

acetate ion.³⁻⁵ The expected product is the Δ^2 -3'-OAc cephem **7a**. However, at the reaction temperature of 126 °C, isomerization of the Δ^2 double bond occurs and a 3:1 ratio of Δ^2 : Δ^3 isomers is obtained. That high temperature isomerizes the double bond is proven by heating to 70 °C, at which temperature only the Δ^2 product and starting material are obtained.⁶

We found this method to be generally applicable. Apparently, variation of the penicillin side chain is permissible. Thus, thiopheneacetyl-*exo*-methylenecephem sulfoxide **1b** reacts under the above conditions to yield **7b** and **4b** ($R =$ thiopheneacetyl) (IR (CHCl_3) 1785 cm^{-1} ; NMR (CDCl_3) δ 6.4 (br s, 1, Δ^2 -C₂ H), 5.6 (dd, 1, C₇ H), 4.6 (br s, 2, C_{3'} methylene), 3.8 (s, 2, C₇ side-chain methylene), 3.8 (s, 2, C₇ methylene), 2.05 (s, 3, 3'-acetoxyl), which ultimately can be converted to **4c**, an important antibiotic.

Another interesting variation of this method is to change the anhydride and acid. For example, a mixture of propionic anhydride and propionic acid at 120 °C converts **1a** to the 3'-propionate **7c**: NMR (CDCl_3) δ 6.45 (br s, 1, Δ^2 -C₂ H), 5.7 (dd, 1, C₇ H), 2.3 (q, 2, methylene of propionoxy), 1.1 (t, 3, methyl of propionoxy).

Optimal conditions for the conversion are to heat **1a** in a 2:1 mixture of acetic anhydride-acetic acid, at reflux (126 °C) for 2 h. The mixture of Δ^2 , Δ^3 -3'-acetoxycephems **7a** and **4a** ($R =$ phenoxyacetyl) is isolated in high yield.

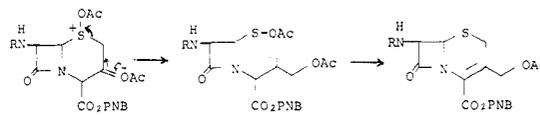
The mixture of isomers is then treated with *m*-chloroperbenzoic acid in methylene chloride and 2-propanol at 0 °C for 45 min. This efficiently yields crystalline Δ^3 -3'-acetoxycephem sulfoxide **8**.

The yield for the two steps from **1a** \rightarrow **8** is 84%. **8** is subsequently treated with PCl_3 and PCl_5 and finally deblocked to yield 7-ACA (**5**).⁷

This adaptation of a 1,4 Pummerer reaction, when combined with the ring expansion of penicillins to **1** as reported by Kukulja, provides a facile and efficient conversion of penicillins to 3'-ester cephalosporins.

References and Notes

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- All reported compounds gave satisfactory elemental and mass spectral analyses.
- For another example of a 1,4 Pummerer reaction, see Uda, *J. Chem. Soc., Chem. Commun.*, 193 (1975).
- Under standard Pummerer conditions (e.g., acetic anhydride, reflux) we obtained a very low yield of **7a** and **4a**.
- An alternate mechanism for the conversion (**1a** \rightarrow **7a** and **4a**) would be an $\text{S}_\text{N}2'$ displacement followed by readdition of sulfenate. However, the major product should be Δ^3 , **4a**. At low temperature, the product is exclusively Δ^2 , **7a**.



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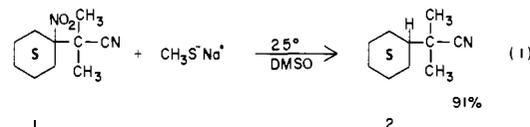
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Replacement of the Nitro Group by Hydrogen¹

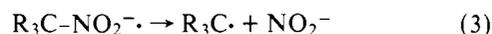
Sir:

It was not until 1954 that the first useful synthesis of tertiary nitroparaffins was described. Since then a number of other reactions which also give excellent yields of pure aliphatic and alicyclic tertiary nitro compounds have been found.¹⁻¹⁰ All of these reactions employ mild conditions and most of them are carbon-carbon bond-forming processes. It is of especial interest that they give rise to highly branched compounds—many of them all but unobtainable by other means. Still another important feature of these reactions is that they are capable of providing tertiary nitro compounds in which other functional groups are present, e.g., cyano, keto, and ester.

