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On the Mechanism of the Reaction of 2,4-Dinitrobenzenesulfenyl Chloride with Ketones

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The reaction between 2,4-dinitrobenzenesulfenyl chloride (I) and some α-, β-, and γ-diketones, α-chloroketones and 1-indanones have been studied. It was found that α-diketones and α-chloroketones do not react under the conditions used, while 1-indanones react very rapidly. The product formed in the reaction of I with optically active 2-methyl-1-indanone was found to be optically inactive. The reaction mechanism is proposed to be an electrophilic attack by the sulfenyl chloride upon the enol form of the ketone.

In a previous paper we have described the effect of ketone structure upon the product distribution and relative rates of substitution in the reaction between 2,4-dinitrobenzenesulfenyl chloride (I) and ketones.[1] In order to study the mechanism of the reaction, we have now extended our investigation to some other ketones, halogenated ketones, and α-, β-, and γ-diketones.

The mechanism of the reaction has been discussed by Kharasch.[2] On the basis of unpublished results he suggests that it is a reaction between the enol and sulfenyl chloride (or polarized sulfenyl chloride), but he also discusses the possibility of a direct attack by sulfenyl chloride molecules on the unenolized ketone.[2]

Valuable information about the suggested enol mechanism was obtained from experiments with optically active ketones. We chose to study the reaction with active 2-methyl-1-indanone, which ketone was found to racemize slowly under the experimental conditions. The crude product showed a trace of optical activity, but repeated recrystallizations gave a completely racemic product while the mother liquors showed a weak optical activity, probably because of the presence of starting ketone, which had not been completely racemized during the experiment. The ketone could also be detected by NMR. The mother liquors were found to racemize on treatment with a few drops of trifluoroacetic acid. As the substituted product has no enolizable α-hydrogens, it cannot be racemized after its formation. This experiment seems to be a

strong indication that the substitution proceeds *via* a symmetric form of the ketone, *i.e.* the enol.

It has recently been found that the orientation of the acid-catalyzed bromination and deuteration of ketones which also proceeds *via* the enol, are solvent depending.[3-5] However, in the present reaction the product distribution was found to be independent of the solvent used; see Table 1. The differences found are small and within the limits of experimental error.

Table 1. K_{SCl}-values [a] for some ketones in different solvents.

Ketone	CCl_4	$CHCl_3$	CH_3COOH
2-Butanone	16	15	17
3-Methyl-2-butanone	10	11	11
4,4-Dimethyl-2-pentanone	0.16	0.16	0.15
Phenylacetone	>100	>100	>100

[a] K_{SCl}-values are defined as methylene or methine-substitution/methyl substitution.[1]

Recently it was also found that the acid-catalyzed bromination of 2-butanone in deuterating solvents yielded halogenated ketones as well as deuterated ketones.[5] The inference drawn was that the halogenating and deuterating agents compete in capturing the enol which in turn means that although the acid-catalyzed halogenation proceeds *via* the enol, enolization is *not* the rate determining step of the reaction.[5]

Table 2. Comparison between product distribution in the crude products and orientation of acid-catalyzed deuteration.[6]

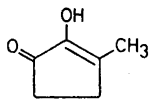
Ketone	K_{SCl}	K_D[a]
2-Butanone	16	1.9
2-Pentanone	8	1.6
2-Hexanone	6.4	1.7
2-Heptanone	4.3	1.5
2-Octanone	3.4	—
3-Methyl-2-butanone	10	0.8
3-Methyl-2-pentanone	4.3	0.19
4-Methyl-2-pentanone	2.2	—
4,4-Dimethyl-2-pentanone	0.16	0.29
Phenylacetone	>100	—
Methyl cyclopropyl ketone	0	0
Methyl cyclobutyl ketone	4.5	—
Methyl cyclopentyl ketone	5.7	—
Methyl cyclohexyl ketone	4.9	—

[a] see Ref. 6.

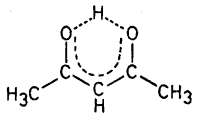
When excess of ketone (acetone, 2-butanone, 3-methyl-2-butanone, or phenylacetone) was treated with equimolar amounts of 2,4-dinitrobenzenesulfenyl chloride and acetic acid-d_1 or trifluoroacetic acid-d_1 in a carbon tetrachloride solution, it was found that the deuterium exchange of α-protons in the starting ketones was almost complete while the sulfide formation was still hardly detectable by NMR. The deuterating agent is much more efficient than I in capturing the enol.

