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One Pot Michael Addition, Vinylsulfone Isomerization and Alkynyl to Alkenyl Triple Bond Reduction. Synthesis of a Carbasugar Related to Rancinamycin III

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Dedicated to Prof. Henry Rapoport

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Abstract: Cyclohexenylsulfones 2 show a different behaviour in their reactions with Na/MeOH system depending on the nature of protecting groups R. In the case of R= TMS, the observed sequence Michael addition-vinylsulfone isomerization-alkynyl to alkenyl reduction has been used for the synthesis of a carbasugar related to the antibiotic Rancinamycin III. © 1998 Elsevier Science Ltd. All rights reserved.

In connection with some studies concerning the synthetic application of functionalized cyclohexenylsulfones 2 obtained by S_N2' ring opening of oxanorbornenic derivatives 1 by reaction with lithium acetylides,¹ we have studied the reaction of sulfones 2a and 2b with Na/MeOH system in order to achieve the transformation 2 to 4. In this way, we have observed a different behaviour of both compounds 2a and 2b depending on the nature of the substituent R attached to the exocyclic triple bond (Scheme 1).



Scheme 1

Thus, reaction of 2b with Na, MeOH at 0 °C gave the expected conjugated sulfone 4b. However, in the case of 2a in the same conditions, one pot sequence Michael addition of methoxide to the vinylsulfone moiety with concommitant vinylsulfone isomerization and triple to double bond reduction was observed. It should be pointed out that the use of other basic reagents, such as NaH in THF at 0 °C, affords exclusively sulfones 4a and 4b, starting from 2a and 2b, respectively.

0040-4039/98/\$19.00 © 1998 Elsevier Science Ltd. All rights reserved. *PII:* S0040-4039(98)00109-9 A probably reaction pathway for the transformation 2a to 3 involves the previous deprotection of the acetylenic moiety to produce the tridentate anion 5. Reprotonation at the terminal allenic position gives 6^2 which after conjugate addition of methoxide anion affords, finally, compound 3 (Scheme 2).³



Scheme 2

In the case of 2b, this compound does not undergo elimination of the TBS group and thus the alkyneallene isomerization is prevented. Final protonation on the less hindered position of the ambidentate anion gives the conjugated enyne 4b (Scheme 3).





It should be pointed out that methoxysulfone $7a^4$ shows a different behaviour in Na/MeOH system. Thus, deprotection of TMS group and 1,3-hydrogen shift rendered the allylic sulfone 8. In the same conditions, the analogous sulfone 7b did not react (Scheme 4).



Compound 3 has been used for the synthesis of carbasugar 9 related to the general structure of the antibiotic Rancinamycin III^5 and with a well defined stereochemistry in the four chiral centers (Figure 1).



Figure 1

Bishydroxilation of 3 afforded 55 % of 10 after column chromatography.⁶ NaIO₄ oxidation of diol 10 produced aldehyde 11. Also, oxidation of 3 with NaIO₄ and RuCl₃ gave directly 11. At this stage, desulfonylation of 11 was not possible and under a variety of experimental conditions, extensive decomposition of the starting material was observed (Scheme 5).



Scheme 5

Therefore, we decided to change the order of experimental operations. In this way, desulfonylation of 3 was achieved using Na-Hg to give 12. Finally, direct oxidation of exocyclic double bond in 12 with NaIO₄, RuCl₃ afforded 9^7 (Scheme 6).



Reagents and conditions: a) Na-Hg, , Na₂HPO₄, MeOH, -20 °C to rt, 80 %. b) NaIO₄, RuCl₃·H₂O, CH₃CN:CCl₄:H₂O 3:3:4, 50 %. Scheme 6

In summary, an interesting, unprecedent transformation of alkynylcyclohexenylsulfones such as 2 was achieved involving a Michael addition, vinylsulfone isomerization and triple bond reduction. This transformation has been used for the synthesis of carbasugar 9 related to Rancinamycin III. Alternatively, vinylsulfone isomerization was observed depending on the nature of the substituent attached to the alkynyl moiety. Other useful transformations are now under active research in our laboratory.

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References and notes.

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- 3. This reaction pathway appears to be reminiscent of those proposed for organocopper reagents mediated 1,6-additions to alkenynones and alkenylnoates: Frederick, M. A.; Hulce, M.; *Tetrahedron* 1997, 53, 10197-10277. See pp. 10204-10206.
- 4. Compounds 7 were prepared by Diels-Alder cycloaddition of 2-methoxyfuran and *trans*-1,2-*bis*-(phenylsulfonyl)-ethylene followed by chemical elaboration of the resulting adducts. Full details wil be given elsewhere.
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- 6. A 18 % yield of compound 13 has been found in bishydroxylation of compound 3.
- 7. All new compounds showed spectroscopic and analytical data consistent with the assigned structures. In the case of ¹H-RMN, selective decoupling experiments were used for stereochemical determination.

