Stereospecific Synthesis of *N*-Benzoyl-L-daunosamine and L-Ristosamine

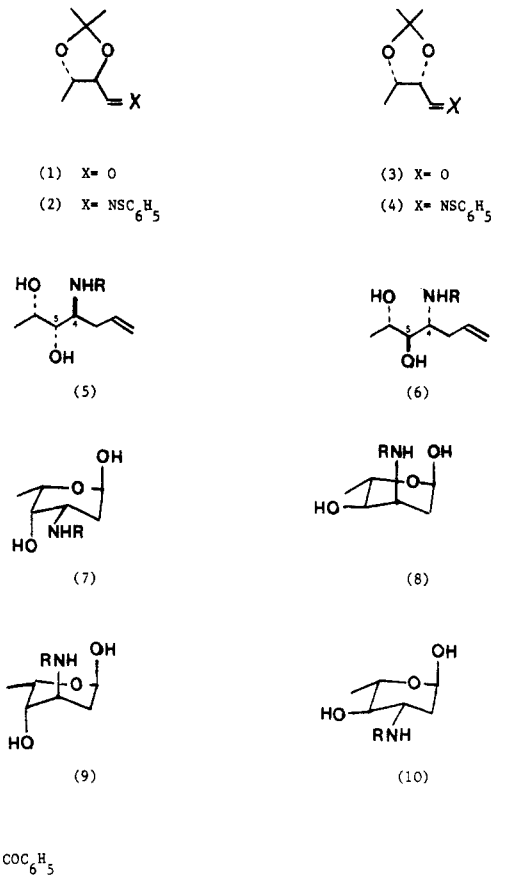
Summary: The synthesis of *N*-benzoyl-L-daunosamine (**7**) and L-ristosamine (**8**) from the C_4 2*R*,3*S* and 2*S*,3*S* aldehydes **1** and **3** through the intermediacy of the C_7–N adducts **5** and **6**, formed by erythro addition of diallylzinc onto the phenylsulfenimines **2** and **4**, is reported.

Sir: The amino deoxy sugar L-daunosamine (**7**, R = H; see Chart I) occurs as a glycoside component in the therapeutic agents daunomycin and adriamycin.[1] There are several syntheses of enantiomerically pure forms of *N*-acyl derivatives of this important amino sugar, most of which are based on natural carbohydrates as starting materials.[2] More recent approaches to the framework of **7** start off with a set of chiral synthons of different origin.[3] A feature which is common to the two types of approaches is the chemical manipulation of the chiral centre(s) in intermediates already possessing three adjacent optically active carbon atoms, required for assessing the "all down" L-lyxo configuration of **7**.

We now present a synthesis of *N*-benzoyl-L-daunosamine (**7**) from the C_4 2*R*,3*S* aldehyde **1**[3b] where the RR^1CH–N chirality present in position 3 of **7** is formed during the process of construction of the carbon skeleton by erythro stereoselective addition of diallylzinc[4] onto the phenylsulfenimine **2**. Thus, the aldehyde **1**, prepared from commercially available D-threonine[3b] or from the 2*S*,3*S* aldehyde **3**[3a] by α epimerization using potassium carbonate in methanol, is converted by treatment with $(C_6H_5S)_2$, $AgNO_3$, and ammonia in methanol[5] into the oily phenylsulfenimine **2**, purified by SiO_2 column chromatography, in ca. 75% yield. A sample of **2**, shown by GLC analysis to contain ca. 10% of diphenyl disulfide, showed $[\alpha]^{20}_D$ +9.5° (*c* 1, $CHCl_3$). Addition of an ethereal solution of **2** at −78 °C onto 2 molar equiv of diallylzinc, prepared from 1.5 M $BrMgCH_2CH{=}CH_2$ in ether and $ZnCl_2$, gave, after acid hydrolysis and benzoylation (benzoyl chloride, $NaHCO_3$ in water–acetone), the C_7–N, 4*S*,5*S*,6*S* adduct **5**[3b]: mp 135 °C; $[\alpha]^{20}_D$ +21° (*c* 1, EtOH); ca. 60% yield. Ozonolysis of **5** in methanol, followed by Me_2S treatment, gave *N*-benzoyl-L-daunosamine (**7**): 85% yield; mp 152 °C; $[\alpha]^{20}_D$ −108° (*c* 0.5, EtOH, equilibrium). From the mother liquors of **5**, on ozonolysis as above and after separation by SiO_2 column chromatography, was obtained *N*-benzoyl-2,3,6-trideoxy-3-amino-L-*xylo*-hexose (**9**).[6] The ratio between the two isomers **7** and **9**, isolated from the whole reaction as pure, crystalline materials, is ca. 75:1.

