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IONIC CHLORINATION OF ALKANES WITH SULFURYL CHLORIDE-SULFOLANE

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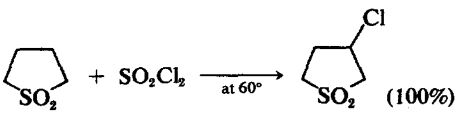
Abstract—Very facile chlorination of saturated hydrocarbons with sulfuryl chloride in sulfolane giving unrearranged chloroalkanes was observed. Hydrocarbons investigated were adamantane, norbornane, cyclohexane, n-hexane and isooctane. Adamantane gave 1-chloroadamantane almost exclusively, indicating that the present chlorination proceeded via an ionic mechanism. The relative reactivity of tertiary, secondary and primary hydrogen of isooctane was found to be 0:3:1, suggesting that the steric requirement of the reaction is considerably large.

Although the direct radical chlorination of alkanes seems to be one of the most important processes in organic syntheses, it has found limited use in laboratory preparation[1] because of its poor regioselectivity. The ionic regioselective chlorination of diethyl sulfone or sulfolane (tetrahydrothiophene-1,1-dioxide) with sulfuryl chloride (the latter case is shown in Eq. (1)) reported,[2] stimulated us to investigate the direct ionic chlorination of saturated hydrocarbons with sulfuryl chloride in sulfolane in expectation of the more facile chlorination of alkanes than that of dialkyl sulfones on the assumption of the probable hydride abstraction mechanism as an initiation step of the chlorination (i.e. a strong electron withdrawing sulfonyl group should destabilize the carbonium ion to be formed via the hydride abstraction).



(1)

The chlorination of cyclohexane and other typical alkanes with sulfuryl chloride in sulfolane were examined and found to give the corresponding chlorides in practically quantitative yields, in a marked contrast to the treatment of cyclohexane with sulfuryl chloride in a nonpolar solvent* where no appreciable amount of chloride has been detected even after 6 hr refluxing as reported by Kharasch and Brown.[3] Although sulfuryl chloride has been used as one of the most common radical chlorination reagents,[4] it has, to the authors' survey, never been used as an ionic chlorination reagent for saturated hydrocarbons. In this article, we wish to describe the profile of the chlorination of the saturated hydrocarbons with sulfuryl chloride in sulfolane, especially about its anomalous facility and unexpected regioselectivity with nearly complete retention of the skeletal structure.

RESULTS AND DISCUSSION

Adamantane, norbornane, cyclohexane, isooctane, and n-hexane were examined as the typical saturated hydrocarbons. Thus, in a reaction vessel,† fitted with an efficient reflux condenser connected with a calcium chloride tube and covered with aluminium foil to cut off light, a mixture of a saturated hydrocarbon, sulfuryl chloride and sulfolane was heated at 60° for appropriate hours. Separation and purification of the products were carried out by means of distilation and GLC and their structures were determined by comparing spectra (NMR, IR) of isolated products with those of the corresponding authentic compounds. Reaction conditions and product distributions are summarized in Table 1.

Chlorination of adamantane. Adamantane seems to be a convenient substrate to investigate the aliphatic reaction mechanism in a sense that the radical chlorination of adamantane is known to give both 1-chloro and 2-chloroadamantanes in the comparable amounts,‡ while the ionic chlorination[6] or bromination[7] of adamantane was reported to give 1-haloadamantanes exclusively.

The chlorination of adamantane with sulfuryl chloride in sulfolane gave 1-chloroadamantane (more than 97·5%) selectively (Eq. 2). Accordingly, the present chlorination may be concluded to proceed not via a radical process but an ionic one and this could be supported also by our preliminary re-

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*Usually hydrocarbon itself was used as a solvent.

†It should be carefully washed with fuming HNO_3 and with distilled water to avoid contamination with a trace of any radical chain initiator.

