Tributyltin Hydride Addition to Nitroalkenes: A Convenient Procedure for the Conversion of Nitroalkenes into Nitroalkanes and Carbonyl Compounds

Claudio Palomo,* Jesús M. Aizpurua, Fernando P. Cossío, Jesús M. García, M. Concepción López, and Mike Oiarbide

Departamento de Química Orgánica, Facultad de Química, Universidad del País Vasco, Apdo. 1072, 20080 San Sebastián, Spain

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A new procedure for the reduction of nitroalkenes by using n-tributyltin hydride as reducing agent is described. The reaction proceeds under almost neutral conditions and works well even in the presence of other reducible functionalities. Hydrolysis and Nef reaction of the resulting nitronates furnished nitroalkanes and carbonyl compounds respectively in high yields. Application of this methodology to the preparation of 6-lactam building blocks is also made.

The conversion of nitroalkanes into carbonyl compounds, usually called the Nef reaction, is a transformation of widespread utility in organic synthesis. Several methods and reagents have been developed to convert nitroalkanes into the corresponding carbonyl compound as the intermediate and by the use of readily available starting materials. Among many suitable methods for the reduction of nitroalkenes, the most widely used involves so-

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(4) Scheme I

\[ \text{R}_1 \text{R}_2 \text{CHNO}_2 \xrightarrow{\text{MeO}^+ \cdot \text{MeOH}} \text{R}_1 \text{R}_2 \text{C}=\text{O} \]

(1) Nef, J. u.


(7) For a recent review, see: Seppen-Penne, J. In Rédactions par les Alumino-et Borohydrures en Synthèse Organique; Lavoisier: Paris, 1988, p 117.

Figure 1. Tributyltin hydride reduction of p-chloro-β-nitro-
styrene under different conditions.

such as carbonyl groups. Recently, we have found\(^9\) that
tributyltin hydride reduction of nitroalkenes afforded
stannyl nitronates,\(^{10}\) which upon oxidative Nef reaction
furnished the expected carbonyl derivatives in excellent
yields. Consequently we rationalized that we could utilize
the tributyltin hydride procedure\(^{11}\) for the preparation of
10 starting from nitroalkenes of type 11. In this paper we
report details of this new procedure for the conversion of
nitroalkenes into carbonyl compounds as well as nitro-
alkanes with emphasis on its utility in β-lactam chemistry.

**Results and Discussion**

As previously described,\(^8\) we found that treatment of
nitroalkene 5 with tributyltin hydride in nearly equimolar
amounts smoothly produced intermediate stannyl nitro-
nate 6 (M = SnBu\(_3\)-n), which could be in situ oxidized to
the corresponding carbonyl compound 8 or hydrolyzed to
the corresponding nitroalkane 7 (Scheme I). Among the
solvents examined, methanol and methylene chloride were
found to be the most satisfactory to obtain the best results
in terms of rapidity. For example, tributyltin hydride
reduction of p-chloro-β-nitrostyrene (Figure 1) in methy-
lene chloride gave a 50% conversion after 2 h of reaction
at room temperature. The reduction could be accelerated
either in refluxing methylene chloride or by the use of
methanol as cosolvent. Tributyltin trifluoro methanesul-
fonate\(^{12}\) also enhanced the reduction of nitroalkenes but
in diethyl ether, tetrahydrofuran, and dimethoxyethane
the reaction was extremely slow even in the presence of
this catalyst.

Results of reduction of some β-nitroalkanes in methy-
lene chloride as solvent are summarized in Table I. These
results suggest that there is a remarkable influence on the


ried out by using McMurry’s procedure,15a nitroalkenes were often produced as a mixture of cis and trans isomers at C3-C4 of the β-lactam ring, probably by the excess of base present in the reaction media, and generally in low yield. Better yields were obtained when dehydration of nitro aldols was carried out under Miyashita reaction conditions.15b In this case the expected nitroalkenes 14–16 were obtained as single cis isomers at C3-C4 of the β-lactam ring. The assignment of a cis or a trans stereochemistry to these compounds was made by examining the values of the coupling constant J3,4. The typical values of J3,4 for trans isomers are between 1.5 and 2.5 Hz and for the cis isomers larger than 5 Hz. Similarly, the geometrical assignment of the carbon–carbon double bond of these compounds was unequivocally determined by 1H NMR spectroscopy.16

As expected, conversion of nitroalkenes 14–16 into their tin nitronates 17 proceeds completely at room temperature within 20 and 24 h in methylene chloride or in methylene chloride–methanol. The conversion could be monitored by TLC analysis of the reaction mixture and, after completion, primary nitroalkenes 18 were separated by evaporation of the solvent, trituration of the resulting oil with methanol or ethanol, and further crystallization or isolation by column chromatography. The results obtained illustrate the efficiency, the applicability, and the scope of the present method. As shown in Scheme II the reaction conditions are mild enough to be applied to compounds possessing other reducible functionalities such as keto and alkoxycarbonyl groups.