The acid-catalyzed deuteration has previously been investigated for some of the ketones studied in the present reaction with I.[6] A comparison between the orientation of the deuteration and the reaction with I can also be interpreted in terms of different efficiency in capturing the enol; see Table 2. In several cases there are big differences between the two reactions, for instance for 2-butanone, 3-methyl-2-butanone, and 3-methyl-2-pentanone. If the enolization was found to proceed exclusively in one direction, the substitution gave exclusively the corresponding product, for instance phenylacetone, 2,4-pentanedione, and methyl cyclopropyl ketone.

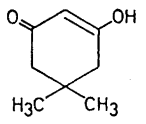
The relative rates of the α-, β-, and γ-diketones, chloroketones and 1-indanones studied in the present investigation are collected in Table 3. The investigated α-diketones, 2,3-butanedione, and 3-methyl-1,2-cyclopentanedione (II),



II



III



IV

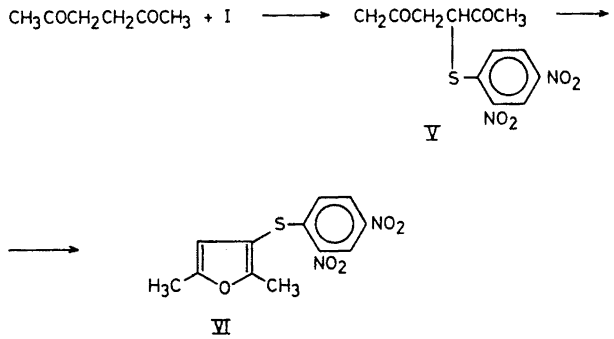
did not react at all. This is unexpected since II is completely enolized,[7,8] and steric effects seem to be negligible. The low reactivity seems to be due to the inductive effect of the unenolized keto group, which results in lower electron density and lower reactivity of the enol double bond towards the electrophile I. The inductive effect and lower electron density may also explain the low reactivity of the α- and β-chloro ketones studied and for 3-carboxymethylthio-2,4-pentanedione; see Table 3. A mixture of 4-chloro-2-butanone and I (1.7:1 by moles) in carbon tetrachloride was refluxed for 45 h. A weak evolution of hydrogen chloride was observed but no reaction product was detectable by NMR.

Table 3. Relative rate of substitution at various groups.

Ketone	CH_3-	$-CH_2-$	$-\overset{|}{\underset{|}{CH}}$
2,3-Butanedione	<0.1		
3-Methyl-1,2-cyclopentanedione		<0.1	<0.1
2,4-Pentanedione	<0.1	2.7	
3-Methyl-2,4-pentanedione [15]	<0.1		1.1
3-Chloro-2,4-pentanedione [16]	<0.1		<0.1
3-Carboxymethylthio-2,4-pentanedione [17]	<0.1		<0.1
Dimedone		<0.1	15
2,5-Hexanedione	0.2	0.5	
Chloroacetone	<0.1	<0.1	
1,3-Dichloroacetone		<0.1	
4-Chloro-2-butanone [18]	<0.1	<0.1	
1-Indanone		27	
2-Methyl-1-indanone [19]			60
3-Methyl-1-indanone [20]		12	
Isobutyrophenone			0.2
Phenylacetone	<0.1	3.4	

The rather slow reaction rate of 2,4-pentanedione and 3-methyl-2,4-pentanedione is also a little unexpected since these compounds are known to have a high enol content.[9] Delocalization of the enol double bond due to intramolecular hydrogen bonding (III) might be one explanation. In dimedone (IV) where intramolecular hydrogen bonding is impossible, the enol double bond is localized and has a greater electron density. This compound consequently reacts much faster.

The low reactivity of α- and β-diketones and α-chloroketones has a parallel in the addition of sulfenyl chlorides to olefinic double bonds. It has been shown that no addition takes place between 2-nitro-4-chlorobenzenesulfenyl chloride and chloro substituted ethylenes or to olefins with the double bond conjugated with a carbonyl group.[10]