‡e.g., With chlorine in CCl_4, 1-chloro- and 2-chloroadamantanes are obtained in the yields of 37% and 63%, respectively, i.e., the statistically corrected reactivity of tertiary to secondary is 1·8.[5a] The regio-selectivity of tertiary to secondary in radical halogenation is also dependent on the reaction condition used especially halogenating reagent.[5b]

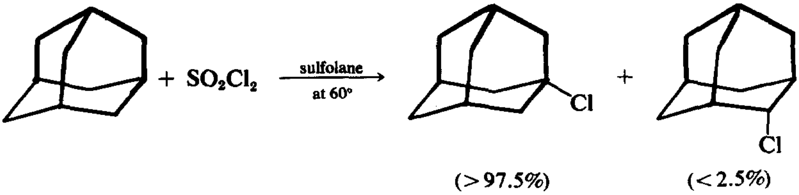
Table 1. Chlorination condition of alkanes[a] and product distributions

Substrate	Sulfuryl chloride (mole/mole substrate)	Time (hour)	Conversion (%)	Product Distribution
Adamantane[b]	2·0	16	79	1-Chloroadamantane (97·2%), 2-Chloroadamantane (2·5%)
Cyclohexane	1·3	18	62	Cyclohexyl chloride ($\sim$ 100%)
Norbornane[c]	1·5	14	50	2-*exo*-Chloronorbornane ($\sim$ 100%)
iso-Octane	3·7	4	30	3-Chloro-2,2,4-trimethylpentane (28%), 1-Chloro-2,2,4-trimethylpentane (43%), 1-Chloro-2,4,4-trimethylpentane (29%)
n-Hexane	3·1	18	40	1-Chlorohexane (20%), 2-Chlorohexane (56%), 3-Chlorohexane (24%)

[a] at 60°.

[b] A small amount of 1,2-dichloroethane was added.

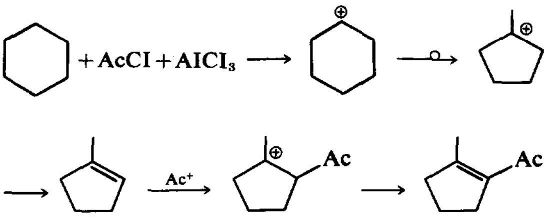
[c] A small amount of methylene chloride was added.



(2)

sults of the chlorination of toluene with the present chlorinating system; *o*- and *p*-chlorotoluenes were obtained quantitatively and neither benzyl chloride nor *m*-chlorotoluene was obtained in detectable amount.*

Chlorination of cyclohexane. The chlorination of cyclohexane with sulfuryl chloride in sulfolane gave mainly skeletally retained cyclohexyl chloride (more than 94%) together with a minor rearranged product, 1-methylcyclopentyl chloride (less than 6%), in an interesting and noteworthy contrast to the facile rearrangement of the cyclohexyl cation to the more stable methylcyclopentyl cation.† On treatment with acetyl chloride and aluminium chloride was converted cyclohexane to 1-acetyl-2-mentylcyclopent-1-ene[9]‡ as shown in Eq. 3.



(3)

On the contrary, skeletally retained nitrocyclohexane was obtained by treating cyclohexane with $NO_2^+PF_6^-$ in CH_2Cl_2-sulfolane.[11]

Thus a conclusion may be drawn that the present chlorination of cyclohexane also proceeds via a pentacoordinated carbonium ion transition state[12] rather than a free carbonium ion just like the nitration of cyclohexane mentioned above. (Fig 1).

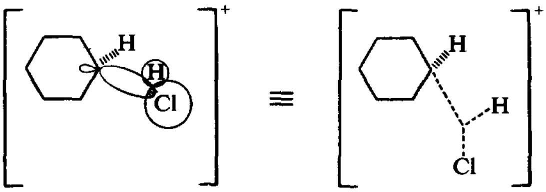


Fig 1.

However, a possibility of a simultaneous hydride abstraction-chloride addition process cannot be eliminated in this stage. Stereochemical investigations to elucidate the detailed mechanisms are under progress.

Chlorination of norbornane. 2-*exo*-Chloronorbornane was obtained selectively in the present chlorination in accord with the Schmerling's observation[13] that 2-*exo*-chloronorbornane had been obtained selectively in 50% yield on treatment of norbornane with a complex of t-butyl chloride and aluminium chloride. In the radical chlorination of norbornane with SO_2Cl_2 initiated by benzoyl peroxide, 2-*exo*-chloro- and 7-chloronorbornanes are obtained in the yields of 95 and 5%, respectively.[14]

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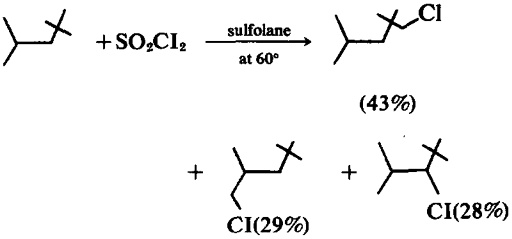
*The chlorination of substituted benzenes with sulfuryl chloride in sulfolane will be reported.

