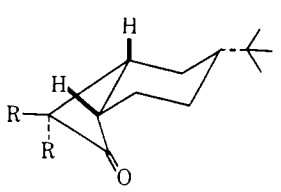
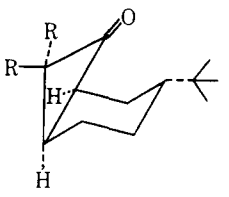
and in a ratio of 87:13 by glc. Separation by preparative glc yielded the two components A and B (ir 1770 $cm^{-1}$),[12] each of which was in turn resolved upon analytical glc into two peaks in the ratio of *ca.* 3:2.

Oxidation of the major component A with *m*-chloroperbenzoic acid produced two isomeric lactones[12] (ir 1780 $cm^{-1}$). Glc indicated two peaks in a ratio of *ca.* 2:1. At 100 MHz the nmr spectrum in the region of the proton next to oxygen was resolved into two multiplets (in a ratio of 2:1) at $\tau$ 5.5 and 5.36, each with a half-width of less than 9 Hz,[13] indicating that these protons were in an equatorial configuration. This indicates that both lactones contain the alkyl oxygen atom in an axial configuration relative to the cyclohexane ring, hence they must have structures **12** and **13** and have arisen from ketones **8** and **9** (R = H).

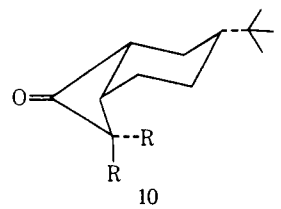
Hydrolysis of the lactone mixture gave hydroxy acids which, on methylation with diazomethane and $CrO_3$ oxidation, yielded ketoesters[12] **14** and **15** (ir 1740 and 1720 $cm^{-1}$) in the ratio of 3:2. The major component of the ketoesters was shown to be **14** by glc comparison with an authentic sample prepared by alkylation of the pyrrolidine enamine of 4-*tert*-butylcyclohexanone.



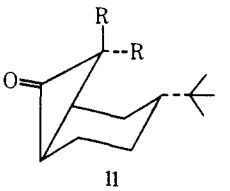
8



9

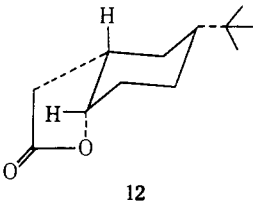


10

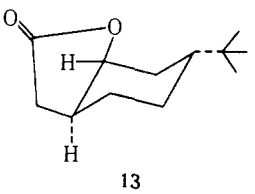


11

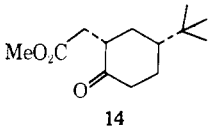
Preliminary attempts to add dichloroketene, generated from dichloroacetyl chloride and triethylamine,[14] to **7** have been unsuccessful. This suggests that possibly the additions we have observed involve a zinc-complexed ketene and therefore have a great deal of electrophilic character, in keeping with the stereoelectronic effects observed.



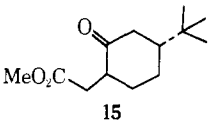
12



13



14



15

(12) Consistent elemental analysis and nmr spectra were obtained for all compounds or isomeric mixtures isolated.

(13) For the use of half-width in conformational assignments, see A. Hassner and C. Heathcock, *J. Org. Chem.*, **29**, 1350 (1964).

(14) H. C. Stevens, D. A. Reich, D. R. Brandt, K. R. Fountain, and E. J. Gaughan, *J. Amer. Chem. Soc.*, **87**, 5257 (1965).

It is clear that in cyclohexene systems, unlike in many open-chain olefins,[15] ketene cycloaddition is not only stereospecific but highly regioselective. Namely, *the newly formed bond of the carbonyl carbon will prefer to be axial with respect to the six-membered ring* (chair conformation).

(15) Our preliminary results indicate that cycloaddition of 4,4-dimethylcyclohexene with dichloroketene leads predominantly to one regioisomer, as predicted from the orbital considerations discussed above. On the other hand, a most recent report by N. S. Isaacs and P. F. Stanbury, *Chem. Commun.*, 1061 (1970), indicates that ketene cycloaddition to 2-pentene is nonregioselective.

