2



The reaction of α-methylthio-isobutyrophenone *anti*-oxime tosylate (**13b**) in 80% ethanol (buffered with triethylamine) was more complicated than that of the lower homologue, *anti*-**12b**, in that fragmentation was accompanied by cyclization to the 1,2-thiazetin-1-ium ion **27** (*Scheme 2*). This follows from the products, namely 53% benzonitrile beside methanethiol, 13% α-methylthio-isobutyrophenone (**20**) and 28% of the corresponding sulfoxide **30**. These products were determined by quantitative gas-chromatography and identified by comparison with authentic samples. They were separated on a preparative scale by chromatography on a silica gel column.

The IR. spectrum of the oily and hygroscopic sulfoxide **30** showed bands at 1069 and 1665 cm^{-1}, which correspond to the sulfoxide and carbonyl group, respectively. The geminal methyl groups gave rise to two singlets in the NMR. spectrum at 1.54 and 1.59 ppm, a consequence of the neighbouring assymmetrical sulfoxide group [13]. The terminal methyl group led to a singlet at 2.31 ppm. The same sulfoxide **30** was obtained upon oxidation of the keto sulfide **20** with sodium periodate in aqueous

[5]) Less than 1% of benzonitrile was detected. This is probably derived from trace amounts of *anti*-**12b**, which are formed from the *syn*-oxime **12a** during tosylation.

[6]) The UV. spectra of acetanilide and N-methyl-benzamide absorb at 238 nm (log ε 4.02) [10] and 225 nm (log ε 4.01) [11], respectively.

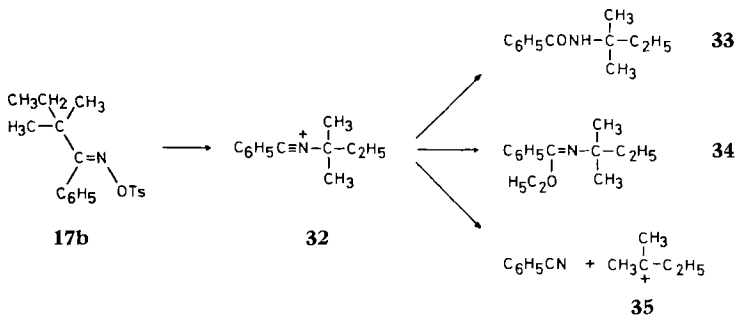
dioxane [14]. Further oxidation of the sulfoxide **30** with hydrogen peroxide led to the crystalline sulfone **31** (*Scheme 2*).

The formation of the keto sulfide **20** and the keto sulfoxide **30** is readily explained on the basis of an intermediate 1,2-thiazetin-1-ium ion **27**. Hydrolysis of the strained imine group in **27** leads to the aminosulfonium ion **28**, which is deprotonated in the basic medium to the sulfimine **29** [15]. The latter class of compounds are known to undergo hydrolysis to sulfoxides and to decompose readily to form sulfides and imine (NH), which disproportionates spontaneously to nitrogen and ammonia [15]:

$$R_2S{=}O + NH_3 \xleftarrow{H_2O} R_2S{=}NH \longrightarrow R_2S + NH$$

Reaction of 1-phenyl-2,2-dimethyl-1-butanone *anti*-oxime tosylate (**17b**), the homomorph of **13b**, in 80% ethanol led to 79% of the amide **33** and 4% of ethyl benzoate by rearrangement, beside 16% benzonitrile by fragmentation (*Scheme 3*).

Scheme 3



These products are in agreement with the results of an earlier study of the *Beckmann* rearrangement/fragmentation of *anti-t*-alkyl ketoxime tosylates [16]. Thus, rearrangement leads to the nitrilium ion **32**, which is converted by solvent to the

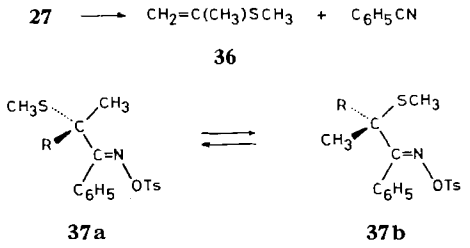
Table 2. *First order rate constants for R-phenyl* anti-*ketoxime* p-*toluenesulfonates* (10^{-3} M in 80-vol.% ethanol with triethylamine (2×10^{-3} M); mean deviation *ca.* 1%)

R	t (°C)	$k \times 10^6$ (s^{-1})	k_{rel} (23°)	$H^{\neq}$ kcal/mol	$S^{\neq}$ cal/mol
CH_3SCHCH_3 (**12b**)	13.0	11.28			
	23.0	39.01	6.4	18.9	−5.7
	31.0	95.44			
	41.0	237.78			
$CH_3SC(CH_3)_2$ (**13b**)	13.0	23.43			
	23.0	78.11	12.8	19.0	−3.9
	31.0	179.97			
$CH_3CH_2CHCH_3$ (**16b**)	23.0	6.11	1	20.1	−5.1
	31.0	16.51			
	41.5	48.83			
$CH_3CH_2C(CH_3)_2$ (**17b**)	23.0	8.55	1.4	21.2	−1.0
	31.0	22.09			
	41.0	71.17			

amide **33** and to the imino ether **34**, the precursor of ethyl benzoate. In a competing reaction, the benzonitrilium ion **32** is cleaved to benzonitrile and the *t*-amyl cation **35**, thus completing the fragmentation.

