ACTA CHEMICA SCANDINAVICA 22 (1968) 2927–2933

The Effect of Ketone Structure upon the Product Distribution in the Reaction of 2,4-Dinitrobenzenesulfenyl Chloride with Ketones

CHRISTOFFER RAPPE and ROLAND GUSTAFSSON

Institute of Chemistry, University of Uppsala, Box 531, S-751 21 Uppsala 1, Sweden

The reaction between some symmetric and unsymmetric ketones and 2,4-dinitrobenzenesulfenyl chloride in carbon tetrachloride solution has been studied. The structures of the products have been determined by NMR and the relative rates of substitution in different positions in the ketones have been measured. It was found that substitution in general preferentially takes place at the most branched α-carbon, but the substitution seems also to be influenced by steric hindrance.

In connection with work on β-keto sulfides [1,2] and on the orientation of the enolization of ketones [3–5] it was of interest to study the reaction of 2,4-dinitrobenzenesulfenyl chloride with ketones. This reaction is reported to give β-keto sulfides in good yields and in fact it can be used for the characterization of ketones.[6,7] The mechanism of the reaction has been discussed by Kharasch,[8] who considers the reaction to be one with at least two available mechanistic pathways; attack by sulfenium ions or sulfenyl chloride on the enol or the parent ketone.

In spite of the fact that 2,4-dinitrobenzenesulfenyl chloride has been used for characterization of a number of unsymmetric ketones, the resulting structures of the β-keto sulfides formed in these reactions seem not to have been determined. In the present work we investigated the 2,4-dinitrobenzenesulfide derivatives of a number of unsymmetrical ketones, and the structures were determined by NMR. Moreover, we have determined the orientation of the reaction from the product distribution in the crude mixture. We have defined the orientation as K_{SCl}-values, which are the ratio of 3-sulfide/1-sulfide, and the results are summarized in Table 1.

From this table it can be seen that both 3- and 1-substituted products are formed in the reaction, and that in general it is the 3-substituted derivatives which are in majority. The exceptions to this rule are 4,4-dimethyl-2-pentanone and methyl cyclopropyl ketone.

Table 1. Product distribution in the crude mixtures.

Ketone	K_{SCl}
2-Butanone	16
2-Pentanone	8
2-Hexanone	6.4
2-Heptanone	4.3
2-Octanone	3.4
3-Methyl-2-butanone	10
3-Methyl-2-pentanone	4.3
4-Methyl-2-pentanone	2.2
4,4-Dimethyl-2-pentanone	0.16
Phenylacetone	>100
Methyl cyclopropyl ketone	0
Methyl cyclobutyl ketone	4.5
Methyl cyclopentyl ketone	5.7
Methyl cyclohexyl ketone	4.9
2-Methyl-3-pentanone	1.2 [a]

[a] counted as 2-substitution/4-substitution.

Data of the crystalline compounds isolated in pure form are collected in Tables 2 and 3. Here it can be seen that due to variation in crystallizing properties in some cases, the isolated product is not the dominating isomer in the crude product. For instance, the derivative of 4-methyl-2-pentanone described in Ref. 7 is that one where the substitution has taken place in the methyl group. This isomer is, however, formed only in minor amounts. In a few cases it has not been possible to obtain any crystalline products at all, but it has always been possible to establish the composition of the crude products by NMR.

By determining the composition of the product mixture from the reaction when 2,4-dinitrobenzenesulfenyl chloride was allowed to react with a tenfold excess of a mixture (1:1) of acetone and another ketone in carbon tetrachloride, it was possible to determine *the relative rates of substitution* at various position of the ketone. The rate of substitution at *one* methyl group of acetone was taken as unity (*i.e.* the amount of derivative from acetone was divided by 2). The results from these investigations are collected in Table 4.

From Tables 1 and 4 conclusions could be drawn concerning 1) the influence of β-substituents on the reaction rate at the α- and α'-carbon, 2) the influence of various α-substituents on the reaction rate at the α'-carbon, and 3) the rate of substitution at methyl, methylene, and methine groups, respectively.