The generality of the method can be further shown in the conversion of tin nitronates 17 into carbonyl compounds 19–20. Thus, when a α-substituted nitroalkene 15 was subjected to treatment with tributyltin hydride in methylene chloride as solvent followed by ozonolysis of the in situ generated tin nitronate 17 the corresponding carbonyl compound 19 was obtained in good yield. Similarly, nitroalkene 16 upon treatment with tributyltin hydride and further oxidative Nef reaction afforded the β-keto ester 20 in good yield. The transformations depicted in Scheme II illustrate the wide scope of the method. For example,

**Scheme II**

1. **Reagents and conditions:** (i) O3, CH3Cl, then Me3S; (ii) R2CH2NO2, NEt3; (iii) MeSO2Cl, NEt3, CH2Cl2; (iv) n-Bu3SnH, CH2Cl2, or CH2Cl2-MeOH, room temperature; (v) n-Bu3SnH, CH2Cl2, or MeOH-H2O; (vi) AcOH, or MeOH or MeOH-H2O-AcOH.

**Scheme III**

1. **Reagents and conditions:** (i) I2, CH3CN-H2O; (ii) Me2SBr2, NEt3, CH2Cl2; (iii) R2CH2NO2, NEt3, or R2CH2NO2, t-BuOK, THF; (iv) MeSO2Cl, NEt3, CH2Cl2; (v) n-Bu3SnH, CH2Cl2; (vi) AcOH, MeOH-H2O; (vii) CF3SO2Me or BSA, DBU, CH2Cl2, then MCPBA; (viii) O3, -78 °C, CH2Cl2, then Me3S.

The nitroalkene 15d, which possesses the labile chloroacetetyl moiety, could be transformed into the ketone 19e in good overall yield. It is also worth noting that the N-(p-anisyl) group in these β-lactams can be removed under mild conditions with cerium(IV) ammonium nitrate (CAN)17 and the resulting N-H azetidin-2-ones further elaborated to the corresponding bicyclic compounds.20 Particularly, the β-keto ester 20 thus prepared provides a new entry to the bicyclic ring system following Merck’s methodology.18

In view of the results obtained we next extended the tin hydride reduction of nitroalkenes to β-lactams 24 and 25 in order to obtain side chains at the C3 position of the β-lactam ring suitable for further chemical elaboration to potentially valuable intermediates for β-lactam antibiotic synthesis.19 Our approach (Scheme III) involved first the preparation of azetidin-2,3-diones 23 followed by the Henry reaction and subsequent dehydration of the resulting nitro aldo. The starting products 23 were prepared either by oxidative hydrolysis of 3,3-bis(ethylthio) β-lactams 21 or by oxidation of β-hydroxy β-lactams 22 by means of a dimethylbromosulphonium bromide-trimethylamine system.21 Formation of nitroalkenes 24 was achieved according to Sheehan’s procedure20 and preparation of nitroalkenes 25 could be carried out in high yields by using the same procedure as described for nitroalkenes 14. The stereochemistry of the double bond on these nitroalkenes was deduced on the basis of 1H NMR nuclear Overhauser effect experiments in which presaturation of the α-methyl group did not lead to any detectable enhancement of the signal corresponding to the C3H proton. This result suggests that these groups are in a trans relationship. This high stereoselectivity could be attributed


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to electrostatic and steric repulsions between the nitro group and the \( \beta \)-lactam carbonyl that could prevent the formation of the \( Z \) isomer.