Finally, the reaction rates of the α-methylthio *anti*-ketoxime tosylates **12b** and **13b** and their homomorphs **16b** and **17b**, respectively, were measured in 80 vol. % ethanol. The first order rate constants and the derived activation parameters are listed in Table 2.

Discussion. – Fragmentation is the only observable reaction of α-methylthiopropiophenone *anti*-oxime tosylate (**12b**), and *Beckmann* rearrangement the only reaction of the *syn*-isomer. α-Methylthio-isobutyrophenone *anti*-oxime tosylate (**13b**), however, undergoes competitive fragmentation and cyclization to the 1,2-thiazetin-1-ium ion **27**. There is no evidence that this type of intermediate leads to fragmentation products, as assumed by *Autrey & Scullard* [3]. Rather, **27** is hydrolyzed to a sulfimine, as evidenced by the isolation of the keto sulfide **20** and the keto sulfoxide **30** from the reaction of **13b**. Furthermore, any enethiol ether **36**, which should have been formed by the fragmentation mechanism proposed by these authors[7]), would be stable under the basic conditions employed and therefore have been detected.



37a **37b**

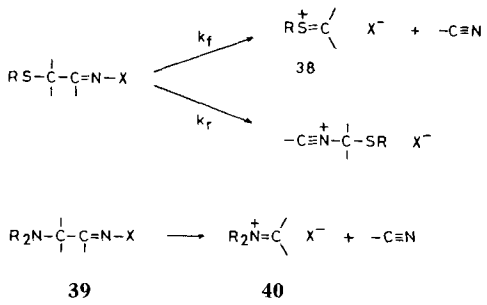
It is surprising that the α-dimethylated *anti*-oxime tosylate **13b** cyclizes, but the α-monomethylated homologue **12b** does not. This observation appears explicable on steric grounds. Space models show that rotation around the C(α)–C(oxime) bond is severly hindered in the *anti*-oximes and that the phenyl group is twisted out of conjugation with the oxime double bond, as evidenced by the UV. spectra (Table 1). Conformation **37a** is more favorable than conformation **37b** when R = H, because the bulky sulfur atom is turned away from the phenyl group and the N-electron pair. However, when R = CH_3, conformation **37b**, which leads to cyclization, becomes practically equivalent.

The question whether the sulfur atom participates in the fragmentation and cyclization of the *anti*-oxime tosylates **12b** and **13b** is answered by a comparison of their rates and those of the corresponding homomorphs **16b** and **17b** (Table 2). Thus, **12b** and **13b** react six and nine times, respectively, as fast as **16b** and **17b**. While the rate ratios clearly show that the sulfur atom assists ionization, they none the less provide only a lower limit for the magnitude of the frangomeric effect, *i.e.* for the rate increase due to concerted fragmentation. This effect can be defined as

[7]) As exemplified by the conversion of **9** to **10**. The latter was probably formed by a normal fragmentation reaction.

the ratio of the rates of fragmentation k_f and rearrangement k_r in *Scheme 4*. However, since rearrangement does not occur in the case of the *anti*-oxime tosylates **12b** and **13b**, the rates of rearrangement of the homomorphs **16b** and **17b**, respectively, are taken as models for the determination of k_r, even though they do not take account of the inductive effect of sulfur. This effect was directly measured in the case of thian-3-one *syn*-oxime tosylate (**5**), which rearranged *ca.* 100 times more slowly than cyclohexanone oxime tosylate (Part VI [1]). The corrected value for k_r in *Scheme 4* is therefore *ca.* one hundredth the rate of the corresponding homomorph.

Scheme 4



The acceleration due to the concerted fragmentation of **12b** and **13b** is therefore of the order 10^2 to 10^3. The same applies to the anchimeric effect for cyclization of **13b** to the thiazetin-1-ium ion **27**, which is responsible for *ca.* 50% of the rate.