1) From Table 1 it can be seen that branching at the β-carbon causes a higher tendency for α'-substitution, and from Table 4 it can be seen that this is due to decreased rate for the α-substitution while the rate of α'-substitution is rather unaffected. This can be well understood from increasing steric interaction opposing the α-substitution when a β-alkyl group is introduced.

2) A general feature of the data in Table 4 is the decreased rate of substitution at the α'-carbon caused by substitution of alkyl groups on the α-carbon.

Table 2. Isolated crystalline compounds. Recrystallized from ethanol where not otherwise stated.

Compound Ph=2,4-$(NO_2)_2C_6H_3$	Yield[a] %	M.p. °C	Empiric formula		Composition C %	H %	S %	N %
$CH_3COCHCH_3$ | S–Ph	87	93–94.5	$C_{10}H_{10}N_2O_5S$	Calc.	44.44	3.73	11.86	10.36
				Found	44.42	3.77	11.85	10.23
$CH_3COCHCH_2CH_3$ | S–Ph	84	77–78[b]	$C_{11}H_{12}N_2O_5S$	Calc.	46.47	4.25	11.28	9.85
				Found	46.58	4.21	11.29	9.74
$CH_3COC(CH_3)_2$ | S–Ph	79	92–93	$C_{11}H_{12}N_2O_5S$	Calc.	46.47	4.25	11.28	9.85
				Found	46.42	4.30	11.28	9.79
$CH_3COC(CH_3)CH_2CH_3$ | S–Ph	37	69–70	$C_{12}H_{14}N_2O_5S$	Calc.	48.32	4.73	10.75	9.39
				Found	48.32	4.61	10.74	9.33
$CH_2COCH_2CH(CH_3)_2$ | S–Ph	16	94.5–95.5 93–94[7]	$C_{12}H_{14}N_2O_5S$	Calc.	48.32	4.73	10.75	9.39
				Found	48.32	4.72	10.73	9.12
$CH_2CO(CH_2)_5CH_3$ | S–Ph	7	94–95	$C_{14}H_{18}N_2O_5S$	Calc.	51.52	5.56	9.82	8.58
				Found	51.50	5.57	9.72	8.52
$CH_3CH_2COCHCH_3$ | S–Ph	94	89–90	$C_{11}H_{12}N_2O_5S$	Calc.	46.47	4.25	11.28	9.85
				Found	46.60	4.14	11.27	9.86
$CH_3CHCOCH(CH_3)_2$ | S–Ph	30	98–99.5[c]	$C_{12}H_{14}N_2O_5S$	Calc.	48.32	4.73	10.75	9.39
				Found	48.38	4.98	10.72	9.42
$CH_2CO-CH(CH_2)_2$ | S–Ph	92	122–123 119–120[7]						
$CH_3CHCO-CH(CH_2)_2$ | S–Ph	85	111–112	$C_{12}H_{12}N_2O_5S$	Calc.	48.64	4.08	10.82	9.45
				Found	48.44	4.01	10.79	9.34
$CH_3COC(CH_2)_3$ | S–Ph	71	114–115[b]	$C_{12}H_{12}N_2O_5S$	Calc.	48.64	4.08	10.82	9.45
				Found	48.66	4.06	10.75	9.49
$CH_3COC(CH_2)_4$ | S–Ph	60	116–117[b]	$C_{13}H_{14}N_2O_5S$	Calc.	50.31	4.55	10.33	9.03
				Found	50.32	4.57	10.32	8.86
$CH_3CHCOC_6H_5$ | S–Ph	90	149–150[b]	$C_{15}H_{12}N_2O_5S$	Calc.[d]				8.43
				Found				8.38

[a] Yield counted on purified product. [b] Recrystallized from carbon tetrachloride. [c] Recrystallized from acetone-light petrol. [d] C, H, and S analyses not possible to perform due to explosion.

Table 3. NMR-data of isolated crystalline compounds. Trifluoroacetic acid used as solvent when not otherwise stated. The aromatic peaks were throughout: 3 H: $\delta = 8.85-9.17$ ppm (d), $J_{35} = 2.5$ Hz; 5 H: $\delta = 8.41-8.51$ ppm (q), $J_{35} = 2.5$ Hz, $J_{56} = 9$ Hz; 6 H: $\delta = 7.42-7.83$ ppm (d), $J_{56} = 9$ Hz. s=singlet, d=doublet, t=triplet, q=quartet, qi=quintet, m=multiplet.