Reaction between 24 and tributyltin hydride in methylene chloride for 20–24 h followed by addition of methanol to the in situ generated tin nitronate 26 furnished the expected nitroalkane 28. As mentioned above, \( \alpha \)-substituted tin nitronates were stable under these workup conditions and isolation of secondary nitroalkanes 29 might be accomplished under acetic acid conditions. Hydrofluoric acid and hydrochloric acid caused formation of oximes and ketones as byproducts. In all cases the yields were high and the nitro compounds were generally obtained as a mixture of cis and trans isomers at C3–C4 of the \( \beta \)-lactam ring. The isomer ratio of these \( \beta \)-lactams was easily determined, from the crude reaction mixture, by examining the coupling constants between the C3 and C4 protons in either the intermediate tin nitronates or nitronates. Although the configuration of the double bond in tin nitronates was not determined, we found that the stereoselectivity of the hydride addition reaction seems to be dependent of the bulkness of the substituents at the C4 position of the \( \beta \)-lactam ring. For example, while compound 24a upon treatment with tributyltin hydride gave a mixture of cis and trans isomers of 28a in approximately equal amounts, compound 24c provided the nitro compound 28c as a cis isomer. Similar results were obtained when the hydride addition was performed on nitroalkenes 25. For instance, whereas nitro compound 29a was produced as a mixture of cis and trans isomers in nearly equal amounts, the cis-\( \beta \)-lactam 29b was formed as main product (cis:trans ratio 80:20). As expected, the hydride reagent showed marked stereoselectivity for the nitroalkane 25c, producing 29c as a single cis isomer. The stereoselectivity of the reaction could be attributed to the preference of the hydride attack from the less hindered face of the starting nitroalkenes. The change of the \( \alpha \)-methylstyril group in 25c by the less hindered styril one caused a loss of selectivity and a mixture of cis and trans isomers of 29d was produced in a 40:60 ratio, respectively. Particularly interesting is the fact that in the case of the isomer syn-29c no nuclear Overhauser enhancement was detected at the C3-H signal when the methyl group was irradiated. The assignment for the anti and syn isomers of \( \beta \)-lactams 29 could also be established by examining the coupling constants between the H-3 and H-1' protons in both isomers. In fact, anti-29c (eq 3) upon treatment with triethylamine led to complete isomerization into the thermodynamically more stable syn-29c. These arguments are consistent with NOE experiments made on both epimers. Thus, presaturation of their respective methyl groups led to the enhancements indicated in eq 3 (R1 = \( \alpha \)-methylstyril, R2 = \( p \)-methoxyphenyl). Particularly interesting is the fact that in the case of the isomer syn-29c no nuclear Overhauser enhancement was detected at the C3-H signal when the methyl group was irradiated. The assignment for the anti and syn isomers of \( \beta \)-lactams 29 could also be established by examining the coupling constants between the H-3 and H-1' protons in both isomers. Thus, in our compounds \( J_{1,3} \) for the syn cis isomer is greater than that for the anti cis isomer and \( J_{1,1'} \) for the syn trans isomer is lower than that for the anti trans isomer, in agreement with similar values made on related compounds. On the basis of this assignment for the stereochemistry at the C3(1') position, we tried to correlate the structure of these epimeric \( \beta \)-lactams with their \( ^{13} \)C NMR spectra as Seebach et al. and Kamimura and Ono did in the case of O-silylated and O-benzylated nitro aldols, established on the basis of their respective \( ^{1} \)H NMR spectra. As can be seen by inspection of Dreiding models, the cis relationship between the C3 and C4 substituents on tin nitronates restricts strongly the number of accessible conformations for the epimers of the \( \beta \)-lactams 29. Assuming that intermediate 27U (Figure 3) is unfavorable by steric and electrostatic repulsions, it is possible to rationalize the behavior of intermediate 27F toward pro- 24.


Figure 3. Different possible conformations of cis nitronates 27 showing the diastereofacial selectivity toward protonation. Only one enantiomer is drawn.

Table II. Distribution of the Products Corresponding to the Sequence Indicated in Scheme IV

<table>
<thead>
<tr>
<th>Substr 25</th>
<th>Nitronates 27 (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Nitro Compounds 29 (%)&lt;sup&gt;b&lt;/sup&gt;,&lt;sup&gt;c&lt;/sup&gt;</th>
<th>cis</th>
<th>trans</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>syn</td>
<td>anti</td>
<td>syn</td>
</tr>
<tr>
<td>a</td>
<td></td>
<td>4 (78.39)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>46 (79.60)</td>
<td>23 (79.37)</td>
</tr>
<tr>
<td>b</td>
<td></td>
<td>31 (78.52)</td>
<td>69 (79.56)</td>
<td>0 c</td>
</tr>
<tr>
<td>c</td>
<td></td>
<td>100 (73.45)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>d</td>
<td></td>
<td>28 (79.00)</td>
<td>15 (79.41)</td>
<td>20 (79.22)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Stereochemistry assigned by measuring $J_{3,4}$ coupling constants and applying Karplus equation.  
<sup>b</sup> $^{13}$C NMR signals corresponding to the CHNO$_2$ group assigned by correlation with the corresponding $^1$H NMR spectra of both isomers and by isomerization (see text for details).  
<sup>c</sup> Hydrolysis not observed: the starting tin nitronate trans-27 was recovered unchanged.  
<sup>d</sup> Chemical shifts obtained by basic isomerization of the kinetic product anti-29.

respectively. These authors made their assignments for the syn and anti isomers on the basis of the major $^{13}$C chemical shifts of the carbon signals corresponding to the methine-NO$_2$ group of the syn isomers. However in our case, Table II, the $^{13}$C chemical shifts of the methine signals are in the inverse relative relationship for all compounds 29.

Compounds 29 thus prepared could be transformed into ketones 30 by silylation and further oxidation by means of m-chloroperbenzoic acid (MCPBA).<sup>46</sup> These methyl ketones could be directly obtained from the corresponding tin nitronates 27 according to the McMurry procedure.<sup>7</sup> In all cases ozonolysis of tin nitronates led to oxidation and concomitant isomerization at C$_3$-C$_4$ of the $\beta$-lactam ring, affording trans methyl ketones 30 in good yields. Particularly, the $\beta$-acetyl $\beta$-lactam 30c bearing a C$_4$-styryl moiety can be further elaborated to the known (+)-thienamycin precursor 31 according to an established protocol.<sup>25</sup>

Conclusion

From the results reported here the tributyltin hydride reduction of nitroalkenes seems to be of general application since a wide range of nitroalkanes, including those bearing reduceable or base-sensitive functionalities, could be prepared. As demonstrated here, the method has been successfully applied to the elaboration of $\beta$-lactams leading to a variety of bicyclic $\beta$-lactam precursors. The procedure is experimentally simple and may be readily extended to further applications, not only in the $\beta$-lactam area but also in other fields of chemistry.