†The facile rearrangement of cyclohexane and its derivatives to methylcyclopentyl cation in strong acid media was observed NMR spectroscopically.[8]

‡Similarly, only 1-methylcyclopentylcarboxylic acid was obtained by the Koch-Haaf carboxylation of cyclohexyl alcohol in 80% yield.[10]

Chlorination of isooctane. In the chlorination of isooctane by the present system, 1-chloro-2,2,4-trimethylpentane, 1-chloro-2,4,4-trimethylpentane and 3-chloro-2,2,4-trimethylpentane were obtained in 43, 29 and 28%, respectively (Eq. 4), of the total products. It is interesting to note that any tertiary chloride[*] expected from the formation of a stable tertiary carbonium ion, 2,4,4-trimethylpent-2-yl cation, was not obtained. The statistically corrected reactivity ratio of tertiary:secondary:primary in the present chlorination was found to be 0:3:1. One reasonable explanation of the anomalous inertness of the tertiary position and the restricted reactivity of the secondary may be made by assuming that an attacking cationic species is too bulky to approach very closely to the highly hindered tertiary position of isooctane.[†] The restricted reactivity of the secondary may be interpreted on similar grounds. However, our attempted detection of the "bulky" chlorinating species (by means of IR, NMR spectroscopy) was not yet successful.



(4)

Chlorination of n-hexane. n-Hexane was chlorinated with sulfuryl chloride in sulfolane at 60° to give 1-chloro, 2-chloro- and 3-chlorohexane in the yields of 20, 56 and 24%, respectively. Again, the bulkiness of an attacking cationic species seems to control the regioselectivity, that is, the less hindered positions have higher reactivity than those expected from the cation stability.

As a conclusion, use of sulfolane as a solvent (as well as a reagent) caused the remarkable acceleration of the chlorination of aliphatic compounds by sulfuryl chloride (in the absence of sulfolane, the chlorination did not take place appreciably[4]). That regioselectivity was determined by cation stability as well as steric requirement of the reaction site and that minor or no skeletal rearrangement was accompanied with were also the characteristics of the present chlorination systems.

EXPERIMENTAL

Sulfolane was dried over barium oxide by heating at about 100° ~ 110° for 2 days and distilled under reduced pressure (138 ~ 139°/17 mmHg). Sulfuryl chloride was distilled twice under atmospheric pressure (69·3° ~ 69·4°) through 10 cm Vigreux-column and stored in the dark. A reaction vessel and a reflux condenser were washed carefully and repeatedly with fuming HNO$_3$ and distilled water to avoid contamination with a trace of any radical chain initiator.

Chlorination of adamantane In a 20 ml round bottom flask, fitted with an efficient reflux condenser connected with a CaCl$_2$ drying tube and covered with Al-foil to prevent light, were added 0·5 g (3·7 mmole) adamantane, 4 ml sulfolane and 1·0 g (7·4 mmole) sulfuryl chloride, then, 2 ml of 1,2-dichloroethane was added to dissolve adamantane (a small portion of adamantane remained undissolved even at elevated temp). The mixture was heated at 60° for 16 hr. Then, the mixture was poured into 30 ml of ice-water and extracted once with 30 ml n-pentane. After neutralization with NaHCO$_3$, the organic layer was washed twice with 10 ml water to extract sulfolane and dried over Na$_2$SO$_4$ and condensed through 10 cm Vigreux-column to *ca* 2 ml. Conversion of adamantane to the chlorinated products was determined to be *ca* 79% by means of GLC using diphenyl as an internal standard for calibration and products were determined to be 1-chloro- and 2-chloroadamantanes by comparing the retention times and the IR spectra with those of the authentic compounds. 1-Chloroadamantane and 2-chloroadamantane were obtained in more than 97·5% and less than 2·5% of the total products, respectively.