The frangomeric effect of sulfur is substancially smaller than that of nitrogen in α-amino ketoxime derivatives **39**, for which values as large as 10^8 have been observed [17]. The main reasons for the different frangomeric effects of sulfur and nitrogen are: i) Methylideniminium ions **40** are formed more readily than methylidenesulfonium ions **38** because π-bonds involving overlap of $2p$-$2p$ orbitals are stronger than those involving $2p$-$3p$ orbitals [18][8]. ii) The electron withdrawing inductive effect of nitrogen is smaller than that of sulfur[9]. These factors will tend to increase the electrofugal activity of methylideniminium ions **40** relative to methylidenesulfonium ions **38**. For this reason *syn*-α-aminoketoxime derivatives readily undergo concerted *syn*-fragmentation, although this process is stereoelectronically less favorable and therefore much slower than *anti*-fragmentation [17]. *syn*-α-Alkylthio ketoxime derivatives, such as *syn*-**5** and *syn*-**12b**, on the other hand, undergo *Beckmann* rearrangement predominantly or even exclusively.

This work was supported by the «*Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung*», grant no. 2.320.70.

[8] *Brown*'s substituent constants σ_p^+ also show that conjugative electron release towards a cationic centre is far greater in the case of nitrogen [20]. In addition, the chemical and physical properties of α-haloamines show that they are salts **40** [21], and that α-halo sulfides and α-halo ethers are covalent compounds [22].

[9] The pK_A values of 4-methylamino- and of 4-methylthio-quinuclidine in water are 10.28 and 9.46, respectively [19].

Experimental Part[10])

α-Methylthio-acetophenone syn-*oxime* (**11a**) was obtained from the ketone **18** [6] by treatment with hydroxylamine hydrochloride in abs. pyridine at 22° for 10 h. From pentane m.p. 59–60.5°. – UV. and NMR. spectra *cf.* Table 1.

$C_9H_{11}NOS$	Calc.	C 59.66	H 6.12	N 7.73	S 17.17%
(181.259)	Found	,, 59.48	,, 6.20	,, 7.91	,, 17.41%

The anti-*Oxime* (NMR.: 3.56 (2 H, *s*) SCH_2CO) isomerized rapidly to the *syn*-isomer. Addition of a solution of cupric sulfate in 70% aqueous ethanol to the former gave an immediate green colour, but not with the *syn*-isomer.

α-Methylthio-propiophenone (**19**). To a suspension of 12.2 g (0.253 mol) sodium hydride (50% suspension in oil) in 250 ml of abs. tetrahydrofuran (THF) was added a solution of 40 g (0.241 mol) of α-methylthio-acetophenone (**18**) in 300 ml of THF with ice cooling. The reaction mixture was stirred for 2 h at 22° and then warmed to 40° until the evolution of H_2 subsided. After cooling, 36 g (0,253 mol) of methyl iodide in 250 ml of abs. THF were added, the reaction mixture refluxed for 4 h, filtered and the filterate evaporated *in vacuo*. The solution of the residue in 500 ml of ether was washed with water, dried over Na_2SO_4 and evaporated *in vacuo* to give 47 g oil, which upon distillation yielded 31.4 g of material, b.p. 80–82°/0.05 Torr. Gas/liquid chromatography (GLC.) showed the presence of traces of starting ketone **18** and *ca.* 10% of the dimethylated ketone **20**. Distillation of the crude product through a spinning band column yielded 12.6 g of pure **19**, b.p. 69–71°/0.03 Torr. – NMR. (CCl_4): 1.47 (3 H, *d*, J = 7.0 Hz) CH_3; 1.88 (3 H, *s*) S–CH_3; 4.18 (1 H, *d*, J = 7.0 Hz) CH. – IR. (CCl_4): 1679 (CO).

$C_{10}H_{12}OS$ (180,264) Calc. C 66.65 H 6.71 S 17.78% Found C 66.89 H 6.96 S 17.74%

syn- *and* anti-*oximes* **12a**. A solution of 14.62 g (81.2 mmol) of the ketone **19** and 16.9 g (244 mmol) of hydroxylamine hydrochloride in 76 ml of pyridine was stirred at 22° for 15 h. The mixture was diluted with ice and hydrochloric acid and extracted with ether. The ether extracts were washed, dried and evaporated *in vacuo* leaving 19,2 g of an oil, which partly solidified in a refrigerator to yield 4.08 g of the *anti*-oxime. The filtrate of the latter was chromatographed on silica gel. Elution with pentane/benzene 1:3 gave 5.85 g of the *syn*-oxime, m.p. 94.5–95.5° after recrystallization from hexane (UV. and NMR. spectra *cf.* Table 1). Elution with benzene/ether 1:1 afforded 4.3 g of *anti*-oxime, m.p. 102.5–103.5° from hexane (UV. and NMR. spectra *cf.* Table 1), which developed a green colour with cupric sulfate.

