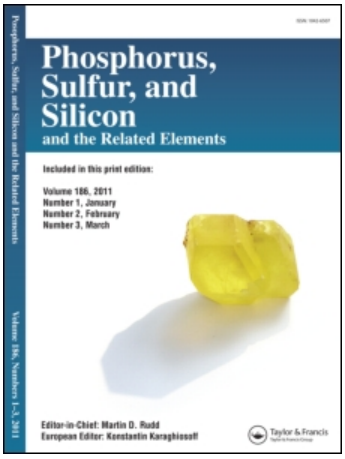

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β-KETOSULFINYL CHLORIDES AND RELATED COMPOUNDS

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β-KETOSULFINYL CHLORIDES AND RELATED COMPOUNDS

by

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ABSTRACT

Isopropyl β-ketosulfinyl chlorides may be prepared in high yields by treating the appropriate isopropyl ketone with thionyl chloride under mild conditions. β-Ketosulfinyl chlorides do not appear to have been previously reported in the literature. Analytical and spectral data indicate that in cases where α and α′ protons are adjacent to the carbonyl group only the α-proton of the isopropyl group is substituted giving a monosulfinyl chloride. In certain cases where the α′-proton is activated cyclization and reduction may occur to give the substituted thietan-3-one. Comparable chloro-compounds have been prepared by treating the ketone with sulfuryl chloride. Anomalous nmr spectra obtained for certain compounds have been further studied using variable temperature techniques and various solvents. An attempt was made to prepare the β-ketosulfinamides, and the compounds obtained were found to be unstable.

Various studies on the reaction between thionyl chloride and numerous compounds containing active methylene groups have led us to propose sulfinyl chlorides as intermediates in both our synthesis of tetra-substituted alkenes[1] and during the formation of sulfides and polysulfides from certain compounds with a relatively high enol content.[2] Thus, we decided to investigate further their preparation in an effort to determine the synthetic possibilities of this type of reaction. We have found that a number of sulfinyl chlorides may be prepared by treating the appropriate carbon acid with thionyl chloride. A similar reaction has been used by Steeter *et al.*[3] to prepare adamantane-1-sulfinyl chloride. We extended their procedure and prepared a number of previously unreported isopropyl β-ketosulfinyl halides by treating the appropriate isopropyl ketones with thionyl chloride under mild conditions (Table I).

The formation of the isopropylsulfinyl chloride appears to depend on the presence of the keto-group or enol function. Thus isobutyronitrile, cumene, and isopropyl acetate do not react with thionyl chloride under similar mild conditions. This suggests that the reaction proceeds *via* an enolic structure rather than

TABLE I

β-Ketosulfinyl Chlorides

$RCOCHMe_2 \rightarrow RCOCMe_2SOCl$

	Reactant		Product	Yield %	mp/bp
1.	$CH_3COCHMe_2$	6.	CH_3COCMe_2SOCl	90	80°/2mm.
2.	$CH_3CH_2COCHMe_2$	7.	$CH_3CH_2COCMe_2SOCl$	not isolated	
3.	$(CH_3)_2CHCOCHMe_2$	8.	$(CH_3)_2CHCOMe_2SOCl$	90	90-91°/1mm.
4.	$C_6H_5COCHMe_2$	9.	$C_6H_5COCMe_2SOCl$	91	*not detm.*
5.	$1\text{-}C_{10}H_7COCHMe_2$	10.	$1\text{-}C_{10}H_7COCMe_2SOCl$	85	74-75°
11.	$C_6H_5CH_2COCHMe_2$	12.	$C_6H_5CH_2COCMe_2SOCl$	not isolated	

via a carbanion-type intermediate. It should be noted that compounds containing highly active α′-protons, such as benzyl (**11**) and ethyl (**2**) isopropyl ketones

$$C_6H_5CH_2^{\alpha'}COCH^{\alpha}Me_2$$

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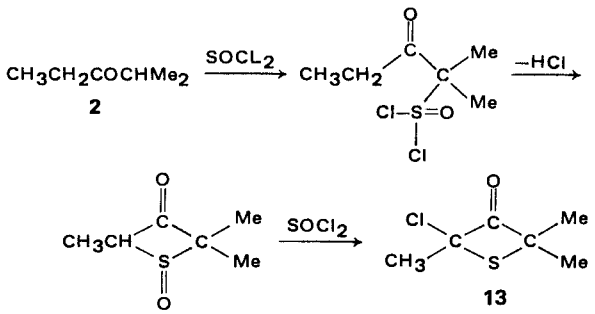
give thietan-3-ones rather than the expected sulfinyl chloride. Thus ethyl isopropyl ketone (**2**) on treatment with thionyl chloride at room temperature for 4 days gave a precipitate of 2-chloro-2,4,4-trimethylthietan-3-one (**13**), presumably *via* the route shown.