Chlorination of cyclohexane. A mixture of 2·1 g (16 mmole) sulfuryl chloride, 25 ml sulfolane and 1·0 g (12 mmole) cyclohexane was heated for 18 hr while stirring vigorously with magnetic stirrer at 60°. Similar treatment as used for adamantyl chlorides, produced cyclohexyl chloride in quantitative yield (based on cyclohexane consumed). Conversion was determined to be 62%. In a

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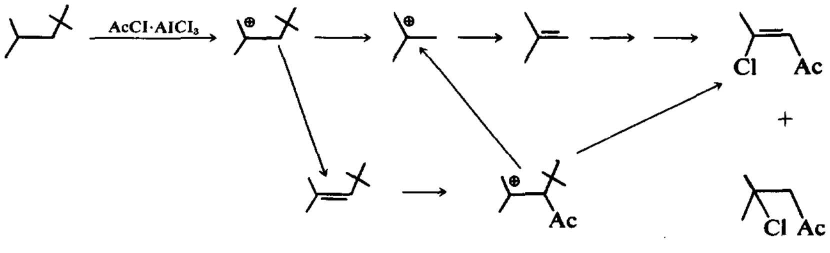
[*] The chlorination of isooctane with an acetyl chloride-aluminium chloride complex was found to give 1-acetyl-2-methylprop-1-ene and 1-acetyl-2-chloro-2-methylpropane and this result was rationalized as the fragmentation products from a tertiary carbonium ion as shown:[15]



[†] In the radical chlorination of isooctane, the similar, but lax inertness of tertiary position, which was explained in terms of conformational effects that shield the methine H atom from radical attack, was observed.[16]

separate run under similar conditions, cyclohexyl chloride and 1-methylcyclopentyl chloride were obtained in 94% and 6% yield, respectively.

Chlorination of norbornane. A mixture of 0·2 g (2 mmole) norbornane, 0·42 g (3·1 mmole) sulfuryl chloride, 2 ml sulfolane, and 0·5 ml CH_2Cl_2 was heated at 60° for 14 hr. After similar work up (isopentane was used as an extracting solvent), conversion was determined to be *ca* 50% by means of GLC using adamantane as an internal standard for calibration, and 2-*exo*-chloronorbornane was found to be the sole product.

Chlorination of isooctane. A mixture of 4 g (35 mmole) isooctane, 17 g (130 mmole) sulfuryl chloride and 10 ml sulfolane was heated with stirring at 60° for 4 hr. After the similar work up, distillation under reduced pressure (78 ~ 82°/60 mmHg) gave 1·6 g of monochloro derivatives (yield was *ca* 30%). The chlorinated products were separated by means of preparative GLC and assigned to 3-chloro-2,2,4-trimethylpentane (28% of the total products) and 1-chloro-2,4,4-trimethylpentane (29% of the total products) on the bases of NMR, IR, mass spectroscopies and relative retention times.[16]

3-Chloro-2,2,4-trimethylpentane; NMR (CCl_4) δ 3·60 (doublet J = 0·75 Hz, 1 proton), δ *ca* 2·2 (multiplet, 1 proton), δ 1·05 (singlet, 9 protons), δ *ca* 1·1 (doublet, $J =$ 3 Hz, 3 protons) and δ 0·93 (doublet, J = 3 Hz, 3 protons); IR (in cyclohexane) 1370 cm^{-1} (s), 820 cm^{-1} (s). Mass spectrum, *m/e* 97, 77 and 57.

1-*Chloro*-2,2,4-*trimethylpentane* and 1-*chloro*-2,4,4-*trimethylpentane*. The separation of these two isomers was unsatisfactory and spectra were measured in an impure state; NMR, (CCl_4). The α protons to chlorine of 1-chloro-2,4,4-trimethylpentane exhibited a typical ABX coupling pattern centered at δ 3·35. The α protons to chloride of 1-chloro-2,2,4-trimethylpentane showed a singlet at δ 3·29. The composition ratio of 1-chloro-2,2,4-trimethylpentane to 1-chloro-2,4,4-trimethylpentane was determined to be 1·5 on the basis of the area intensities; IR (liq. film), 1470 cm^{-1}(s), 1370 cm^{-1}(s), 765 cm^{-1}(s), and 721 cm^{-1}(s). Mass spectrum, *m/e* 99, 77 and 57.

Chlorination of n-hexane. A mixture of 6·6 g (77 mmole) n-hexane, 33 g (240 mmole) sulfuryl chloride and 15 ml sulfolane was heated with stirring at 60° for 18 hr. After similar work up, distillation gave 3·7 g chlorohexanes (70 ~ 75°/135 mmHg) (yield was *ca* 40%). One of the two peaks (GLC, He carrier gas, 5 m SiDC 550, PEG), which took a shorter retention time, was collected and determined to be a mixture of 2-chlorohexane (56% of the total products) and 3-chlorohexane (24% of the total products) by NMR spectroscopy and comparing GLC with those of the authentic compounds. Another peak was determined to be 1-chlorohexane (20% of the total products) on the basis of NMR spectrum and GLC comparing with those of the authentic compound.

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