Compound Ph=2,4-$(NO_2)_2C_6H_3$	ppm	Integrated areas	Fine structure	Coupling constant in Hz
CH_3COCH_2-S-Ph	2.61	3	s	—
	4.29	2	s	—
$CH_3COCHCH_3$	1.80	3	d	7.5
|	2.86	3	s	—
S−Ph	4.45	1	q	7.5
$CH_3COCHCH_2CH_3$	1.25	3	t	7
|	2.18	2	qi	7
S−Ph	2.51	3	s	—
	4.19	1	t	7
$CH_3COC(CH_3)_2$	1.76	6	s	—
|	2.65	3	s	—
S−Ph				
$CH_3COC(CH_3)CH_2CH_3$	1.08	3	t	7
|	1.67	3	s	—
S−Ph	2.13	2	q	7
	2.61	3	s	—
$CH_2COCH_2CH(CH_3)_2$	1.03	6	d	6
|	~2.25	1	m	—
S−Ph	2.77	2	d	6.5
	4.18	2	s	—
$CH_2CO(CH_2)_5CH_3$	0.8−2.1	11	m	—
|	2.90	2	t	7.5
S−Ph	4.20	2	s	—
$CH_3CHCOCH(CH_3)_2$	1.22	6	t[a]	7
|	1.76	3	d	7
S−Ph	3.36	1	m	7
	4.49	1	q	7
$CH_3CHCOCH_2CH_3$	1.17	3	t	7
|	1.77	3	d	7
S−Ph	2.92	2	q	7
	4.44	1	q	7
$CH_2CO-CH(CH_2)_2$	1.20−1.45	4	m	—
|	2.50	1	m	—
S−Ph	4.32	2	s	—
$CH_3CHCO-CH(CH_2)_2$	1.12−1.42	4	m	—
|	1.85	3	d	7
S−Ph	2.60	1	m	6
	4.54	1	q	7
$CH_3COC(CH_2)_3$	2.0−3.3	6	m	—
|	2.46	3	s	—
S−Ph				

Table 3. Continued.

$CH_3COC(CH_2)_4$ $\vert$ $S-Ph$	1.8—3.0 2.61	8 3	m s	— —
$CH_2COC_6H_5$ $\vert$ $S-Ph$	5.11	2	s	—
$C_6H_5COCHCH_3$ $\vert$ $S-Ph$	1.63 5.77	3 1	d q	7 7

[a] The two methyl groups in the isopropyl group are not magnetically equivalent.

This is the case for both methyl, methylene, and methine substitution and can be explained by steric factors. In the case of acid-catalyzed deuteration of the same ketones no obvious trend was observed.[3]

3) Examining the rate of methyl substitution in Table 4 showed that acetophenone and methyl cyclopropyl ketone were two exceptions where higher rates of substitution was observed than in acetone. This is probably due to conjugation and electronegativity effects.

Introduction of one methyl group at one of the carbons of acetone increases the rate of reaction at this carbon, while it diminishes the rate of substitution at the other side of the carbonyl group. The increased reactivity of the methylene group can be the result of an inductive effect or hyperconjugation. Thus methylene substitution dominates over methyl substitution. The only excep-

Table 4. Relative rate of substitution at various groups.

Ketone	CH_3-	$-CH_2-$	$-\overset{\vert}{\underset{\vert}{CH}}$
Acetone	1.0		
2-Butanone	0.4	5.6	
2-Pentanone	0.3	3.4	
3-Pentanone		2.3 [a]	
3-Methyl-2-butanone	0.3		3.8
3-Methyl-2-pentanone	0.5		2.4
4-Methyl-2-pentanone	0.7	1.5	
4,4-Dimethyl-2-pentanone	0.7	0.09	
2-Methyl-3-pentanone		1.0	1.2
2,4-Dimethyl-3-pentanone			0.33
Pinacolone	0.2		
Methyl cyclopropyl ketone	1.3		0
Ethyl cyclopropyl ketone		3.3	0
Acetophenone	3.0		
Ethyl phenyl ketone		5.7	

[a] The observed value divided by 2.

tion among the ketones studied is 4,4-dimethyl-2-pentanone. From Table 4 it is seen that the reactivity of the methylene group is diminished by introduction of alkyl groups in the β-position, probably due to steric effects.