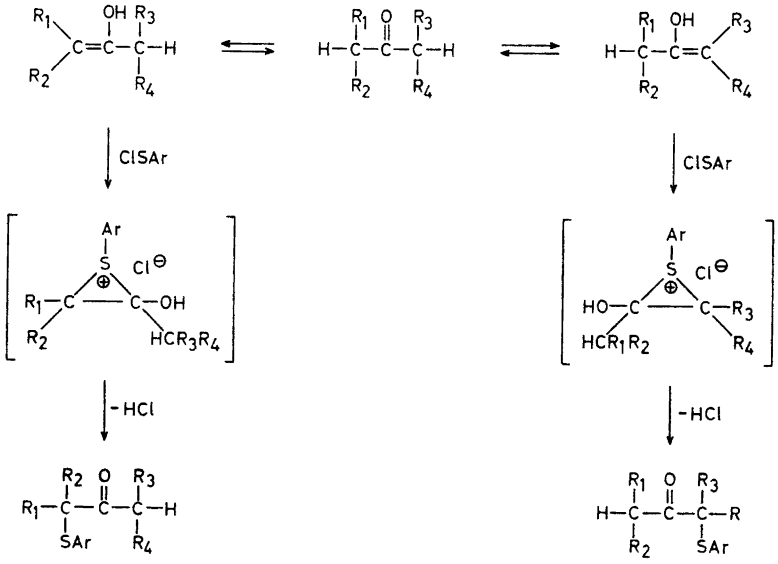


Scheme 1

From the reaction between 2,5-hexanedione and I in carbon tetrachloride a 2,5-dimethylfuran (VI) was isolated; see Scheme 1. It can be assumed that in this reaction the substituted γ-diketone V is an intermediate. When the reaction was performed in chloroform for 2.0 h it was possible to isolate the substituted ketone V, while prolonged treatment resulted in ring closure, and shorter time gave partly starting material back. If V is treated with trifluoroacetic acid it is rapidly and quantitatively converted to the furan VI.

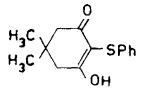
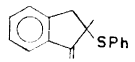
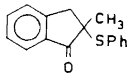
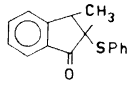
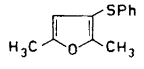
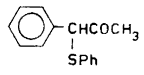
Relative rates for the substitution of the 1-indanones were found to follow the general rules for α- and β-alkyl substituents given in Ref. 1. It can be seen from Table 3 that there is more than a hundredfold difference in reaction rate between 2-methyl-1-indanone and isobutyrophenone. The relative rate of substitution at the isopropyl group of 3-methyl-2-butanone, 2-methyl-3-pentanone, 2,4-dimethyl-3-pentanone, and isobutyrophenone is 3.8, 1.2, 0.3, and about 0.2, respectively,[1] which probably reflects the increased steric interaction. Ring closure of isobutyrophenone to 2-methyl-1-indanone decreases the steric hindrance somewhat and consequently increases the reaction rate, but it is difficult to see how this change alone can explain the observed difference. One possible explanation may be that contrary to isobutyrophenone the enols of the indanones must be planar.

Substitution of 3-methyl-1-indanone can give two isomeric *cis-trans* compounds. The coupling constants of 3-methyl-1-indanone have been determined by Agahigian *et al.* thus providing a possibility for the identification of the two isomers.[11] The reaction was studied at 30 min intervals and it was completed in 2 h. All samples were analyzed by NMR, and in all samples both isomers were found to be present in a ratio *cis:trans*=1:3. Although it



Scheme 2

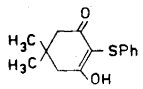
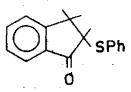
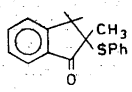
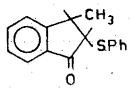
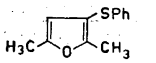
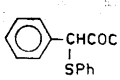
Table 4. Isolated crystalline compounds.

Compound Ph = 2,4-$(NO_2)_2C_6H_3$-	Yield %	Recrystallized from	M.p. °C	Empiric formula	Composition C % H % S % N %
$CH_3COCHCOCH_3$ SPh	94	CCl_4	151–152	$C_{11}H_{10}N_2O_6S$	Calc. 44.29 3.38 10.75 9.39 Found 44.30 3.41 10.65 9.31
$CH_3COC(CH_3)COCH_3$ SPh	89	CCl_4	92–93	$C_{12}H_{12}N_2O_6S$	Calc. 46.15 3.87 10.27 8.97 Found 45.98 3.83 10.20 8.94
	77	CH_3COOH	210–211 (d)	$C_{14}H_{14}N_2O_6S$	Calc. 49.70 4.17 9.48 8.28 Found 49.65 4.13 9.35 7.94
	73	CH_3COOH	174–176 (d)	$C_{15}H_{10}N_2O_5S$	Calc. 54.54 3.05 9.70 8.48 Found 54.59 2.96 9.62 8.66
	80	CH_3COOH	165–166	$C_{16}H_{12}N_2O_5S$	Calc. 55.82 3.51 9.31 8.13 Found 55.77 3.57 9.24 8.03
	47	CH_3COOH	176–177 (d)	$C_{16}H_{12}N_2O_5S$	Calc. 55.82 3.51 9.31 8.13 Found 55.80 3.64 9.23 8.00
$CH_3COCH_2CHCOCH_3$ SPh	39	CCl_4–C_2H_5OH	127–128	$C_{12}H_{12}N_2O_6S$	Calc. 46.15 3.87 10.27 8.97 Found 46.09 3.88 10.26 8.70
	42	C_2H_5OH	112–113	$C_{12}H_{10}N_2O_5S$	Calc. 48.98 3.43 10.90 9.52 Found 49.02 3.55 10.64 9.42
	68	C_2H_5OH	126–127	$C_{15}H_{12}N_2O_5S$	Calc. 54.21 3.63 9.65 8.43 Found 54.10 3.68 9.62 8.45