The same high erythro stereoselectivity was observed in the addition of diallylzinc onto the phenylsulfenimine **4**, prepared in 80% yield from the 2*S*,3*S* aldehyde **3**.[3a] A sample of **4**, containing ca. 5% of the sulfenimine of benzaldehyde, showed $[\alpha]^{20}_D$ −30.4° (*c* 0.5, $CHCl_3$). From **4**, under the above-mentioned conditions, was isolated the C_7–N 4*R*,5*R*,6*S* adduct **6** [an oil which solidified on standing, $[\alpha]^{20}_D$ +6.4° (*c* 1, EtOH)] as the sole reaction product. The latter material, on ozonolysis and Me_2S treatment gave rise to *N*-benzoyl-L-ristosamine (**8**): mp 132 °C; $[\alpha]^{20}_D$ −12.4° (*c* 1, EtOH, 10 min).[7]

Chart I



However, when the two phenylsulfenimines **2** and **4** were reacted with allylmagnesium bromide in ether at −78 °C, the stereochemistry of the addition was different. From the threo α,β-dialkoxy phenylsulfenimine **2** the lyxo and xylo amino sugar derivatives **7** and **9**, obtained from the adducts as above, resulted in a ca. 5.5:4.5 ratio. Thus, the 4,5-erythro adduct **5** is formed in a 5.5:4.5 ratio with its 4,5-threo 4*R*,5*S*,6*S* isomer.

From the erythro phenylsulfenimine **4** with $BrMgCH_2CH{=}CH_2$ in ether was obtained the 4,5-erythro adduct **6** in a ca. 3:7 ratio with its 4,5-threo 4*S*,5*R*,6*S* isomer, $[\alpha]^{20}_D$ −14.5 (*c* 1, EtOH). From the latter material was obtained *N*-benzoyl-L-acosamine (**10**)[8] in the usual way. The yields in the addition of allylmagnesium bromide to **2** and **4** were ca. 70%.

The results mentioned above thus show an almost complete erythro stereoselectivity in the addition of diallylzinc onto the sp^2 carbon of the threo and erythro phenylsulfenimines **2** and **4** to give adducts **5** and **6**, respectively. The same substrates (**2** and **4**) add allylmagnesium bromide to give the products of the erythro and threo modes of addition in 5.5:4.5 and 3:7 ratios, respectively. The same trend in the stereochemistry of the addition was observed when the above reagents reacted with the aldehydes **1** and **3**. Diallylzinc gives the products of erythro addition, whereas allylmagnesium bromide gives rise to the erythro and threo adducts in a ca. 7:3 ratio.[9]

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Apart from the mechanistic interest of the present work, the experiments reported above represent a simple, stereoselective route to the important amino deoxysugar derivatives **7** and **8** and a general entry to chiral secondary amines. Further synthetic applications of the stereochemically rich, highly functionalized chiral synthons **5** and **6** are in progress.

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Registry No. 1, 84519-53-9; 2, 84472-94-6; 3, 82010-51-3; 4, 84519-54-0; 5 (isomer 1), 81069-01-4; 5 (isomer 2), 81130-78-1; 6 (isomer 1), 84519-55-1; 6 (isomer 2), 84519-56-2; 7, 81176-31-0; 8, 84519-57-3; 9, 81176-32-1; 10, 81176-33-2; diallylzinc, 1802-55-7; allyl bromide, 106-95-6.

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Claudio Fuganti,* Piero Grasselli
Giuseppe Pedrocchi-Fantoni
Istituto di Chimica del Politecnico
Centro del CNR per la Chimica
delle Sostanze Organiche Naturali
20133 Milan, Italy
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Application of the Catalytic Two-Phase System to Carbanionic Reactions of Allyl Sulfones[1]

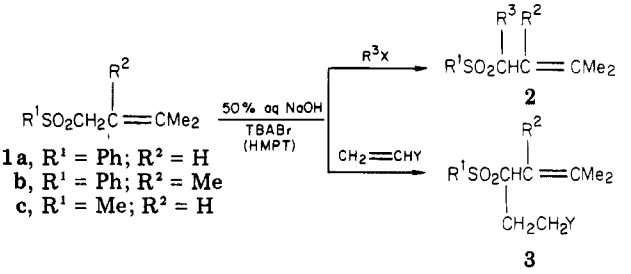
Summary: Allyl sulfones are easily converted into carbanions in the presence of concentrated aqueous NaOH solution and a quaternary ammonium catalyst. These carbanions readily react with alkyl halides, electrophilic alkenes, or perchloroalkanes.