$C_{10}H_{13}ONS$ (195.285)	Calc.	C 61.52	H 6.71	N 7.18	S 16.42%
syn-**12a**	Found	,, 61.34	,, 6.95	,, 7.26	,, 16.70%
anti-**12a**	Found	,, 61.60	,, 6.63	,, 7.18	,, 16.17%

α-Methylthio-isobutyrophenone (**20**). To a suspension of 3 g (62.5 mmol) of sodium hydride in 100 ml of abs. THF was added a solution of 10.2 g (56.6 mmol) of the ketone **18** and the mixture warmed to 50° for 1.5 h. After cooling, 10.5 g (73.7 mmol) of methyl iodide in 20 ml abs. THF were added and the mixture was refluxed for 4 h. The precipitated salt was filtered and the filtrate evaporated *in vacuo*. The residue was taken up in ether, the solution washed with water, dried and evaporated. The oily residue (13 g) was distilled and yielded 8.25 g (75%) ketone **20**, b.p. 71–73°/0.05 Torr; n_D^{25} 1.5475. – IR. (CCl_4): 1666 (C=O). – NMR. (CCl_4): 1.50 (6 H, *s*) $C(CH_3)_2$; 1.95 (3 H, *s*) S–CH_3.

$C_{11}H_{14}OS$ (194.297) Calc. C 68.02 H 7.27 S 16.50% Found C 68.11 H 7.27 S 16.30%

anti-*Oxime*-**13a**. 13 g (67 mmol) of the ketone **20** and 18.8 g (269 mmol) of hydroxylamine hydrochloride in 60 ml of pyridine were warmed to 60° for 14 h. The pyridine was removed *in vacuo* and the residue worked up as described for **12a**. The residue, 11.23 g (80%), was crystallized from hexane, m.p. 130–130.5°, and gave a green colour with cupric sulfate. – NMR. ($(CD_3)_2SO$): 1.37 (6 H, *s*) $C(CH_3)_2$; 2.01 (3 H, *s*) SCH_3; 10.66 (1 H, *s*) N–OH.

$C_{11}H_{15}ONS$	Calc.	C 63.14	H 7.23	N 6.69	S 15.32%
(209.312)	Found	,, 63.16	,, 7.43	,, 6.60	,, 15.60%

1-Phenyl-2-methyl-1-butanone (**21**) was prepared as described [7], b.p. 87.5–89°/4 Torr. n_D^{25} 1.5083. – IR. (CCl_4): 1680 (C=O).

[10]) For the recording of physical data *cf.* Part VI [1].

syn- *and* anti-*Oximes* **16a**. 21.6 g (0.133 mol) of the ketone **21** and 20.4 g (0.294 mol) of hydroxylamine hydrochloride in 200 ml of methanol were added to 16.5 g (0.294 mol) of KOH in 70% aqueous methanol. The mixture was stirred for 14 h at 22° and then evaporated to dryness *in vacuo*. The residue was taken up in ether and water, the ether solution dried and evaporated *in vacuo*. Crystallization of the residue, 23.5 g (98%), from hexane yielded 5.46 g of *syn*-oxime. The residue from the mother liquor, 18.14 g, was chromatographed on 440 g of silica gel. Elution with benzene/hexane 7:3 gave a further 4.74 g of *syn*-oxime (total yield 42.4%). Elution with benzene gave 3.99 g of a mixture of *syn*- and *anti*-oximes, and further elution with benzene/ether 10:3 9.07 g of *anti*-oxime (38.4%).

The *syn*-oxime crystallized as platelets from hexane, m.p. 103–104° (Lit. [23]: m.p. 99°). The *anti*-oxime crystallized as needles, m.p. 79–80°. (UV. and NMR. spectra *cf.* Table 1.)

$C_{11}H_{15}ON$ (177.248)	Calc.	C 74.54	H 8.53 N 7.90%
syn-**16a**	Found	,, 74.38	,, 8.60 ,, 7.62%
anti-**16a**	Found	,, 74.72	,, 8.61 ,, 8.11%

1-Phenyl-2,2-dimethyl-1-butanone (**22**). To sodium amide (prepared from 4.4 g (0.19 g-atom) of sodium and 250 ml of liquid ammonia) was added 250 ml of abs. 1,2-dimethoxyethane and the suspension heated to 70° for 7 h under N_2. 20 g (0.123 mol) of the ketone **21** in 150 ml of dimethoxyethane were added and the mixture heated to 70° for 2 h, when the evolution of ammonia subsided. 287 g (2.02 mol) of methyl iodide were added, the mixture heated to 85° for 5 h and then evaporated to dryness *in vacuo*. The residue was taken up in ether and water, the ether layer washed, dried and evaporated. The oily residue, 20.88 g, was distilled and yielded 16.52 g (76%) of the ketone **22**, b.p. 108–109°/10 Torr (Lit. [24]: b.p. 78–79°/1 Torr); n_D^{25} 1.5040. – IR. (CCl_4): 1673 (C=O). – NMR. (CCl_4): 0.82 (3 H, two *t*, J = 6.9 and 1.5 Hz) CH_3; 1.25 (6 H, *s*) $C(CH_3)_2$.

anti-*Oxime* **17a**. This was prepared from 1.76 g of the ketone **22** and 2.09 g of hydroxylamine hydrochloride in 20 ml of methanol, to which were added 1.51 g of KOH in 10 ml of 70% aqueous methanol, by refluxing for 4.5 h. After working up, as described for the oximes **16a**, 1.72 g (89%) of **17** were obtained. From hexane needles, m.p. 140–141° (Lit. [25]: m.p. 139°) (*cf.* Table 1).