was found that the *cis*-ketone isomerized completely into the *trans*-form by heating, the conclusion could be drawn that *trans*-substitution predominates, which is in accordance with the theory of steric hindrance.

This investigation shows that the reaction between I and ketones is analogous in many respects to the addition of I to olefinic double bonds. The mechanism involves an electrophilic attack on the enol double bond; an intermediate episulfonium ion is probably formed, which after fission gives the β-ketosulfide; see Scheme 2.

Table 5. NMR-data of isolated crystalline compounds. Data of aromatic protons omitted. s=singlet, d=doublet, q=quartet, m=multiplet.

Compound Ph=2,4-$(NO_2)_2C_6H_3$-	Solvent	δ ppm	Integrated areas	Fine structure	Coupling const. (Hz)
$CH_3COCHCOCH_3$ SPh	CF_3COOH	2.51	6	s	—
$CH_3COC(CH_3)COCH_3$ SPh	CF_3COOH	1.94 2.56	3 6	s s	— —
	DMSO-d_6	1.11 2.56	6 4	s s	— —
	$C_6H_5NO_2$	3.13 4.02 4.66	1 1 1	q q q	4 (*trans*), 18 (*gem*) 8 (*cis*), 18 (*gem*) 4 (*trans*), 8 (*cis*)
	$C_6H_5NO_2$	1.79 3.52	3 2	s s	— —
	$C_6H_5NO_2$	1.67 3.4 4.18	3 1 1	d m d	7 4.5
$CH_3COCH_2CHCOCH_3$ SPh	CD_3COCD_3	2.20 2.35 3.32 4.76	3 3 2 1	s s q q	— — J_{AB} = 18.5 J_{AX} = 9.0, J_{BX} = 4.5
	CF_3COOH	2.33 6.00	6 1	s s	— —
	CF_3COOH	2.45 5.63	3 1	s s	— —

EXPERIMENTAL

The NMR-spectra were recorded on a Varian A-60 spectrometer with TMS as internal standard. The micro analyses were performed by the Analytical Department at this Institute.

The ketones used were redistilled or recrystallized commercial samples or were prepared by known procedures.[15–20]

Preparation of the sulfides. 1.17 g (0.005 mole) of 2,4-dinitrobenzenesulfenyl chloride and an excess of ketone in 10 ml carbon tetrachloride was refluxed for 5 h. For dimedone and 1-indanones a twofold excess of ketone was used, for less reactive ketones the excess was tenfold. The solvent and if possible the ketone was evaporated in *vacuo*. The residue was recrystallized from carbon tetrachloride, ethanol, or acetic acid. Yields, melting points and analyses are given in Table 4, the NMR-data in Table 5.

2,5-Hexanedione reacted somewhat abnormal. A fivefold excess of ketone was used. After evaporation and recrystallization from acetone-light petrol and finally from ethanol, 0.45 g (31 %) of the furan VI (Scheme 1) was isolated, and 0.95 g of tarry by-product was discarded. By refluxing in chloroform for 5 h the yield was raised to 42 %. When the reaction in chloroform was stopped after 2 h, it was possible to isolate the substituted ketone, V, which was recrystallized from a mixture of carbon tetrachloride and ethanol.

Determination of the relative rates of substitution. A mixture 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. For dimedone the proportions used were 2:2:1 and for 1-indanone 4:4:1 instead of 5:5:1. After evaporation the crude product was dissolved in trifluoroacetic acid or nitrobenzene and analyzed by NMR. The amount of substituted product from acetone and from both α-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 of each group in the other ketone could be calculated. No correction was made for different numbers of hydrogens in various groups. The results are collected in Table 3.