The rapid chlorination and reduction of the sulfoxide to the α-chlorosulfide is analogous to that encountered under similar conditions with dimethyl sulphoxide.[4] The infrared spectrum of the reaction mixture after ten minutes showed a large peak at 1155 cm^{-1}, presumably due to the sulphinyl chloride, a broadened peak at 1720–1695 cm^{-1} probably due to the initial ketone and the sulphinyl chloride, and a very small peak at 1782 cm^{-1} corresponding to the carbonyl group of the thietanone. The nmr spectrum gave results in accordance with the above assignments. As the reaction time increased the relative size of the peaks changed and after two hours the three peaks at 1155 cm^{-1}, 1720–1695 cm^{-1}, and 1782 cm^{-1} were of the same intensity. After four days the peak at 1155 cm^{-1} had disappeared while that at 1782 cm^{-1} was the sole peak observed in the carbonyl region of the spectrum. Analytical results for the thietanone (**13**) agree with the postulated structure and are given in the Experimental Section.

It appears from our results that cyclization does not involve a Pummerer-Type rearrangement[5] as at no time do we observe the formation of an α′-chloro-α′-chlorosulfenyl group. For a Pummerer rearrangement to take place substitution must occur on the α′-carbon atom whereas we have observed experimentally that only the α-hydrogen is substituted.

The reaction between benzyl isopropyl ketone and thionyl chloride appears to follow a similar course although the structure of the products has not been fully elucidated. The crude oil obtained from the reaction had 2 singlets at τ8.19 and τ8.56 of comparable areas, the *gem*-dimethyl peaks of the cyclic sulfide, and two singlets at τ6.10 and τ8.37, presumably due to the sulfinyl chloride, whilst the infrared spectrum gave ν_{max} at 1775, 1700 and 1148 cm^{-1} corresponding to the carbonyl of the thietanone, the carbonyl of the sulfinyl halide, and the sulfoxide of the sulfinyl chloride. A peak corresponding to the sulfoxide function in the cyclic sulfoxide was not observed. Hence we propose that the crude oil contains the sulfinyl chloride and the thietanone. On further heating with thionyl chloride the sulfoxide peak of the sulfinyl chloride slowly disappears while the carbonyl peak at 1775 cm^{-1} increases in size. Distillation of the reaction product gives almost pure thietanone (**14**). In both the above cases the thietanone has been found to be unstable to atmospheric moisture, and we are investigating the structure of the decomposition products. When the α′-proton is not activated by two adjacent groups, as in isopropyl methyl ketone (**1**), then only the α-proton reacts with thionyl chloride. Thus both methyl isopropyl (**1**) and di-isopropyl (**3**) ketones gave the corresponding monosulfinyl chlorides on treatment with thionyl chloride.

The treatment of di-isopropyl ketone (**3**) with thionyl chloride gave the monosulfinyl chloride (**8**) in high yield rather than the expected disulphinyl chloride. Further treatment with excess thionyl chloride in the presence of aluminium chloride or further heating did not give the disubstituted product. The nmr spectrum of **8** showed it to exist as the keto- rather than the enol-form. Thus the reaction may not proceed further due to the non-formation of the enol. Models show that formation of the enol is sterically possible and that chelation within the keto-form with the prevention of enol formation is improbable. Hence it is felt that electronic interactions rather than steric hindrance are responsible for the sole formation of a monosubstitution product. To investigate this further the ketone (**3**) was treated with excess sulfuryl chloride and again only a monosubstitution product was formed. This monochloride also exists as the keto-form and did not react when treated with thionyl chloride. It should be noted however, that treatment of both isopropyl methyl ketone (**1**) and benzyl isopropyl ketone (**11**) with excess sulfurylchloride resulted in the formation of the αα′-dichloro-compound. The anomalous results shown by the formation of the monosulphinyl chlorides (**6**, **8**) and by di-isopropyl ketone (**3**) in its reactions with sulphuryl chloride are being further studied.