$C_{12}H_{17}NO$ (191,275) Calc. C 75.35 H 8.96 N 7.32% Found C 75.59 H 8.95 N 7.60%

Preparation of oxime p-*toluenesulfonates*. To a solution of 1.0 mmol of the oxime in 10 ml of abs. ether a solution of 1.0 mmol of titrated butyllithium in hexane [26] was added with a syringe under N_2 with stirring at – 15°. In most cases the lithium salt precipitated after stirring for 1.5 to 3 h. 1.05 mmol of *p*-toluenesulfonyl chloride in 10 ml of abs. ether was then added with ice cooling and the mixture stirred for 2 to 4 h. 5 to 10 ml of pentane were then added to precipitate lithium chloride, which was filtered off. The filtrate was evaporated *in vacuo* at 20° and the crude tosylate purified by crystallization.

1-Phenyl-2-methylthio-1-propanone anti-*oxime tosylate* (**12b**). From ether/pentane; m.p. 67–68° (75%).

$C_{17}H_{19}NO_3S_2$ (349.571) Calc. C 58.45 H 5.48 N 4.01% Found C 58.56 H 5.65 N 4.15%

1-Phenyl-2-methyl-2-methylthio-1-propanone anti-*oxime tosylate* (**13b**). Unstable powder, which decomposes upon recrystallization (92%). – IR. (CCl_4): 1130, 1140 and 1384 (–SO_2–). – NMR. ($(CD_3)_2CO$: 1.34 (6 H, *s*) $C(CH_3)_2$; 1.75 (3 H, *s*) S–CH_3.

1-Phenyl-2-methyl-1-butanone anti-*oxime tosylate* (**16b**). From pentane; m.p. 74–75° (61%).

$C_{18}H_{21}NO_3S$ (331.434) Calc. C 65.24 H 6.39 N 4.23% Found C 65.33 H 6.58 N 4.19%

1-Phenyl-2,2-dimethyl-1-butanone anti-*oxime tosylate* (**17b**). From pentane; m.p. 56–57° (82%).

$C_{19}H_{23}NO_3S$ (345.464) Calc. C 66.07 H 6.71 N 4.06% Found C 66.13 H 7.00 N 4.20%

Preparative solvolyses of oxime tosylates. All runs were repeated at least once. *Solvolysis of* anti-**12b**. 5.0 ml of a solution of 52.5 mg (0.15 mmol) **12b** and 30 mg (0.30 mmol) of triethylamine in 80% ethanol were reacted at 22° for 10 h. The solution was analyzed by quantitative GLC. (10% carbowax on 45–60 mesh Chromosorb W), the peak area of *benzonitrile* being compared to that of a solution of a known concentration of benzonitrile. The mean yield of four runs was 99.8 ± 0.5%.

The above reaction was repeated in a sealed ampoule and the solution subsequently treated with excess aqueous 0.1N iodine and titrated with 0.1N sodium thiosulfate [27]. The mean value

from several runs indicated the formation of 96 ± 2% of *methanethiol*, which was characterized as the mercuric methyl sulfide.

In a repetition of the reaction on a preparative scale, the ethanol was slowly distilled off through a *Widmer* column. Extraction of the aqueous residue with ether and careful removal of the latter after drying afforded 97% of benzonitrile.

Solvolysis of syn-**12b**. 300 mg of the *syn*-oxime **12a** were converted to the tosylate **12b**, as described above, and the latter reacted without purification in 5 ml of 70% aqueous dioxane, containing 300 mg of triethylamine, for 14 h at 22°. The solvent was removed *in vacuo* and the residue partitioned between benzene and water. The washed and dried benzene solution was evaporated *in vacuo*, leaving 297 mg (99%) of *α-methylthio-propionanilide* (**23**). From hexane and a trace of benzene, m.p. 123.5–124.5°. – UV. (ethanol): 244 nm (log ε 4.14). – NMR. ($CDCl_3$): 1.52 (3 H, *d*, *J* = 7.5 Hz) CH_3; 2.10 (3 H, *s*) S—CH_3; 3.43 (1 H, *q*, *J* = 7,5 Hz) CH; 7.0–7.6 (5 H, *m*) C_6H_5; 8.50 (1 H, br.) NH.