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## A New 1:1 Adduct of Trimethylamine and Trichlorosilane, Trimethylammonium Trichlorosilyl

*Sir:*

Benkeser and coworkers[1] have recently demonstrated the usefulness of trichlorosilane–tertiary amine combinations in both organic and organosilicon chemistry. They postulated that the reactive species was the trichlorosilyl anion. Evidence for the existence of this anion in solution has now been obtained.[2,3] Bis(trichlorosilyl)mercury has also recently been obtained.[4] We wish to describe our results concerning a *new* 1:1 adduct of $N(CH_3)_3$ and $HSiCl_3$ which we believe must be $HN(CH_3)_3{}^+SiCl_3{}^-$.

It has been reported[5,6] that trimethylamine and trichlorosilane form a 1:1 adduct at −70° which decomposes below 0°. We have verified this result with the same quantities used by Burg ($HSiCl_3$, 0.19 mmol; $N(CH_3)_3$, 0.32 mmol). However, when larger quantities of reactants were used (see Table I), a different result was obtained. The trimethylamine and the trichlorosilane were condensed into a reaction tube at −196° (−78°). As the mixture warmed to room temperature, some of the condensate transformed into another white solid. The volatile fraction was recondensed and then allowed to warm to room temperature. This procedure was repeated until all or most of the trichlorosilane was consumed. We propose that the first condensate contained the complex observed by Burg which, in the presence of liquid trimethylamine, transferred a proton to form $(CH_3)_3NH^+SiCl_3{}^-$.

The results in Table I demonstrated that a 1:1 adduct was formed when a 2:1 excess of the amine was used. The solid had a vapor pressure of less than 1 mm at 25°. The infrared spectrum in Nujol contained the following absorptions ($cm^{-1}$): 2920 (vs), 2860 (vs), 2520 (vw), 2480 (w), 1460 (s), 1380

(1) R. A. Benkeser and W. E. Smith, *J. Amer. Chem. Soc.*, **90**, 5307 (1968); **91**, 1556 (1969); R. A. Benkeser, J. M. Gaul and W. E. Smith, *ibid.*, **91**, 3666 (1969).

(2) R. A. Benkeser, K. M. Foley, J. B. Grutzner, and W. E. Smith, *ibid.*, **92**, 697 (1970).

(3) S. C. Bernstein, *ibid.*, **92**, 699 (1970).

(4) C. R. Bettler, J. C. Sendra, and G. Urry, *Inorg. Chem.*, **9**, 1060 (1970).

(5) A. B. Burg, *J. Amer. Chem. Soc.*, 76, 2674 (1954).

(6) H. J. Campbell-Ferguson and E. A. V. Ebsworth, *J. Chem. Soc. A*, 705 (1967).

Table I. Reactions of $Cl_3SiH$ with $N(CH_3)_3$

| Reactant, mmol $N(CH_3)_3$ | Reactant, mmol $Cl_3SiH$ | Condensation temp, °C | No. of condensations | Volatile products (total mmol) |
|---|---|---|---|---|
| 1.85 | 1.73 | −196 | 15 | $HSiCl_3$, $SiCl_4$, $N(CH_3)_3$ (0.042) |
| 1.43 | 1.20 | −196 | 10 | $HSiCl_3$, $SiCl_4$, $N(CH_3)_3$ (0.52) |
| 1.61 | 0.79 | −196 | 10 | $N(CH_3)_3$ (0.81) |
| 2.08 | 1.07 | −196 | 6 | $N(CH_3)_3$ (1.04) |
| 2.56 | 1.39 | −196 | 10 | $N(CH_3)_3$ (1.17) |
| 2.40 | 1.09 | −196 | 8 | $N(CH_3)_3$ (1.30) |
| 0.92 | 0.61 | −78 | 8 | $HSiCl_3$, $SiCl_4$, $N(CH_3)_3$ (1.19) |
| 1.20 | 0.56 | −78 | 10 | $SiCl_4$,[a] $N(CH_3)_3$ (0.65) |
| 1.87 | 0.88 | −78 | 10 | $N(CH_3)_3$ (0.98), $SiCl_4$ (0.04) |

[a] Very small quantity.