With such a wide variety of unusual structures readily available it is apparent that any process which results in the replacement of a nitro group by other atoms or groups of atoms has considerable value. In this communication we describe a new reaction—the replacement of a nitro group by hydrogen. This occurs at room temperature when the nitro compound is treated with the sodium salt of methyl mercaptan. Equation 1 is illustrative and Table I summarizes our results; it should be emphasized that yields refer to pure, isolated products.



The mechanism of this transformation appears to be



The first two steps (eq 2 and 3) are fully consistent with what is known about electron-transfer reactions of aliphatic nitro compounds.¹⁰ The last two (eq 4 and 5), which provided the initiative for this work, were suggested by the studies of Bunnett, Boyle, and Wamser¹¹ on the free-radical chemistry of methoxide ion. Although mechanistic studies are not yet complete, it has already been established that several of the reactions of Table I are completely inhibited by 20 mol % of di-*tert*-butyl nitroxide. This, and the fact that these reactions are greatly accelerated by exposure to two 20-W ordinary fluorescent lights, provides support for the proposed electron-transfer chain mechanism of eq 2-5.¹⁰

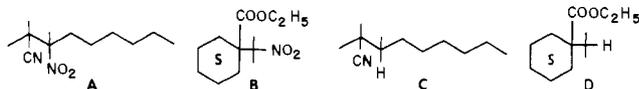
A typical example follows. Under N_2 the sodium salt of methyl mercaptan¹² (10.50 g, 150 mmol) was dissolved in 150 mL of $\text{Me}_2\text{SO}^{13}$ and, then, 9.80 g (50 mmol) of **1**⁷ was added without opening the system. The resulting solution was stirred for 10 h, under N_2 , with exposure to two 20-W fluorescent lights and, then, was poured into water. The aqueous Me_2SO solution was extracted with pentane, the pentane was washed

Table I. The Replacement of the Nitro Group by Hydrogen at 25°C^a

| A | Solvent | Reaction time, h | Yield, % ^b |
|---|---------|------------------|-----------------------|
| | | | |
| H | HMPA | 8 | 94 |
| CN | DMF | 15 | 91 |
| C ₆ H ₅ C(=O)- | DMF | 18 | 76 |
| C ₆ H ₅ SO ₂ - | DMF | 8 | 83 |
| 3,5-(CF ₃) ₂ | DMF | 20 | 84 |
| | | | |
| CN | HMPA | 16 ^c | 82 |
| C ₆ H ₅ C(=O)- | HMPA | 12 ^c | 80 |
| C ₆ H ₅ SO ₂ - | HMPA | 10 ^d | 80 |
| 3,5-(CF ₃) ₂ | HMPA | 16 ^c | 77 |

| Nitro compd | Solvent | Reaction time, h | Product | Yield, % ^b |
|-------------------|--------------------|------------------|----------------|-----------------------|
| tert-Nitrooctane | HMPA | 46 | Isooctane | 55 |
| 1-Nitroadamantane | HMPA | 42 ^e | Adamantane | 71 |
| A ^f | Me ₂ SO | 17 | C ^f | 92 |
| 1 | Me ₂ SO | 10 | 2 | 91 |
| B ^f | Me ₂ SO | 24 | D ^f | 83 |

^aAll reactions were carried out with exposure to two 20-W ordinary fluorescent lights unless otherwise noted. ^bPure, isolated, product. ^cIn total darkness. ^dRoom light. ^eAt 100 °C. ^fFor structures A-D, see below.



with water and dried (MgSO₄), and the solvent was removed. This gave 8.09 g of a yellow oil which was dissolved in an ethyl ether-pentane mixture (1:3) and passed through a column of silica gel (90%)–silver nitrate (10%). Removal of solvents followed by distillation at 7 mm gave 7.05 g (91% yield) of pure 2, bp 84–86 °C.¹⁴

Acknowledgment. We thank the National Science Foundation and Hoffmann-La Roche, Inc., for generous support.