TABLE II

Characteristic Absorption of Products and Related Compounds

No.	Compound	ν_{SO}	ν_{CO}	τH^1	τH^2	τH^3
6	$Me^1COCMe_2^2SOCl$	1155	1703	s, 7.7	s, 8.42 s, 8.35	–
7	$Me^1CH_2^2COCMe_2^3SOCl$[a]	1155	1700	t, 8.88	q, 7.30	s, 8.40 s, 8.42
8	$Me_2CH^1COCMe_2^2SOCl$	1156	1696	septet, 6.87	s, 8.30 s, 8.38	–
9	$C_6H_5COCMe_2^2SOCl$	1150	1658	–	s, 8.18	–
10	α-$C_{10}H_7COCMe_2^2SOCl$	1152	1675	–	s, 8.35	–
12	$C_6H_5CH_2^1COCMe_2^2SOCl$[a]	1148	1700	s, 6.10	s, 8.37	–
13	$Me^1\overline{C(Cl)SCMe_2^{2,3}C}=O$	–	1782	s, 7.96	s, 8.10	s, 8.35
14	$C_6H_5{}^1\overline{C(Cl)SCMe_2^{2,3}C}=O$	–	1775	m, 2.2-2.8	s, 8.19	s, 8.56
15	$Me_2CH^1COCMe_2^2Cl$	–	1722	septet, 6.57	s, 8.33	–
16	$C_6H_5COCMe_2^2Cl$	–	1684	–	s, 8.2	–
17	$CH_2{}^1ClCOCMe_2^2Cl$	–	1740	s, 5.36	s, 8.25	–
18	$C_6H_5CH^1ClCOCMe_2^2Cl$	–	1735	s, 3.84	s, 8.51	–
19	$C_{10}H_{15}SONH'C_6H_5$	1068	–	s, 3.56	s, 8.25	–
20	$C_{10}H_{15}SOCl$	1150	–	–	–	–

[a] This compound was not isolated, and the peaks recorded were found in the crude reaction product.

All nmr shifts were determined using carbon tetrachloride as a solvent.

The chloro-compounds from ketones (**1**, **3**, **4**, **11**) have been prepared by treating the parent compound with sulfuryl chloride and in the case of 1,3-dichloro-3-methylbutan-2-one (**17**), 2-chloro-2,4-dimethylpentan-3-one (**15**) and 1,3-dichloro-3-methyl-1-phenylbutan-2-one (**18**) the compound was obtained as the keto rather than the enol form.

The nmr and infrared spectra of the sulfinyl chlorides and chloro-compounds have been studied and certain characteristic absorptions are given in Table II. It should be noted that the sulfoxide absorption of β-ketosulfinyl chlorides, occurring at $1152 \pm 4\ cm^{-1}$, does not differ from that given by other sulphinyl chlorides. The nmr spectrum of 2,4-dimethyl-3-oxopentane-2-sulfinyl chloride (**8**) and 2-methyl-3-oxopentane-2-sulphinyl chloride (**7**) is unusual in that the *gem*-methyl groups on the carbon attached to the sulfinyl chloride occur as two singlets. The monochloro-compound derived from di-isopropyl ketone shows these groups absorbing as one singlet as do other similar isopropyl compounds shown in Table II. Stereochemical models of **8** indicate possible steric effects and this was studied by observing the nmr spectrum at various temperatures and in different solvents. A further consideration of the diastereotopic effects noted in certain of the β-ketosulphinyl chlorides will be published shortly.

In an effort to further characterize the sulfinyl chlorides an attempt was made to prepare the substituted amides by treating the chloride with aniline. *N*-methylaniline or piperidine. In no case was the expected stable sulfinamide obtained; a compound was isolated which rapidly decomposed. The sulfinanilide (**19**) derived from adamantane was prepared *via* the sulphinyl chloride and was found to be stable as is a sulfenamide, *NN'*-bis(2,4-dimethyl-3-oxo-2-pentanesulfenyl)-2,2,4,4-tetramethyl-1,3-cyclobutanediamine,[6] derived from di-isopropyl ketone. Hence it is postulated that β-ketosulfinamides possessing a tertiary carbon atom *alpha* to the sulfoxide group are inherently unstable. It is known that β-ketosulphoxides possessing a similar structure are stable[7] and work is in progress to study the source of the instability of the sulfinamide and also to determine the nature of the decomposition products. The decomposition does not appear to follow the normal disproportionation route, *e.g.*

$$2RSONH_2 \rightarrow RSNH_2 + RSO_2NH_2$$

Further work has shown that the carbon-sulfur bond in both β-ketosulfinyl chlorides and β-ketosulfinamides is readily cleaved by bases to give the original ketone and a product derived by nucleophilic attack of the sulfoxide function.[8]