(s), 1255 (m), 1240 (w), 1158 (w), 980 (m), 797 (s), 716 (m), 615 (m), 595 (m), and a broad band (m) with possible absorptions at 550, 525, 500, and 465. The infrared spectrum of an authentic sample of $(CH_3)_3NH^+Cl^-$ (prepared from $(CH_3)_3N$ and HCl) in Nujol contained only the first ten bands listed plus the band at 716 $cm^{-1}$, all with the same relative intensities as found in the spectrum of our 1:1 adduct. This result strongly suggested that the $(CH_3)_3NH^+$ ion was present in our adduct. This point was confirmed by the adduct proton nmr spectrum in acetonitrile which contained only one resonance at $\delta$ 2.38, while the methyl resonance in $(CH_3)_3NH^+Cl^-$ was observed at $\delta$ 2.46. Our failure to observe the N–H resonance in either compound was presumably due to line broadening from the nitrogen quadrupole moment.

Both of the adduct spectra were obtained at high gain. The fact that no silicon–hydrogen stretching frequency (2300–2000 $cm^{-1}$) and no silicon–hydrogen resonance were found is evidence that compounds containing a silicon–hydrogen bond $[(CH_3)_3NSiHCl_3]$ were absent or present in only very small quantities.

In Table II we list the X-ray powder photograph of the new adduct and that of an authentic sample

Table II. X-Ray Powder Photographs

| $HN(CH_3)_3^+Cl^-$ (*d*) | Adduct ($HN(CH_3)_3^+SiCl_3^-$) (*d*) |
|---|---|
| 6.40 (m) | 5.75 (w) |
| 5.86 (vs) | 5.19 (vs) |
| 4.90 (m) | 5.14 (m) |
| 4.40 (vs) | 5.10 (m) |
| 3.81 (m) | 5.05 (m) |
| 3.73 (w) | 4.86 (s) |
| 3.63 (m) | 4.60 (m) |
| 3.44 (w) | 4.37 (vs) |
| 3.35 (s) | 4.24 (w) |
| | 4.00 (w) |
| | 3.84 (w) |
| | 3.62 (m) |

of $(CH_3)_3NH^+Cl^-$. It is apparent that $(CH_3)_3NH^+Cl^-$ was absent from our 1:1 adduct or was present in only a very small quantity.

Our adduct did not yield hydrogen when treated with water or 4 *N* NaOH.[7] Therefore the new adduct did not contain $H^-$ ions or species containing silicon–silicon or silicon–hydrogen bonds. The only formulation that could fit these results, the stoichiometry, and our spectral data is $(CH_3)_3NH^+SiCl_3^-$.

The 1:1 adduct, $HN(CH_3)_3^+SiCl_3^-$, was found unreactive toward gaseous methyl chloride or ethyl chloride; however, in 10 min, hydrogen chloride (1.50 mmol) reacted with $HN(CH_3)_3^+SiCl_3^-$ (0.79 mmol) to produce $HSiCl_3$ (0.24 mmol), while 0.60 mmol of hydrogen chloride was consumed. The solid product was then treated with 2 *N* NaOH and 0.30 mmol of hydrogen was produced. In a separate experiment, we demonstrated that $HN(CH_3)_3^+SiCl_3^-$ reacted with $HSiCl_3$ to produce a solid that yielded hydrogen when treated with 2 *N* NaOH.

The adduct $HN(CH_3)_3^+SiCl_3^-$ was also treated with a DCl–HCl mixture of about 70% DCl, yielding a $DSiCl_3$–$HSiCl_3$ mixture of about 50% $DSiCl_3$. The reaction between hydrogen chloride and $HN(CH_3)_3^+SiCl_3^-$ was also carried out in propyl ether, where the silanes produced ($HSiCl_3$ with some $H_2SiCl_2$ and $SiCl_4$) were reduced with $LiAlH_4$ to produce silane in a 62% overall yield. These results demonstrate that as expected, the $SiCl_3^-$ ion extracts a proton from hydrogen chloride, producing trichlorosilane which unfortunately also reacts with the $SiCl_3^-$ ion. A sequence of steps that would fit our data can be represented by the following equations

