The Journal of Organic Chemistry

VOLUME 54, NUMBER 11 MAY 26, 1989

Communications

Influence of the N-Protecting Group on the Stereochemical Course of (4 + 2) Cycloaddition of 1-Ethoxy-3-[(trimethylsilyl)oxy]buta-1,3-diene to α-Amino Aldehydes

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Received December 11, 1988

Summary: The $ZnBr_2$-catalyzed (4 + 2) cycloaddition of Danishefsky's diene (1) to variously N-protected D-alaninals (2) was studied, and a large difference between the N-protecting groups replacing either one or two amino protons was observed.

Sir: We recently described high-pressure (4 + 2) cycloaddition of 1-methoxybuta-1,3-diene to α-amino aldehydes[1] and demonstrated that the configuration of the product can be controlled under high-pressure conditions.[2] We observed that there is a large difference between the N-protecting groups replacing either one or two amino protons. When we used N,N-diprotected α-amino aldehydes instead of N-monoprotected ones, the direction of asymmetric induction was reversed. We explained this was a result of substantial changes in the nature of the α-amino group: from steric to chelating character.[3] We considered it very interesting, especially from the synthetic point of view, to study this type of reaction at ambient pressure but with the application of Lewis acid catalysts. In view of the known strong tendency of α-amino aldehydes[4] to react via their α-chelate conformers, it was very important to find a kind of N-protection that will enhance the population of the "steric Cram conformer".

D-Alaninal (2) variously N-protected was chosen as the simplest chiral α-amino aldehyde. Danishefsky's diene (1)[5] gives adducts with these aldehydes, which are easily correlated. The reaction is shown in Scheme I. The results of our preliminary experiments are shown in Table I.

Scheme I

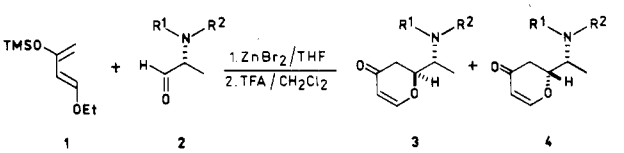

Table I. Results of (4 + 2) Cycloaddition of Danishefsky's Diene (1) to N-Protected D-Alaninals (2)[a]

entry	R^1	R^2	yield,[b] %	diastereoisomeric ratio[c] (3/4)
a	H	Boc	75	25/75
b	H	Cbz	78	33/67
c	H	Tos	74	50/50
d	Bn	Bn	80	90/10
e	Bn	Tos	91	91/9
f	Bn	Boc	85	93/7

[a] Boc = CO_2Bu^t; Cbz = CO_2Bn. 1.0 equiv of $ZnBr_2$ in THF was used. [b] Yield calculated on isolated pure compounds. [c] Ratio determined by ^1H NMR spectroscopy (500 MHz).

The data show that NHBoc-protected alaninal **2a** gives, via α-chelated conformer A (Figure 1), syn-adduct 4 as a main one. Similar diastereoselectivity was observed for NHCbz-protected alaninal **2b**, which is easily explained by the strong interactions between the nitrogen atom and Lewis acid.

In NHTos-protected alaninal **2c**, the blocking group is intermediate between the chelating and steric types. The sulfonyl function strongly deactivates the nitrogen center, but the remaining amino proton can still affect α-chelation-controlled addition.

The anti selectivity was obtained with the doubly N-protected alaninals **2d–f**. For these types of aldehydes, conformation B (Figure 1) dominates. Clearly for doubly N-protected alaninals, the diastereoselectivity of the re-

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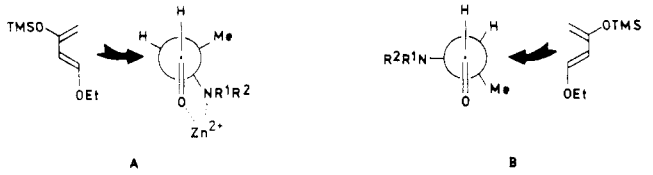
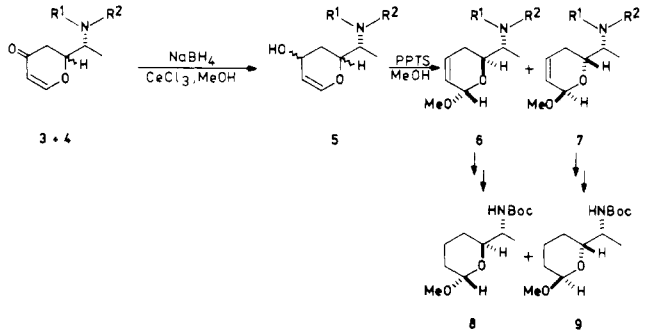


Figure 1.