For 2,5-hexanedione the value for methylene substitution is calculated from amount formed furan compound VI. As some other by-products are formed, both values given are less reliable than for other ketones.

(+)-2-Methyl-1-indanone. α-Benzylpropionic acid was prepared by the method given by Conrad and Bischoff.[12] The total yield from diethyl malonate was 30 %, b.p. 168°C/12 mm, m.p. 35–36°C (m.p. 37°C is given in Ref. 12). The acid was resolved *via* its quinine salt according to Kipping and Hunter.[13] The (+)-form was obtained sufficiently pure after four recrystallizations from ethanol, $[\alpha]_D^{25} = +15.4°$ (ethanol), yield 60 %. The acid chloride was prepared in small portions by treating the (+)-acid with an equivalent amount of phosphorus pentachloride in light petrol at room temperature for 2 h.[13] Solvent and formed phosphorus oxychloride were removed *in vacuo* at 60°C. The acid chloride was not distilled, $[\alpha]_D^{25} = +15°$ to $+20°$ (light petrol). Yield 70–75 %.

(+)-α-Benzylpropionyl chloride was added dropwise with stirring to twice the equivalent amount of aluminium trichloride in dry carbon disulfide.[14] The mixture was stirred for 3 h at room temperature. It was then poured out in ice-water, extracted with carbon disulfide, dried over sodium sulfate, and evaporated. The resulting somewhat yellow oil had $[\alpha]_D^{25} = +30°$ (ethanol). Rapid distillation at 65°C/0.1 mm gave a product with an optical rotation a few degrees lower. Yield 70–75 %, $n_D^{20} = 1.5534$.

The reaction between 2,4-dinitrobenzenesulfenyl chloride and (+)-2-methyl-1-indanone was performed in the usual way. The crude product was investigated polarimetrically with dioxane as solvent. The individual values for the optical rotation of the crude product varied between 0.03° and 0.008° depending on ratio ketone:I (3:1 to 1:2) and reaction time (3–5 h). After two recrystallizations from acetic acid the product was found to be inactive.

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REFERENCES

1. Rappe, C. and Gustafsson, R. *Acta Chem. Scand.* **22** (1968) 2927.
2. Kharasch, N. In Kharasch, N., Ed., *Organic Sulfur Compounds* I, Pergamon, Oxford 1961, p. 375.
3. Sachs, W. H. and Rappe, C. *Acta Chem. Scand.* **22** (1968) 2031.
4. Gaudry, M. and Marquet, A. *Bull. Soc. Chim. France* **1967** 1849.
5. Rappe, C. *Acta Chem. Scand.* **22** (1968) 1359.
6. Rappe, C. and Sachs, W. H. *J. Org. Chem.* **32** (1967) 3700.
7. Bredenberg, J. B-son *Acta Chem. Scand.* **13** (1959) 1733.
8. Rappe, C. and Norström, Å. *Acta Chem. Scand.* **22** (1968) 1853.
9. Gould, E. *Mechanism and Structure in Organic Chemistry*, Holt, Rinehart, and Winston, New York 1959, p. 379.
10. Turner, R. A. and Connor R. *J. Am. Chem. Soc.* **69** (1947) 1009.
11. Agahigian, G., Plant, H., Vickers, G. D. and van der Veen, J. *Anal. Chem.* **39** (1967) 1583.
12. Conrad, M. and Bischoff, C. A. *Ann.* **204** (1880) 177.
13. Kipping, F. S. and Hunter, A. E. *J. Chem. Soc.* **83** (1903) 1005.
14. Kipping, F. S. *Proc. Chem. Soc.* **18** (1902) 33.
15. *Org. Syn.* **42** (1962) 75.
16. Buchman, E. R and Richardson, E. M. *J. Am. Chem. Soc.* **67** (1945) 398.
17. Rappe, C. and Gustafsson, R. *Acta Chem. Scand.* **22** (1968) 2915.
18. Smith, L. I. and Sprung, J. A. *J. Am. Chem. Soc.* **65** (1943) 1279.
19. Kishner, N. *J. Russ. Phys. Ges.* **46** (1914) 1411; *Chem. Zentr.* **1915 I** 1114.
20. Koelsch, C. F., Hochmann, H. and Le Claire, C. D. *J. Am. Chem. Soc.* **65** (1943) 59.

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