$$SiCl_3^- + HCl \longrightarrow HSiCl_3 + Cl^- \quad (1)$$

$$SiCl_3^- + HSiCl_3 \longrightarrow HSi_2Cl_5 + Cl^- \quad (2)$$

$$SiCl_3^- + HSi_2Cl_5 \longrightarrow HSi_3Cl_7 + Cl^- \quad (3)$$

and/or

$$2HSi_2Cl_5 \longrightarrow HSiCl_3 + HSi_3Cl_7 \quad (4)$$

Reactions 2 and 3 seem reasonable, since at low temperature in butylamine $CCl_4$–$HSiCl_3$ mixtures have yielded $Cl_3SiCCl_3$, presumably from the reaction of the $SiCl_3^-$ ion with $CCl_4$.[1]

$$SiCl_3^- + CCl_4 \longrightarrow Cl_3SiCCl_3 + Cl^- \quad (5)$$

Disproportionation reactions (reaction 4) of hexachlorodisilane are well known.[8] Based on the consumption of HCl (reaction 1), the purity of $(CH_3)_3NH^+SiCl_3^-$ was at least 76%. However, since the product $HSiCl_3$ reacts further with the $SiCl_3^-$ ion, the purity was considerably greater than 76% and not impossibly 100%.

Benkeser and Smith[1] have reported that in butylamine at 40–60°, $CCl_4$–$HSiCl_3$ mixtures produced $HCCl_3$ in an 82% yield along with $SiCl_4$. The reaction of $(CH_3)_3NH^+SiCl_3^-$ (0.84 mmol) with refluxing $CCl_4$ yielded $HCCl_3$ (0.13 mmol) and $SiCl_4$ (0.17 mmol) in 6 hr.

The salt $HN(CH_3)_3^+SiCl_3^-$ was thermally unstable with evidence of some decomposition at 38°. A sample (1.32 mmol) was heated for 10 min at 100°. The volatile products were trimethylamine (0.46 mmol), silicon tetrachloride (0.23 mmol), and trichlorosilane (0.18 mmol). The solid products could be separated into a chloroform-soluble fraction, trimethylammonium

(7) As control experiments, we demonstrated that $HSiCl_3$ and the silicon–chlorine polymer generated in this communication rapidly yield hydrogen when treated with 2 *N* NaOH.

(8) G. D. Cooper and A. R. Gilbert, *J. Amer. Chem. Soc.*, 82, 5042 (1960); A. Kaczmarczyk and G. Urry, *ibid.*, 82, 751 (1960).

chloride (0.78 mmol), and a chloroform-insoluble solid (82.1 mg). The infrared spectrum of this solid had absorptions at 2245 (w), 1050 (vs), 870 (s), and 430 (m) $cm^{-1}$, in addition to weak bands from $HN(CH_3)_3^+Cl^-$. The X-ray powder photograph of the entire solid sampie obtained by heating $HN(CH_3)_3^+SiCl_3^-$ at 100° was essentially identical with that of our authentic sample of $HN(CH_3)_3^+Cl^-$. Therefore, the solid products from the thermal decomposition of $HN(CH_3)_3^+SiCl_3^-$ were $HN(CH_3)_3^+Cl^-$ and a silicon–chlorine polymer.

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## Incomplete Deblocking as a Cause of Failure Sequence in Solid Phase Peptide Synthesis

*Sir:*

The ninhydrin method[1] for measurement of the coupling efficiency of BOC-amino acids with Merrifield resin–peptides showed that the two octapeptides I

b 8 7 b 6 5 4 3 c 2 1
Tyr-Gly-Ser-Leu-Pro-Gln-Lys-Gly-Resin
I

b 8 7 b 6 b 5 4 n 3 2 1
Ser-Met-Glu-His-Phe-Arg-Trp-Gly-Resin
II

13 n12 b11 b10 b9 b8 7 b 6 5 4 3 c 2 1
Ala-Arg-Thr-Thr-His-Tyr-Gly-Ser-Leu-Pro-Gln-Lys-Gly-Resin
III

b13 b12 b11 10 b9 b8 7 t 6 5 4 c 3 2 1
Ser-Tyr-Ser-Met-Glu-His-Phe-Arg-Trp-Gly-Lys-Pro-Val-Resin
IV

and II (where b = benzyl, c = carbobenzoxy, n = nitro, and t = tosyl) were synthesized with coupling efficiencies of 98–100%. Amino acid analysis on the octapeptide resins revealed that in both peptides the seventh amino acid was present in 30–50% yield and the eighth amino acid in 5–10% yield. Since the coupling was essentially complete, a possible explanation of these failures is incomplete deblocking of amino acids six and seven. In the examples cited, the Merrifield deblocking reagent,[2] fresh 50% TFA in $CH_2Cl_2$, was used for 30 min as recommended. Quantitative amino acid analysis on dried weighed resin at different stages of the synthesis showed no loss of peptide during the total synthesis. In any event, cleavage of peptide from the resin cannot explain these results.