Experimental Section

Commercially available compounds were used without further purification unless otherwise noted. Hexane was purified by distillation. Tetrahydrofuran was distilled over sodium with benzophenone as indicator. Methylene chloride was shaken with concentrated H$_2$SO$_4$, dried over K$_2$CO$_3$, and distilled. $\beta$-Lactams 12 were prepared by our procedure<sup>13</sup> and ozonized by using a Fischer 502 ozone generator. All compounds prepared are racemic mixtures. Melting points were determined on either Büchi SMP-20 or Mettler FP61 instruments and are uncorrected. Proton magnetic resonance ($^1$H NMR) spectra were recorded on a Varian VXR 300 spectrometer; chemical shifts are reported as $\delta$ values (ppm) relative to internal tetramethylsilane. The nuclear Overhauser enhancement experiments were run at 300 MHz by preirradiating the desired signals for 15 s with the decoupler channel turned on at 20 dB below 1 W and acquiring the spectrum with the decoupler turned off. A control experiment was created by setting the irradiation away from any signal. The acquisitions

were carried out in groups of four for each irradiated signal, until 32 accumulations were performed. The FID's, acquired with 16K (3000 Hz sweep width), were Fourier transformed to obtain a spectrum (zero-filling) and with a line broadering of 5 Hz. The NOE's were measured by integration of the signals resulting from the respective difference spectra. Infrared (IR) spectra were obtained on a Shimadzu IR-435 spectrometer. For new compounds microanalytical data were obtained in these laboratories on a Perkin-Elmer Model 240 C instrument.

Reduction of β-Nitrostyrenes 5 to Nitroalkanes 7. General Procedure. Reduction of the corresponding nitrostyrene 5 (R1 = Ar, R2 = R = H) (3 mmol) in methylene chloride (7.5 mL) was added tributyltin hydride (0.95 mL, 3.6 mmol), and the resulting mixture was stirred at room temperature. The conversion of the reaction was monitored by 1H NMR spectroscopy from an aliquot of the reaction mixture. When the conversion was total the solvent was evaporated under reduced pressure. The resulting oil was dissolved in methanol and treated with a solution of H2SO4 in methanol. The resulting precipitate tin compounds were filtered off and the residue was subjected to column chromatography to afford the corresponding nitroalkane, which was purified by distillation or crystallization. All compounds exhibited physical and spectral characteristics in accordance with the assigned structures.6a

Preparation of Nitroalkenes 14-16. General Procedure. The solution or suspension of the β-lactam 13 (10 mmol) in nitromethane or nitroethane (15 mL) was added triethylamine (0.2 mL, 1.5 mmol), and the resulting mixture was stirred at room temperature until completion (1-3 h). Evaporation of the solvent under reduced pressure gave a residue, which was dissolved in methylene chloride (40 mL) and dropwise added at -75 °C to a mixture of triethylamine (4.14 mL, 30 mmol) and methanesulfonyl chloride (2.34 mL, 30 mmol) and was stirred for 30 min at -75 °C. Triethylamine (4.14 mL, 30 mmol) was added to the solution at -50 °C and the resulting mixture was gradually warmed to 0 °C during 3 h, poured into water, and extracted with methylene chloride. The organic layer was washed with 0.1 N HCl (3 × 40 mL) and then with aqueous NaHCO3 (40 mL, saturated solution). The organic layer was separated and dried (MgSO4). Evaporation of the solvent at reduced pressure gave the nitroalkenes 14-16, which were purified by crystallization or chromatography on silica gel (eluent methylene chloride–hexane).

cis-1-(4-Methoxyphenyl)-4-(2-nitrovinyl)-3-phthalimidazoetidin-2-one (14a). Following the general procedure starting from 4-nitrophenyl-4-(2-nitrovinyl)-3-phthalimidazoetidin-2-one (13a) (2.97 g, 10 mmol) and nitromethane, the title compound was obtained: yield 2.89 g (85%); mp 125-127 °C (EtOH); IR (KBr) v 1757, 1751, 1393, 1530 cm-1; 1H NMR (CDCl3) δ 7.57-7.55 (d, 1 H, J = 7.7 Hz, Ar), 7.60 (d, 1 H, J = 7.3 Hz, H-3), 5.57 (d, 1 H, J = 5.0 Hz, H-5, 5.08 (m, 1 H, 1 H, H-4)), 3.81 (s, 3 H, OCH3). Anal. Calcd for C18H16NO6: C, 63.71; H, 4.67; N, 8.21.