The rate of methine substitution is slower than that of methylene substitution in ketones where the α'-group is the same (2-butanone and 3-methyl-2-butanone; 3-pentanone and 2-methyl-3-pentanone). If the different numbers of α-hydrogens are taken into account, a methine hydrogen is more easily replaced than a methylene hydrogen.

The size of the group on the other side of the carbonyl group seems to be of importance. The ketone 2-methyl-3-pentanone provided a possibility for a direct comparison of a methylene and a methine group (the group on the other side being changed). In this ketone it was found that the substitution in the methine group is more pronounced than methylene substitution. However, both rates were lower compared with ketones with one methyl group less on the other side (3-pentanone and 3-methyl-2-butanone).

The situation in the methyl cycloalkyl ketones requires some comment. With the exception of methyl cyclopropyl ketone the substitution preferentially takes place in the cycloalkyl group. The reason for the complete inability for substitution in the cyclopropyl group is due to the special hybridization and bonding in this group, see Ref. 5 and references therein.

Additional work is in progress to study the mechanism of the reaction. This work includes a comparison between the orientation of this reaction with that of the acid-catalyzed deuteration and halogenation of the ketones, work with α- and β-diketones with a high enol content, and work with optically active ketones.

EXPERIMENTAL

The NMR spectra were recorded on a Varian model A-60 spectrometer with TMS as internal standard. The micro analyses were performed by the Analytical Department, Chemical Institute, University of Uppsala.

Determination of product distribution. A solution of 0.05 mole ketone in 10 ml carbon tetrachloride was refluxed with 1.17 g (0.005 mole) of 2,4-dinitrobenzenesulfenyl chloride for 5 h. The excess of ketone and the solvent were evaporated *in vacuo*. Part of the residue was dissolved in trifluoroacetic acid and analyzed by NMR, see Table 1. The rest was recrystallized from ethanol, carbon tetrachloride, or acetone-light petrol, see Table 2. The yields, melting points and analyses are given in Table 2, the NMR-data in Table 3.

Determination of the relative rates of substitution. A solution of 0.025 mole of acetone and 0.025 mole of the ketone was dissolved in 10 ml of carbon tetrachloride. 1.17 g (0.005 mole) of 2,4-dinitrobenzenesulfenyl chloride was added and the solution was refluxed for 5 h. After removal of excess of ketone and the solvent, the residue was analyzed as before. The amount of substituted product from acetone and in both positions of the other ketone was determined. When the amount of substitution in *one* methyl group of acetone was assigned unity, the relative rates for substitution in the other groups could be calculated. No correction was made for different numbers of hydrogens in various groups. The results are collected in Table 4.

Acknowledgements. The authors are indebted to Professor Arne Fredga for all facilities placed at our disposal. Grants from *Magnus Bergwalls Stiftelse* to C. R. and from the *Faculty of Mathematics and Natural Sciences, University of Uppsala* to R. G. are gratefully acknowledged.

REFERENCES

1. Rappe, C. and Gustafsson, R. *Acta Chem. Scand.* **21** (1967) 705.
2. Rappe, C. and Gustafsson, R. *Acta Chem. Scand.* **22** (1968) 2015.
3. Rappe, C. and Sachs, W. H. *J. Org. Chem.* **32** (1967) 3700.
4. Rappe, C. and Sachs, W. H. *J. Org. Chem.* **32** (1967) 4127.
5. Rappe, C. and Sachs, W. H. *Tetrahedron* **24** (1968) 6287.
6. Kharasch, N. *J. Chem. Educ.* **33** (1956) 585.
7. Langford, R. B. and Lawson, D. D. *J. Chem. Educ.* **34** (1957) 510.
8. Kharasch, N. In Kharasch, N., Ed., *Organic Sulfur Compounds I*, Pergamon, Oxford 1961, p. 383.

Received April 6, 1968.