The ninhydrin procedure was modified to measure the extent of removal of the BOC group. $CH_2Cl_2$-washed and dried resin (5–10 mg) was used in the assay. The reaction was carried out as previously described[1] on resin unknown, completely deblocked amino acid resin ester, and a glycine color standard. Solutions were diluted to 20 ml with 50% ethanol and read against a reaction blank at 570 mμ in a DB spectrophotometer. The yield was calculated as per cent of deblocking based upon completely deblocked amino acid resin ester.

When the synthesis of I was repeated, see III, the coupling efficiency was again 98–100%. Deblocking of the first five amino acids with reagent A, 50% TFA–$CH_2Cl_2$, reagent B, 5.6 *N* HCl–dioxane, or reagent C, an equivolume mixture of A and B, gave yields of 90% or better with one of these reagents, and 100% after deblocking with a second of these reagents. Amino acids which are deblocked completely in one or two trials with reagents A, B, or C will hereafter be referred to as normal. The sixth amino acid, BOC-serine, was deblocked only 70% after four trials with the reagents listed. Use of a new reagent which contained C plus an equivolume of HCl-saturated $CH_2Cl_2$ raised the yield to 95%. The seventh amino acid, BOC-glycine, was also difficult, but could be deblocked with three trials using the standard reagents A, B, and C.

The eighth amino acid, BOC-tyrosine, deblocked normally. However, the next residue, BOC-histidine, failed to deblock beyond 58% with repeated trials using all of the reagents previously employed. A new reagent, 5.35 *M* HCl–DMSO and $CH_2Cl_2$ (1:1), for 90 min gave 100% yield. The tenth residue, BOC-threonine, again required three trials using reagents A, B, and C. The next residue, BOC-threonine, deblocked normally.

The failure sequence II was also resynthesized, but for reasons not important here, it was decided to elongate the peptide C terminal by three residues. See IV. Coupling efficiency again was 98–100% throughout. Deblocking of the first four amino acids was normal. The fifth residue, BOC-tryptophan, was very difficult to deblock, but was finally accomplished by pretreating the resin with 1.5 *M* urea in DMF, washing with DMF and dioxane, and deblocking for 2 hr with reagent C. Mercaptoethanol was present in all solutions. The next two residues, BOC-arginine and BOC-phenylalanine, deblocked normally. However, the eighth residue, BOC-histidine, required three trials using standard reagents. Five additional residues coupled and deblocked normally.

Peptides I–IV illustrate the following points: (1) when glycine-resin-ester (III) was used in peptide synthesis, the most difficult residues to deblock were no. 6 and 9, residues less difficult were no. 7 and 10; (2) when valine-resin-ester (IV), was used in peptide synthesis, residue no. 5 was most difficult to deblock, residue no. 8 less difficult; (3) all other residues in all peptides deblocked normally; (4) the BOC-glutamic and BOC-methionine which were poorly deblocked in II were normal in IV, alternatively the BOC-tryptophan and BOC-histidine which were difficult to deblock in IV were normally deblocked in II. These findings indicate that the position of the amino acid in the peptide rather than the nature of the amino acid determined the difficulty in deblocking.

A plausible explanation for the difficulty in deblocking various BOC-amino acids is that the terminal amino group is sterically hindered. Since the reactions are carried out in organic solvents, one may visualize around this amino group a cage of hydro-

(1) E. Kaiser, R. L. Colescott, C. D. Bossinger, and P. L. Cook, *Anal. Biochem.*, 34, 595 (1970).
(2) B. Gutte and R. B. Merrifield, *J. Amer. Chem. Soc.*, **91**, 501 (1969).