cis-1-[Methoxybenzyl](methyl)-4-(2-nitrovinyl)-3-phthalimidazoetidin-2-one (14b). Following the general procedure starting from cis-1-(4-acetylamphenyl)-4-formyl-3-phthalimidazoetidin-2-one (13b) (3.16 g, 10 mmol) and nitromethane, the title compound was obtained: yield 2.58 g (85%); mp 111 °C; IR (KBr) v 1735, 1725, 1380 cm-1; 1H NMR (CDCl3) δ 7.91-7.88 (m, 6 H, Ar), 7.44 (d, 1 H, J = 7.7 Hz, H-3), 4.33 (dd, 1 H, J = 7.3 Hz, H-4), 4.28 (d, 2 H, 1 H, J = 5.9 Hz, CH2CO), 2.29 and 2.14 (s, 3 H, CH3). Anal. Calcd for C18H17NO5: C, 63.99; H, 5.04; N, 7.76.

cis-4-(2-Methyl-2-nitrovinyl)-1-[[(methoxycarbonyl)methyl]-3-phthalimidazoetidin-2-one (15). Following the general procedure starting from cis-4-formyl-1-[[(methoxycarbonyl)methyl]-3-phthalimidazoetidin-2-one (15a) (3.38 g, 10 mmol) and nitromethane, the title compound was obtained: yield 2.50 g (67%); mp 155-158 °C (EtOH); IR (KBr) v 1767, 1752, 1728, 1717, 1518, 1396 cm-1; 1H NMR (CDCl3) δ 7.87-7.76 (m, 4 H, Ar), 7.15 (d, 1 H, J = 8 Hz, CH=CH(COMe)N2), 5.31 (d, 1 H, J = 5.7 Hz, H-3), 5.06 (dd, 1 H, J = 7.3 Hz, H-4), 4.54 (dd, 1 H, J = 8.8 Hz, CH2CO), 3.88 (s, 1 H, CH=CHCOOH), 3.80 (s, 3 H, CH3CH2CO2H). Anal. Calcd for C14H13NO5: C, 64.40; H, 5.12; N, 7.90. Found: C, 63.99; H, 5.04; N, 7.76.

Preparation of Azetidines 23-27. Method A. General Procedure. To a solution of 3,3-bis(ethyloxothio) β-lactam 21a (20 mmol) in acetonitrile (200 mL) and water (50 mL) was added iodine (30.45 g, 120 mmol), and the resulting mixture was stirred under reflux for 30-45 min until completion. Then the mixture was cooled at room temperature and diluted with methylene chloride (400 mL) and washed with 40% aqueous sodium hydrosulfite (100 mL). The organic layer was separated and the aqueous phase was extracted with methylene chloride (2 × 100 mL). The methylene chloride solutions were combined and washed with water (2 × 200 mL) and then with aqueous NaHCO3 (200 mL, saturated solution). The organic layer was separated and dried (MgSO4). Evaporation of the solvent at reduced pressure afforded an oil, which was used without further purification. Following the general procedure for nitroalkene formation, the title compound 26f was obtained: yield 1.40 g (30%); mp 208-211 °C (EtOH); IR (KBr) v 1758, 1737, 1710, 1393 cm-1; 1H NMR (CDCl3) δ 7.91-6.92 (m, 9 H, Ar and CH=CH(CONO2)), 5.93 (d, 4 H, J = 6 Hz, H-3), 5.52 (dd, 1 H, J = 6 Hz, J′ = 7.8 Hz, H-4), 3.81 (s, 3 H, CH3CH2CO2H), 3.54 (s, 3 H, CH3COOH), 3.55 (d, 4 H, J = 7.5 Hz, CH2CONHO), 3.46 (2 H, J = 1.5 Hz, J′ = 8.1 Hz, CH3CO2H), 2.99 (s, 3 H, OCH3). Anal. Calcd for C41H39NO10: C, 65.15; H, 4.12; N, 9.03. Found: C, 59.72; H, 4.28; N, 8.87.

Preparation of Azetidine-2,3-diones 23-27. Method A. General Procedure. To a solution of 3,3-bis(ethyloxothio) β-lactam 21b (20 mmol) in acetonitrile (200 mL) and water (50 mL) was added iodine (30.45 g, 120 mmol), and the resulting mixture was stirred under reflux for 30-45 min until completion. Then the mixture was cooled at room temperature and diluted with methylene chloride (400 mL) and washed with 40% aqueous sodium hydrosulfite (100 mL). The organic layer was separated and the aqueous phase was extracted with methylene chloride (2 × 100 mL). The methylene chloride solutions were combined and washed with water (2 × 200 mL) and then with aqueous NaHCO3 (200 mL, saturated solution). The organic layer was separated and dried (MgSO4). Evaporation of the solvent at reduced pressure gave the title compound, which was purified by column chromatography or crystallized from hexane/chloroform.