Experimental Section

The isopropyl ketones used in this study were either purchased and redistilled or prepared by the known route involving interaction between isobutyronitrile and the appropriate Grignard reagent.

2-Acetylpropane-2-sulfinyl chloride (6)

3-Methylbutan-3-one (isopropyl methyl ketone) (8.6 g, 0.1 mol) was placed in a round-bottom flask equipped with a stirrer, dropping funnel, condenser and drying tube. The flask was immersed in an ice-salt bath and freshly distilled thionyl chloride (37.5 g, 0.3 mol) was added dropwise over a period of 30 min. The ice-bath was then removed, and the reaction was stirred for a further 15 hrs. The excess thionyl chloride was removed at 40° using a rotary evaporator, and the residual oil was then distilled under reduced pressure to give an 85% yield of the sulfinyl chloride, bp 90°/4 mm. Hg., τ (CCl_4) 7.7 (3H, s), 8.42 (3H, s) 8.35 (3H, s), υ_{max} 1703, 1155 cm^{-1}.

Anal. Calc. for $C_5H_9ClO_2S$, S, 19.00%, Cl 21.05%; Found: S, 19.39%, Cl, 20.6%.

2,4-Dimethyl-3-oxopentane-2-sulfinyl chloride (8)

2,4-Dimethylpentan-3-one (di-isopropyl ketone) (0.1 mol) was treated with redistilled thionyl chloride (0.3 mol) using the conditions described above to give a 90% yield of the sulfinyl chloride, bp 90–91°/1 mm. Hg., τ (CCl_4) 6.87 (1H, septet), 8.30 (3H, s), 8.38 (3H, s). 8.90 (6H, d), τ (C_6H_6). 8.66 (3H, s), 7.28 (1H, septet), 8.72 (3H, s). 9.17 (3H, d), 9.21 (3H, d), υ_{max} 1696, 1156 cm^{-1}. The molecular weight, by titration, was found to be 197.7; the calculated value for $C_7H_{13}ClO_2S$ is 196.5.

2-Benzoylpropane-2-sulfinyl chloride (9)

α-Methylpropiophenone (0.1 mol) was treated with redistilled thionyl chloride (0.3 mole) using the conditions described above to give a 91% yield of the crude sulfinyl chloride, τ (CCl_4) 2.3 (5H, m), 8.18 (6H, s) υ_{max} 1658, 1150 cm^{-1}.

Anal. Calc. for $C_{10}H_{11}ClO_2S$, S, 13.89%; Cl, 15.40%. Found: S, 13.40%; Cl 16.34%. Distillation resulted in decomposition.

2-1′-Naphthoylpropane-2-sulfinyl chloride (10)

Isopropyl 1-naphthyl ketone (0.1 mol) was slowly treated with redistilled thionyl chloride (0.3 mole) at room temperature and stirred for 18 hrs. Excess thionyl chloride was removed on a rotary evaporator and the residual solid recrystallized from a mixture of 95% petroleum ether (100–120°) and 5% benzene to give an 85% yield of the sulfinyl chloride, mp 74°, τ (CCl_4) 2.40 (7H, m), 8.35 (6H, s) υ_{max} 1675, 1152 cm^{-1}. The mass spectrum of the compound gave molecular ion peaks at m/e 280, 282.

2-Chloro-2,4,4-trimethylthietan-3-one (13)

Ethyl isopropyl ketone (0.1 mol) was treated with redistilled thionyl chloride (0.3 mol) using the conditions described for (6). The reaction vessel was left for four days at room temperature, and the solid thietanone obtained after the excess thionyl chloride had been removed had a mp 45° (crude product), τ (CCl_4) 7.96 (3H, s), 8.10 (3H, s), 8.35 (3H, s), υ_{max} 1782, 1455, 1438, 1078 cm^{-1}. A mass spectrum of the crude material gave a molecular ion peak at m/e 164 with the correct isotopic and fragmentation patterns for the postulated structure. The thietanone was not recrystallized due to its rapid decomposition with atmospheric moisture.