Scheme II



action rises with the steric hindrance of the blocking groups.

The mixtures of adducts **3** and **4** could not be easily separated; they were reduced by means of Luche's method[6] to afford corresponding mixtures of alcohols **5** (Scheme II). Ferrier rearrangement[7] in conjunction with cis → trans isomerization at the anomeric carbon[8] afforded a mixture of adducts **6** and **7**. The absolute configurations of these 5,6-dihydro-2*H*-pyrans were established by means of ^1H and ^{13}C NMR spectroscopy.[9,10] Independently, they were transformed into the known compounds **8** and **9**.[2,10]

The presented results demonstrate that it is possible to control the stereochemistry of Lewis acid catalyzed (4 + 2) cycloaddition with α-amino aldehydes as heterodienophiles, by means of changing the N-protecting groups. The inversion of "natural" syn selectivity[2] can be achieved by the removal of both amino protons.

The diastereoselectivity of the studied reaction depends on the solvent and catalyst concentration and was not optimized toward these parameters.[11] Enlargement upon these findings and the application of the presented approach to the total synthesis of complex amino sugars are matters of continuing interest in this laboratory.

Acknowledgment. Financial support from the Polish Academy of Sciences (Grant CPBP 01.13) is gratefully acknowledged.

Registry No. **1**, 54125-02-9; **2a**, 82353-56-8; **2b**, 82353-55-7; **2c**, 120294-57-7; **2d**, 120205-96-1; **2e**, 120205-97-2; **2f**, 120205-98-3; **3a**, 120205-99-4; **3b**, 120206-00-0; **3c**, 120206-01-1; **3d**, 120206-02-2; **3e**, 120229-29-0; **3f**, 120206-03-3; **4a**, 120206-04-4; **4b**, 120206-05-5; **4c**, 120206-06-6; **4d**, 120206-07-7; **4e**, 120206-08-8; **4f**, 120206-09-9; **5a**, 120206-10-2; **5b**, 120206-11-3; **5c**, 120206-12-4; **5d**, 120206-13-5; **5e**, 120206-14-6; **5f**, 120229-30-3; **6a**, 120294-58-8; **6b**, 120294-59-9; **6c**, 120294-60-2; **6d**, 120206-15-7; **6e**, 120206-16-8; **6f**, 120328-36-1; **7a**, 120294-61-3; **7b**, 120294-62-4; **7c**, 120294-63-5; **7d**, 120294-64-6; **7e**, 120294-65-7; **7f**, 120206-17-9.

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Palladium-Catalyzed Cross-Coupling of Organostannanes with Sulfonyl Chlorides: A Simple Synthesis of Sulfones[1]

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Received February 8, 1989

Summary: The palladium-catalyzed cross-coupling reaction between aryl- and alkylsulfonyl chlorides and substituted vinyl- and allylstannanes proceeds smoothly to provide good yields of sulfones and tolerates a wide variety of functionalities.

Sir: Sulfones are gaining attention as synthetic intermediates and also as medicinally important molecules.[2] Frequently used methods for the preparation of sulfones are the sulfonylation of aromatic hydrocarbons in the presence of a Lewis acid, oxidation of sulfides with peracids or with oxone, and nucleophilic substitution with sulfenic acid salts.[3] Although there are a number of methods available for the preparation of vinyl and allyl sulfones, simple one-step procedures are scarce.[4]

Transition metal catalyzed coupling reactions involving organostannanes have been widely used in the carbon–carbon bond formation.[5] Coupling partners include acyl, aryl, vinyl, and allyl halides, as well as aryl and vinyl triflates.[5,6] The palladium-catalyzed cross-coupling reactions of organostannanes proceed under mild conditions to provide excellent yields of coupling products and tolerate a wide variety of functionalities. However, to date, analogous palladium-catalyzed coupling of organostannanes with sulfonyl chlorides to form sulfones has not been documented. We have found that alkyl- and aryl-

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