Method B. General Procedure. To a solution of dimethyl sulfoxide (0.6 mL, 5.4 mmol) in methylene chloride (10 mL) was added bromine (0.4 mL, 8.4 mmol) in methylene chloride (5 mL) with stirring. After the immediate formation of a yellow precipitate the mixture was stirred at room temperature for 5 min and the corresponding 3-hydroxy β-lactam 22 (8 mmol) was added. The stirring was continued for 2 min at the same temperature and then the solution was cooled at 0 °C. To the above mixture was added triethylamine (2.24 mL, 16 mmol) in methylene chloride (4 mL) dropwise, and the stirring was continued for 1-1.5 h at...
the same temperature until completion. The reaction mixture was washed with H2O (40 mL) and 0.1 N HCl (2 × 10 mL). The organic layer was separated and dried (MgSO4). Evaporation of the solvent at reduced pressure gave the azetidine-2,3-dione 23, which was purified by crystallization.

Preparation of Nitroalkanes 24. General Procedure. A solution of nitromethane (1.35 mL, 20.6 mmol) in tetrahydrofuran (30 mL) under nitrogen was cooled to 0 °C and potassium tert-butoxide (0.55 g, 4.77 mmol) was added. After 15 min a solution of the azetidine-2,3-dione 23 (10 mmol) in tetrahydrofuran (30 mL) was added, and the resulting mixture was stirred at 0 °C for 1–2 h. The mixture was diluted with methylene chloride (150 mL) and washed with H2O (60 mL) and NaCl (60 mL, saturated solution). The organic layer was separated and dried (MgSO4). Evaporation of the solvent gave an oil, which was triturated with ethanol and filtered off to give the corresponding nitroalkane. An analytical sample was obtained by crystallization from ethanol.

Preparation of Secondary Nitroalkanes. General Procedure. To a solution of the corresponding nitroalkane (6 mmol) in methylene chloride (20 mL) and methanol (2 mL) was added tributyltin hydride (1.85 mL, 7.2 mmol), and the mixture was stirred at room temperature for 20 h. Evaporation of the solvent gave a residue, which was triturated with hexane (50 mL) and then with methanol (25 mL, saturated solution). After drying over MgSO4, the solution was evaporated at reduced pressure to give the nitroalkene 6, which was purified by chromatography on silica gel.

cis-1-(4-Methoxyphenyl)-4-(2-nitroethyl)-3-phenoxyazetidin-2-one (18a). Following the general procedure starting from 2.04 g, 6 mmol of the title compound was obtained. Yield: 2.16 g (90%); IR (KBr): v 1744, 1553, 1495, 1392 cm⁻¹; 'H NMR (CDCl₃) δ 7.80-7.00 (m, 10 H, Ar); diastereoisomer mixture B, 2.89 (m, 1 H, CH₂), 2.26 (m, 1 H, CH₂). Anal. Calcd for C₂₃H₂₂NO₅: C, 69.38; H, 5.72; N, 7.95. Found: C, 68.86; H, 5.76; N, 7.78.

Preparation of Nitroalkenes 25. The same procedure as that used for the preparation of 14 was followed.

1,4-Diphenyl-3-(1-nitroethyldene)azetidin-2-one (25a). Following the general procedure starting from 2.32 g (3.07 g, 10 mmol), and nitroethane, the title compound was obtained: yield 2.16 g (78%); mp 90–92 °C (EtOH); IR (KBr) v 1744, 1553, 1495, 1392 cm⁻¹; 'H NMR (CDCl₃) δ 7.52, 6.90 (m, 5 H, Ar), 6.50 (s, 1 H, Ar), 5.62 (d, 1 H, J = 4.9 Hz), 4.77 (dd, 1 H, CH₃). Anal. Calcd for C₁₇H₁₄NO₃: C, 76.93; H, 4.77; N, 9.48. Found: C, 76.93; H, 4.76; N, 9.48.
4.07 (dd, 1 H, =CH, 14.2 Hz), 4.97 (m, 1 H, CHN02), 3.71 (dd, 1 H, H-3, 6.9 Hz), 4.08 (dd, 1 H, CH3, J = 6 Hz), 4.51 (m, 1 H, CHN02, J = 6.6 Hz), J' = 5.1 Hz), 1.78 (d, 3 H, CH3, J = 6.9 Hz); anti-cis diastereoisomer 5.35 (d, 1 H, H-4, J = 6 Hz), 4.07 (dd, 1 H, H-3, J = 6 Hz, J' = 10.2 Hz), 1.21 (d, 3 H, CH3, J = 5.2 Hz), 4.42 (m, 1 H, CHN02, J = 6.8 Hz), J' = 11.7 Hz), 4.27 (dd, 1 H, H-3, J = 5.2 Hz, J' = 11.7 Hz), 1.78 (d, 3 H, CH3, J = 6.9 Hz). Anal. Calc'd for C19H16N2O4: C, 68.84; H, 6.05; N, 7.64. Found: C, 68.25; H, 5.43; N, 9.51.