Sir: Considerable interest has been recently focused on the chemical transformations of allyl sulfones.[2-4] The key step of these transformations is the generation of allylsulfonyl carbanions and their reactions with electrophilic compounds, leading to the formation of new C–C bonds. Subsequently, the RSO_2 group is removed from the product via reduction, elimination, or substitution, affording the target molecule.

A pertinent search of the literature reveals that very strong bases like BuLi or RMgX are usually used for the generation of allylsulfonyl carbanions.[4]

We report that the catalytic two-phase (CTP) system,[5] which consists of a concentrated aqueous NaOH solution and a quaternary ammonium salt as a catalyst, can be successfully applied for generation of allylsulfonyl carbanions[6] and their reactions with a variety of electrophilic compounds. Thus, sulfones **1a–c** react smoothly in the presence of 50% aqueous NaOH solution and tetrabutylammonium bromide (TBABr) as catalyst with alkyl halides or electrophilic alkenes to give respectively products[7] **2** and **3** in high yields (Scheme I, Table I). In the case of less active alkyl halides, the reactions were advantageously carried out with a small amount of aprotic dipolar solvent. Sulfones **1a,b** react in the CTP system with perchloroethane to give either α-mono- or α,α-dichlorinated derivatives. The degree of chlorination is easily controlled by the C_2Cl_6/sulfone ratio (Scheme II). The reaction of **1a** with an excess of CCl_4 resulted in the formation of the cyclopropene derivative **5**[11] in addition to

Scheme I

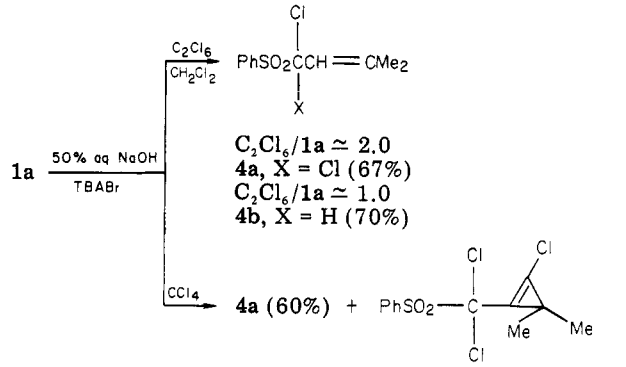


1a, R^1 = Ph; R^2 = H
b, R^1 = Ph; R^2 = Me
c, R^1 = Me; R^2 = H

2

3

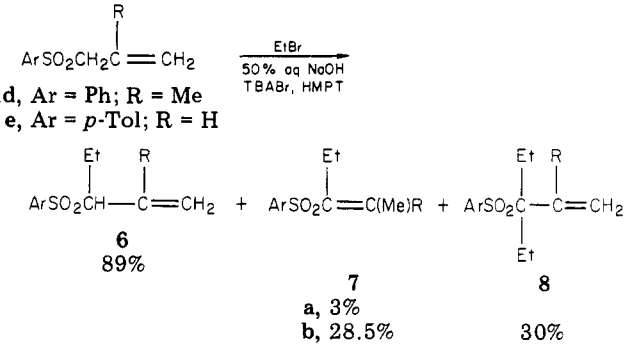
Scheme II[12]



C_2Cl_6/**1a** ≃ 2.0
4a, X = Cl (67%)
C_2Cl_6/**1a** ≃ 1.0
4b, X = H (70%)

5 (12%)

Scheme III



1d, Ar = Ph; R = Me
e, Ar = *p*-Tol; R = H

6
89%

7
a, 3%
b, 28.5%

8
30%

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(6) There are two examples of the application of the CTP system to carbanionic reactions of allyl sulfones: (a) condensation of **1a** with benzaldehyde, leading to 4-methyl-1-phenyl-2-(phenylsulfonyl)penta-1,3-diene, yield 25% (Cardillo, G.; Sovoia, D.; Umani-Ronchi, A. *Synthesis* **1975**; 453) and (b) rearrangement of **1e** to propenyl *p*-tolyl sulfone, yield 63% (Steinbeck, K. *Liebigs Ann. Chem.* **1979**, 920).

(7) The NMR and IR spectra were consistent with the assigned structure; satisfactory combustion analysis were obtained for all compounds.

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