$C_{10}H_{13}NOS$	Calc.	C 61.52	H 6.71	N 7.18	S 16.42%
(195.285)	Found	,, 61.72	,, 6.85	,, 7.28	,, 16.17%

Solvolysis of anti-**16b**. A solution of 255 mg (0.77 mmol) of the tosylate **16b** and 132 mg (1.31 mmol) of triethylamine in 10 ml of 80% ethanol were reacted at 22° for 24 h. Quantitative analysis by GLC. of the solution showed the presence of 13% ethyl benzoate and 87% of amide **25**. The solution was evaporated to dryness *in vacuo*, the residue taken up in ether, the latter washed, dried and evaporated to give 117 mg (86%) of N-*(2-butyl)-benzamide* (**25**). From hexane, needles m.p. 83–83.5°. – UV. (ethanol): 224 nm (log ε 4.04). – NMR. ($CDCl_3$): 0.95 (3 H, *t*, *J* = 7.0 Hz) CH_3; 1.22 (3 H, *d*, *J* = 7.0 Hz) CH_3; 1.52 (2*H*, *quintet*, *J* = 7.0 Hz) CH_2; 4,19 (1 H, *sextet*, *J* = 7.0 Hz) CH; 6.11 (1 H br.) NH.

$C_{11}H_{15}NO$ (177.248) Calc. C 74.54 H 8.53 N 7.90% Found C 74.78 H 8.72 N 7.80%

Solvolysis of syn **16b**. 150 mg of the *syn*-oxime **16a** were converted to the tosylate **16b**, as described above, and the crude product reacted in 2 ml of 70% aqueous dioxane containing 100 mg of triethylamine for 14 h at 22°. The usual isolation procedure yielded 147 mg (99%) of *α-methyl-butyranilide* (**24**). From hexane needles, m.p. 108.5–109.5°. – UV. (ethanol): 242 nm (log ε 4.18). – NMR. ($CDCl_3$): 0.93 (3 H, *t*, *J* = 7.0 Hz) CH_3; 1.20 (3 H, *d*, *J* = 7.0 Hz) CH_3; 1.57 (2 H, *quintet*, *J* = 7.0 Hz) CH_2; 2.21 (1 H, *sextet*, *J* = 7.0 Hz) CH; 7.0–7.7 (5 H, *m*) phenyl; 7.75 (1 H, br.) NH.

$C_{11}H_{15}NO$ (177.248) Calc. C 74.54 H 8.53 N 7.90% Found C 74.73 H 8.51 N 7.92%

Solvolysis of anti-**17b**. A solution of 250.5 mg (0.725 mmol) of the tosylate **17b** and 110 mg (1.1 mmol) of triethylamine in 80% ethanol was reacted at 22° for 14 h and then evaporated *in vacuo*. The residue was dissolved in ether, the latter washed and dried and evaporated *in vacuo* to give 108 mg (78%) of *N-(1,1-dimethylpropyl)-benzamide* (**33**). From hexane needles, m.p. 91.5–92.5°. – UV. (ethanol): 223 nm (log ε 4.03). – NMR. ($CDCl_3$): 0.92 (3 H, *t*, *J* = 7.3 Hz) CH_3; 1.42 (6 H, *s*) $C(CH_3)_2$; 1.87 (2 H, *q*, *J* = 7.3 Hz) CH_2; 5.83 (1 H br.) NH; 7.34–7.55 (3 H, *m*) and 7.63–7.83 (2 H, *m*) phenyl H.

$C_{12}H_{17}NO$ (191.275) Calc. C 75.35 H 8.96 N 7.32% Found C 75.24 H 9.18 N 7.54%

25 mg of **17b** and 15 mg of triethylamine in 2.0 ml of 80% ethanol were reacted for 14 h at 22°. The solution was then analyzed by quantitative GLC., the areas of the three peaks being compared to those of solutions of known concentrations of benzonitrile (16%), ethyl benzoate (4%) and the amide **33** (79%).

Solvolysis of anti-**13b**. 1.0 g (4.79 mmol) of the *anti*-oxime **13a** were converted to the tosylate **13b**, as described above, and the crude product reacted in 10 ml of 80% ethanol containing 500 mg of triethylamine for 3 h at 22°. Ethanol was slowly removed by distillation through a *Widmer* column. The residue was repeatedly extracted with ether, the extracts washed with water and dried over Na_2SO_4 and evaporated carefully at 20°. The oily residue, 819 mg, was chromatographed on 15 g of silica gel. Elution with hexane/ether 10:1 gave 402 mg of a mixture of benzonitrile and the *β-keto sulfide* **20**, which was separated by fractional distillation at 110–115°/13 Torr and 90–95°/0.01 Torr, respectively. Further elution with benzene/ether 15:2 afforded 231 mg of the *β-keto sulfoxide* **30**. The three products were identified by comparison of their IR.- and NMR. spectra and their GLC. retention times with those of authentic samples.