cis-syn-4-(2,5-Dimethylphenyl)-3-(1-nitroethyl)-1-phenylazetidin-2-one (29b). Following the general procedure starting from 25b (0.93 g, 3 mmol), a mixture of epimeric cis-azetidines was obtained, in a ratio of 1:13. After purification by column chromatography, the sole syn diastereoisomer of 29b was obtained: yield 0.29 g (57%); mp 164-166 °C (EtOH); IR (KBr) ν 3378, 1743, 1711 cm⁻¹; 'H NMR (CDCl₃) δ 7.35-7.20 (m, 7 H, Ar), 5.39 (d, 1 H, J = 18.1 Hz, CH3CH2CO), 4.04 (d, 1 H, J = 18.1 Hz, CH3CH2CO), 3.77 (t, 3 H, OCH3), 1.85 (s, 3 H, CH3). Anal. Calc'd for C19H16N2O4: C, 68.84; H, 6.05; N, 7.64. Found: C, 68.25; H, 5.43; N, 9.51.

cis-syn-4-(2,5-Dimethylphenyl)-3-(1-nitroethyl)azetidin-2-one (29c). Following the general procedure starting from 25c (3.64 g, 10 mmol), the title compound was obtained: yield 2.64 g (75%); mp 164-166 °C (EtOH); IR (KBr) ν 3378, 1743, 1711 cm⁻¹; 'H NMR (CDCl₃) δ 7.35-7.20 (m, 7 H, Ar), 6.87 (d, 2 H, Ar, J = 9 Hz), 6.53 (s, 1 H, =CH), 4.96 (qq, 1 H, CH2OH, J = 6.6 Hz, J' = 9 Hz), 4.78 (d, 1 H, H-4, J = 5.2 Hz), 3.97 (dd, 1 H, H-3, J = 6 Hz, J' = 6 Hz), 3.77 (s, 3 H, OCH3), 1.85 (s, 3 H, CH3). Anal. Calc'd for C19H16N2O4: C, 68.84; H, 6.05; N, 7.64. Found: C, 68.25; H, 5.43; N, 9.51.

cis-syn-4-(3-Methylphenyl)-1-(4-methoxyphenyl)-3-nitroazetidin-2-one (29d). Following the general procedure starting from 25d (3.5 g, 10 mmol), the title compound was obtained: yield 2.64 g (75%); mp 164-166 °C (EtOH); IR (KBr) ν 3378, 1743, 1711 cm⁻¹; 'H NMR (CDCl₃) δ 7.35-7.20 (m, 7 H, Ar), 6.87 (d, 2 H, Ar, J = 9 Hz), 6.53 (s, 1 H, =CH), 4.96 (qq, 1 H, CH2OH, J = 6.6 Hz, J' = 9 Hz), 4.78 (d, 1 H, H-4, J = 5.2 Hz), 3.97 (dd, 1 H, H-3, J = 6 Hz, J' = 6 Hz), 3.77 (s, 3 H, OCH3), 1.85 (s, 3 H, CH3). Anal. Calc'd for C19H16N2O4: C, 68.84; H, 6.05; N, 7.64. Found: C, 68.25; H, 5.43; N, 9.51.
IR (KBr) v 1787, 1763, 1758, 1731, 1718 cm\(^{-1}\) (C=O); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 6.92-7.93 (m, 8 H, Ar), 5.61 (d, 1 H, J = H-3, 4.79-4.96 (m, 1 H, H-4), 3.82 (s, 3 H, p-CH\(_3\)OPh), 3.62 (s, 3 H, COCH\(_2\)COOCH\(_3\)), 3.35 (s, 2 H, COCH\(_2\)COOCH\(_3\)), 3.07 (dd, 1 H, J = 8.7 Hz, J' = 17.4 Hz, CH\(_3\)HCO), 2.66 (dd, 1 H, J = 5.1 Hz, J' = 17.4 Hz, CH\(_3\)HCO). Anal. Calcld for C\(_{33}\)H\(_{30}\)N\(_2\)O\(_7\): C, 63.29; H, 5.70; N, 5.28. Found: C, 76.90; H, 5.69; N, 5.00.

trans-3-Acetyl-1,4-phenylazetidin-2-one

Following the general procedure starting from 25a (1.76 g, 6 mmol), the title compound was obtained: yield 1.18 g (78%); mp 90-93 \(^\circ\)C. Anal. Calcld for C\(_{19}\)H\(_{18}\)N\(_2\)O: C, 77.54; H, 6.59; N, 4.67.

trans-3-Acetyl-4-(2,5-dimethylphenyl)-1-phenylazetidin-2-one (30a). Following the general procedure starting from 25a (1.76 g, 6 mmol), the title compound was obtained: yield 1.18 g (75%); mp 90-93 \(^\circ\)C (CHCl\(_3\)/hexane); IR (KBr) v 1740, 1708 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 7.40-7.06 (m, 10 H, Ar), 5.48 (d, 1 H, CH, J = 2.55 Hz), 4.14 (d, 1 H, CH, J = 2.55 Hz), 2.39 (s, 3 H, CH\(_3\)). Anal. Calcld for C\(_{26}\)H\(_{26}\)N\(_2\): C, 76.95; H, 5.70; N, 5.28. Found: C, 76.90; H, 5.69; N, 5.00.