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- The sodium salt of methyl mercaptan is prepared as follows. Under N₂ 9.20 g (0.40 mol) of sodium is added to 350 mL of freshly distilled 2-propanol. The mixture is refluxed until the reaction is complete (~5 h) after which heating is discontinued; the flask is promptly fitted with a Dry Ice condenser and 25 g (0.52 mol) of methyl mercaptan is passed in. 2-Propanol is then removed under reduced pressure at 30–35 °C. When the solution becomes

viscous ~250 mL of cyclohexane is added and the solvents are removed under reduced pressure. Two additional 250-mL portions of cyclohexane are added and the azeotrope is repeated. The resulting white solid is subjected to a vacuum of ~1 mm for 0.5 h (rotary evaporator) and then the free-flowing white powder is transferred to a sintered-glass funnel (protected by an N₂ blanket), and washed with a total of 500 mL of anhydrous ethyl ether. The solid, still moist with ether, is transferred to a round-bottom flask which is evacuated to ~1 mm and heated at 55–60 °C for ~15 h (rotary evaporator). The product, a finely divided, free-flowing white powder, is stored under N₂. It has a neut equiv of 71, calcd 70. Presumably, replacement of nitro by hydrogen would also occur with salt prepared in situ, but this has not yet been tried.

- (13) We thank the Crown-Zellerbach Corp. for a generous supply of Me₂SO.
(14) Satisfactory elemental analyses and NMR spectra were obtained for all new compounds.

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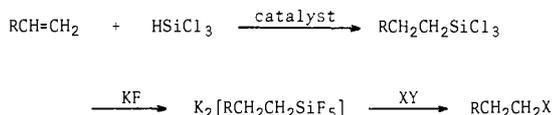
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Organofluorosilicates in Organic Synthesis. 1. A Novel General and Practical Method for Anti-Markownikoff Hydrohalogenation of Olefins via Organopentafluorosilicates Derived from Hydrosilylation Products

Sir:

The addition of silicon hydrides to olefins and acetylenes has become one of the most important methods of forming silicon-carbon bonds.¹ While alkenylsilanes thus obtained have recently been recognized as useful intermediates in various organic syntheses,² use of *alkylsilanes* has been rather limited. The major reason for this situation is that there has been virtually no method for transformation of the *alkyl*-silicon bonds into functional groups.

We report here the first general and practical method for preparing alkyl halides from alkyl-silicon compounds, as outlined in the following equation. This sequence of reactions represents our initial results concerning transformation of



(XY = Cl₂, Br₂, I₂, NBS)

carbon-silicon bonds into functional groups via organopentafluorosilicates which contain a doubly negatively charged hexacoordinate silicon atom, M₂[RSiF₅],³ the reactivities of which are expected to be quite different from those of neutral tetracoordinate organosilanes.⁴

In contrast to the complete inertness of tetracoordinate alkylsilanes towards halogenolysis,⁵ alkylpentafluorosilicates have been found to react almost spontaneously (exothermically) with halogen,⁶ forming alkyl halides in high yields. Organopentafluorosilicates also undergo a rapid reaction with NBS to give alkyl bromides. Representative results are summarized in Table I. The high yields of primary alkyl halides should particularly be noted, because these procedures provide a new convenient route to anti-Markownikoff hydrohalogenation of olefins under neutral reaction conditions.⁷ Another significant feature is that the reaction with NBS can tolerate certain functional groups,⁷ as shown by two examples in Table I. The nature of the reaction medium does not significantly affect the yield, although aliphatic hydrocarbon and alcoholic solvents seem less favorable. The yield dropped with secondary alkyl groups. Unfortunately, NCS gave mainly an organotri-fluorosilane rather than an organic chloride.

The present methodology, of course, applies to the regio- and