2-Methyl-3-oxopentane-2-sulfinyl chloride (7)

A portion of the above reaction mixture was taken after two hrs, the excess thionyl chloride was then removed to give an oil, τ (CCl_4) 7.30 (2H, q), 7.93 (3H, s), 8.10 (3H, s), 8.35 (3H, s), 8.40 (3H, s) 8.42 (3H, s).

8.88 (3H, t), υ_{max} 1782, 1720–1695, 1155 cm^{-1}. The two components of the mixture, the thietanone (13) and sulfinyl chloride (7) could not be separated by fractional distillation.

2-Chloro-4,4-dimethyl-2-phenylthietan-3-one (14)

Benzyl isopropyl ketone (0.1 mol) was treated with redistilled thionyl chloride (0.3 mol) using the conditions described for 6. The crude oil isolated had τ (CCl_4) 2.2–2.8 (m), 6.10 (s), 8.19 (s), 8.37 (s), 8.56 (s), υ_{max} 1775, 1700, 1148 cm^{-1}. From these figures the crude oil was composed mainly of **14** with a little sulfinyl chloride as byproduct in the approximate ratio of 7:3.

On heating the above reaction mixture at 45° for 60 hr the thietanone was obtained, free from sulfinyl chloride, τ (CCl_4) 2.3–3.0 (5H, m), 8.20 (3H, s), 8.54 (3H, s), υ_{max} 1775 cm^{-1}, bp 98–99°/0.4 mm. Hg.

2-Chloro-2,4-dimethylbutan-3-one (15)

Sulfuryl chloride (0.3 mol) was added over a period of 30 minutes to a stirred cooled solution of di-isopropyl ketone (0.1 mol). The solution was further stirred for 15 hr at room temperature, and excess sulfuryl chloride was then removed using a rotary evaporator. The resulting oil was then distilled to give a 90% yield of the chloro-compound, bp 145–146°; Lit[9] bp 143–145°, τ (CCl_4) 6.57 (1H, septet), 8.33 (6H, s), 8.89 (6H, d) υ_{max} 1722 cm^{-1}.

α-Chloro-α-methylpropiophenone (16)

α-Methylpropiophenone (0.1 mol) was treated with sulphuryl chloride (0.3 mole)using the conditions described for (16) to give a 90% yield of the chloro-compound, bp 69–70°/0.4 mm. Hg., τ (CCl_4) 2.30 (5H, m) 8.20 (6H, s), υ_{max} 1684, 1388, 1371 cm^{-1}. Lit[10] bp 108–108.5/17 mm. Hg.

1,3-Dichloro-3-methylbutan-2-one (17)

3-Methylbutan-2-one (0.1 mol) was treated with sulfuryl chloride (0.3 mol) using the conditions described for (15) to give a high yield of the dichloro-compound, bp 174–176°, τ (CCl_4) 5.36 (2H, s), 8.25 (6H, s), υ_{max} 1740, 1388, 1371 cm^{-1}. Lit[11] bp 164–165°.

1,3-Dichloro-3-methyl-1-phenylbutan-2-one (18)

Benzyl isopropyl ketone (0.1 mol) was treated with sulphuryl chloride (0.3 mol) using the conditions described for (15) to give a high yield of the dichloro-compound, bp 107–109°/14 mm. Hg., τ (CCl_4) 2.6 (5H, m), 3.84 (1H, s), 8.51 (3H, s), 8.25 (3H, s) υ_{max} 1735 cm^{-1}.

Adamantane-1-sulfinanilide (19)

Adamantane-1-sulfinyl chloride[3] (0.01 mol) (20) was dissolved in dry diethyl ether, and aniline (0.03 mol) was slowly added with external cooling. The precipitate was filtered off after 1½ hr and the sulfinanilide precipitated from 50% aqueous ethanol to give colorless plates, mp 155° decomp., τ ($CDCl_3$) 2.90 (5H, m), 3.56 (1H, s), 8.05 (15H, m) υ_{max} 3188, 1068 cm^{-1}.

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