trans-3-Acetyl-1,4-(2,5-dimethylphenyl)-1-phenylazetidin-2-one (30b). Following the general procedure starting from 25b (1.86 g, 6 mmol), the title compound was obtained: yield 1.32 g (75%); mp 86-87 \(^\circ\)C (CHCl\(_3\)/hexane); IR (KBr) v 1749, 1715 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 7.27-7.00 (m, 8 H, Ar), 5.66 (d, 1 H, CH, J = 2.63 Hz), 4.07 (d, 1 H, CH, J = 2.63 Hz), 2.39 (s, 6 H, CH\(_3\)), 2.21 (s, 3 H, CH\(_3\)), 1.86 (s, 3 H, CH\(_3\)). Anal. Calcld for C\(_{31}\)H\(_{31}\)N\(_2\): C, 77.79; H, 5.70; N, 4.67.

trans-3-Acetyl-4-(o-methoxyphenyl)-1-(4-methoxyphenyl)-azetidin-2-one (30c). To a solution of anti-29c (1 mmol, 0.36 g) in methylene chloride (3 mL) and N,O-bis(trimethylsilyl)acetamide (BSA) (1.5 mmol, 0.37 mL) cooled to 0 \(^\circ\)C was added 1.8-diazabicyclo[5.4.0]undec-7-ene (DBU) (1 drop). After 15 min of stirring at the same temperature, the resulting solution was added to a cooled (0 \(^\circ\)C) solution of MCPBA (1.2 mmol, 0.26 g) in methylene chloride (3 mL) and stirred at room temperature for 1 h. The mixture was then washed with 1 N NaSO\(_3\), 1 N HCl, and aqueous NaHCO\(_3\) (saturated solution). The organic layer was separated and dried (MgSO\(_4\)) and evaporation of solvent gave a mixture of cis, syn-29c and trans-30c in a ratio of 30:70. Compound 30c was isolated by column chromatography as an oil; yield 50%; IR (CHCl\(_3\)) v 1749, 1715 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 7.38-7.25 (m, 7 H, Ar), 6.85 (d, 2 H, Ar, J = 9 Hz), 6.74 (s, 1 H, =CH\(_3\)), 5.01 (d, 1 H, H-4, J = 2.4 Hz), 4.13 (d, 1 H, H-3, J = 2.4 Hz), 3.77 (s, 3 H, OCH\(_3\)), 2.33 (s, 3 H, CH\(_3\)), 1.86 (s, 3 H, CH\(_3\)), J = 1.5 Hz.

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New Methodologies: Fluorodemetalation of Organogermanium, -tin, and -lead Compounds. Applications with Organometallic Sulfides To Produce Highly Active Anions and Spectroscopic Evidence for Pentavalent Intermediates in Substitution at Tin

Marc Gingras, T. H. Chan, and David N. Harpp* 

Department of Chemistry, McGill University, Montréal, Québec, Canada H3A 2K6 

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The general concept of fluorodemetalation is illustrated with three novel methodologies. Fluoride ion smoothly demetalates organogermanium, -tin, and -lead sulfides under mild and neutral conditions to liberate active nucleophilic sulfur species. Eight different sulfur transfer agents derived from group IV are used to demonstrate fluorodemetalation. The reactions of fluorodecuplumination and fluorodegermanylation are presented for the first time along with a discussion of their potential uses in chemistry. The study of fluoride sources as demetalating agents, solvents, substituents and substrates variation is reported. Mechanistic and kinetic aspects of fluorodemetalation are also discussed. We propose that a metal proximate to an anion will increase the nucleophilicity of the latter. In addition, we present spectroscopic evidence for a pentacoordinated intermediate involved in the mechanism of substitution at tin by the use of low-temperature \(^{19}\)F and \(^{119}\)Sn NMR spectroscopy.

Introduction

While organotins are widely used for industrial applications,\(^1\) in organic synthesis organotin sulfides have not been significantly explored.\(^2-5\) Recently, we reported that bis(trialkyltin) sulfide (2) is useful as a general sulfur transfer agent for the high-yield synthesis of thioethers and related derivatives, albeit under forcing conditions.\(^6\) Further, we communicated that fluoride and cyanide ions attack organotin sulfides and smoothly liberate the corresponding sulfur ligand.\(^7\) While several methods are known for making sulfides, fluorodestannylation\(^8-10\) represents a real improvement in methodology because of the neutrality of the medium, the mildness of the conditions, and the high reactivity of the sulfide ion released. This intriguing reactivity has been exploited by two groups using this methodology since classic procedures had failed.\(^11\) The fast rate of these reactions favors the formation of macrorocyclic sulfides, and the mild and neutral conditions could open new synthetic routes to other interesting structures.\(^12-14\)

\(^{*}\) Present address: Department of Chemistry, University of Wisconsin, Madison, WI 53706.

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