24 mg of the *anti*-tosylate **13b** and 13 mg of triethylamine in 2.0 ml of 80% ethanol were reacted at 22° for 3 h. The solution was then analyzed by quantitative GLC., the peak areas of the three products being compared to those of solutions of known concentrations of benzonitrile, keto sulfide **20** and keto sulfoxide **30**. The mean yield of the three products from several runs was 53% benzonitrile, 13% of **20** and 28% of **30**, respectively, beside 6% of an unknown peak.

α-Methylsulfinyl-isobutyrophenone (**30**). To a solution of 142 mg (0.736 mmol) of **20** in 3 ml of dioxane was added a solution of 196 mg (0.922 mmol) of sodium periodate in 0.9 ml of water at 10°. After stirring at 22° for 20 h the mixture was filtered and the filtrate extracted with ether. The extracts were washed, dried and evaporated to give 145 mg of an oil, which was purified by chromatography on silica gel. Benzene/ether 15:1 eluted 110 mg (70%) of the hygroscopic sulfoxide **30**, which was identical with the sample isolated from *anti*-**13b**. – IR. (CCl_4): 1665 (CO), 1068 (S–O). – NMR. (CCl_4): 1.54 (3 H, *s*) CH_3; 1.59 (3 H, *s*) CH_3; 2.31 (3 H, *s*) $SOCH_3$; 7.36–7.5 (3 H, *m*) and 7.75–8.1 (2 H, *m*) phenyl H.

α-Methylsulfonyl-isobutyrophenone (**31**). A solution of 1.033 g (4.92 mmol) of the sulfoxide **30** and 0.6 ml of 30% aqueous hydrogen peroxide in 1.0 ml of acetic anhydride and 1.5 ml of glacial acetic acid was stirred for 1.5 h at 0° and 6 h at 22°. The reaction mixture was then diluted with 5 ml of ice water and repeatedly extracted with ether. The combined ether extracts were washed with aqueous $NaHCO_3$ solution and with water, dried and evaporated *in vacuo*. The oily residue (880 mg) was chromatographed on 11 g of silica gel. Elution with benzene yielded 650 mg (59%) of the sulfone **31**. From hexane, m.p. 62.5–63.5°. – IR. (CCl_4): 1670 (CO), 1120 and 1310 ($-SO_2-$). – NMR. (CCl_4): 1.69 (6 H, *s*) $C(CH_3)_2$; 2.92 (3 H, *s*) SO_2CH_3; 7.25–7.52 (3 H, *m*) and 7.68–7.90 (2 H, *m*) phenyl H.

$C_{11}H_{14}O_3S$ (226.297) Calc. C 58.40 H 6.24 S 14.17% Found C 58.58 H 6.29 S 14.14%

The *kinetic measurements* (Table 2) were carried out as previously described [1].

Elemental analyses were carried out by Mr. *E. Thommen*, NMR. spectra were measured by Mr. *K. Aegerter*.

REFERENCES

[1] *C. A. Grob & J. Ide*, Helv. *57*, 2562 (1974).
[2] *C. A. Grob & P. W. Schiess*, Angew. Chem., internat. Edit. *6*, 1 (1967).
[3] *R. L. Autrey & P. W. Scullard*, J. Amer. chem. Soc. *90*, 4924 (1968).
[4] *R. K. Hill & D. A. Cullison*, J. Amer. chem. Soc. *95*, 2923 (1973).
[5] *C. A. Grob*, Angew. Chem., internat. Edit. *8*, 535 (1969).
[6] *V. Prelog, V. Hahn, H. Brauchli & H. C. Beyerman*, Helv. *27*, 1209 (1944).
[7] *J. B. Lambert, W. D. Oliver & J. D. Roberts*. J. Amer. chem. Soc. *87*, 5085 (1965).
[8] *H. P. Fischer & C. A. Grob*, Helv. *45*, 2528 (1962).
[9] *G. Slomp & W. J. Wechter*, Chemistry and Ind. *1962*, 41; *K. D. Berlin & S. Rengaraju*, J. org. Chemistry *36*, 2912 (1971).
[10] *H. E. Ungnade*, J. Amer. chem. Soc. *75*, 432 (1953).
[11] *H. Ley & H. Specker*, Ber. deutsch. chem. Ges. *72*, 192 (1939).
[12] *L. G. Donaruma & W. Z. Heldt* in 'Organic Reactions', Vol. 11, p. 1, Wiley, New York 1960.
[13] *M. van Gorkom & G. E. Hall*, Quart. Rev. *22*, 14 (1968); *M. Nishino & T. Ito*, Chem. pharm. Bull. (Tokyo) *13*, 1392 (1965); *15*, 1669 (1967); *17*, 262 (1969).
[14] *N. J. Leonard & C. R. Johnson*, J. org. Chemistry *27*, 282 (1962).
[15] *R. Appel & W. Büchner*, Chem. Ber. *95*, 849, 855, 2220 (1962); *J. B. Lambert, C. E. Mixan & D. S. Bailey*, J. Amer. chem. Soc. *94*, 208 (1972); *N. Furukawa et al.*, Tetrahedron Letters *1972*, 1619.
[16] *C. A. Grob et al.*, Helv. *47*, 1003 (1964).
[17] *H. P. Fischer, C. A. Grob & E. Renk*, Helv. *45*, 2539 (1962), *C. A. Grob et al.*, Helv. *46*, 1190 (1963).
[18] *S. Oae* in 'Chemistry of Organosulfur Compounds', *Kagaku-Dojin*, Kyoto, Vol. *1*, p. 7 (1968).
[19] *E. Ceppi, W. Eckhardt & C. A. Grob*, Tetrahedron Letters *37*, 3627 (1973); *W. Eckhardt*, Dissertation, Basle University 1974.
[20] *H. C. Brown & Y. Okamoto*, J. Amer. chem. Soc. *80*, 4980 (1958).

[21] *H. Böhme, E. Mundlos & O. E. Herboth*, Chem. Ber. *90*, 2003 (1957).
[22] *H. Böhme*, Ber. deutsch. chem. Ges. *74*, 248 (1941).
[23] *T. E. Zalesskaya*, Ž. obšč. Chim. *8*, 1539 (1938).
[24] *T. E. Zalesskaya & T. B. Remizova*, Ž. obšč. Chim. *34*, 3168 (1964); *35*, 31 (1965).
[25] *A. Haller & E. Bauer*, C. r. hebd. séances Acad. Sci. *148*, 72 (1909).
[26] *R. G. Jones & H. Gilman* in 'Organic Reactions', Vol. 6, p. 352, New York 1951.
[27] *J. W. Kimball, R. L. Kramer & E. E. Reid*, J. Amer. chem. Soc. *43*, 1199 (1921).

283. Reversible, thermische Isomerisierung zwischen α,β-γ,δ-ungesättigten Aldehyden und Alkenylketenen durch [1,5]-H-Verschiebung. Valenzisomerisierung von *cis*-Dienonen, V [1]

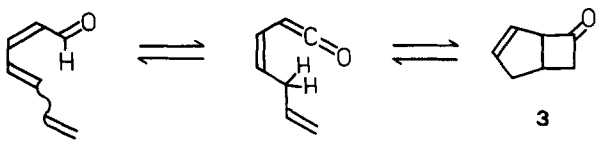
von **Peter Schiess** und **Paul Radimerski**

Institut für Organische Chemie der Universität, St. Johanns-Ring 19, CH–4056 Basel

(15. X. 74)

Summary. Vapor phase pyrolysis of 2,4-pentadienaldehyde, of 6-oxabicyclo[3.1.0]hex-2-ene or of 3-pentenoic acid chloride at 600° (0.1 s/1 Torr) leads to similar mixtures containing the stereoisomers of 2,4-pentadienaldehyde and 1-propenylketene. These compounds, and methyl substituted derivatives thereof, equilibrate at 600° (0.1 s) through intramolecular processes involving *cis/trans*-isomerisations and [1,5]-H-shifts. It is shown that α,β-γ,δ-unsaturated aldehydes can be prepared in high yield through gas phase thermolysis of appropriately substituted acid chlorides.

1. Einleitung. – Kürzlich haben wir beobachtet, dass bei der Thermolyse von Hepta-2,4,6-trienal (**1**) das Bicycloheptenon **3** entsteht [2]. Dieses bildet sich unter intramolekularer Cycloaddition aus dem nur indirekt nachgewiesenen Keten **2**, welches seinerseits durch eine sigmatrope [1,5]-H-Verschiebung aus **1** hervorgegangen ist.



1 **2** **3**

Dieser Hinweis auf die Bildung eines Ketens aus einem konjugiert ungesättigten Aldehyd durch eine thermisch ausgelöste [1,5]-H-Verschiebung hat uns veranlasst, das Verhalten verschiedener α,β-γ,δ-ungesättigter Aldehyde beim Erhitzen zu untersuchen[1]).

2. Thermolyse von 2,4-Pentadienal (4) und 3-Pentensäurechlorid (10). – Der einfachste Aldehyd, welcher eine [1,5]-H-Verschiebung eingehen kann, ist 2,4-Pentadienal (**4**). Diese Verbindung wurde bei 1 Torr durch ein auf 600° geheiztes Quarzrohr destilliert (Kontaktdauer *ca.* 0,1 s). Aus dem bei −78° in Methanol aufgefangenen Pyrolysat liess sich gas-chromatographisch als Hauptprodukt ein

[1]) Vorläufige Mitt. s. [3].