

Synthesis of a Protected Derivative of (±)-1-(hydroxymethyl)conduritol C from 2-(hydroxymethyl)furan

Odón Arjona,* Fátima Iradier, Rosario M. Mañas and Joaquín Plumet*

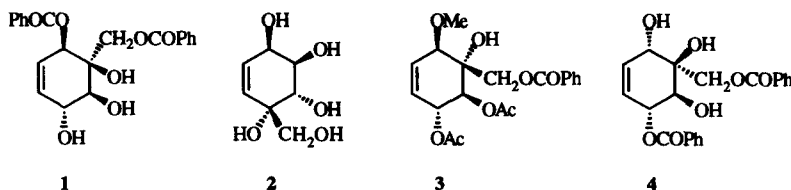
Departamento de Química Orgánica I, Facultad de Química, Universidad Complutense, 28040 Madrid, Spain.

Dedicated to Prof. Joaquín de Pascual Teresa, In Memoriam.

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Abstract: A short and totally stereoselective synthesis of a protected derivative of (±)-1-(hydroxymethyl)conduritol C has been achieved. The key step was the cleavage of the oxygen bridge in a 7-oxanorbomenic sulfone using an acidic medium. © 1998 Elsevier Science Ltd. All rights reserved.

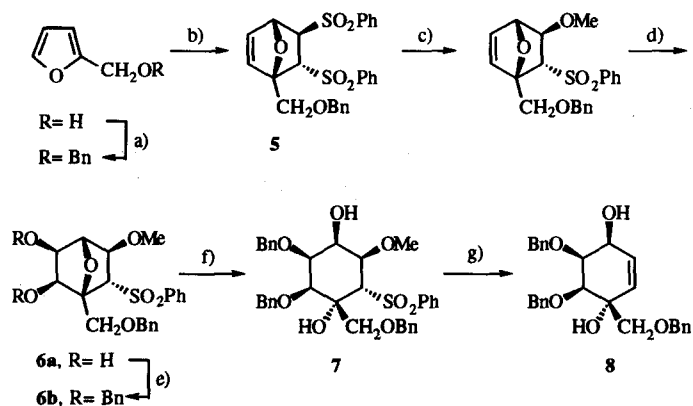
Conduritol derivatives are compounds of biological importance being also starting materials for the synthesis of other biologically important compounds.¹ In the case of (hydroxymethyl)conduritols, some of these compounds have been isolated from natural sources;^{1a} for instance, ferrudiol **1**, piperonol B **2**,² seneol **3**, zeylenol **4** and 1-epizeylenol. From the synthetic point of view only the piperonol B **2**, 1-(hydroxymethyl)conduritol E and its 4-epimer have been, to the best of our knowledge, previously synthesized² (Scheme 1).



Scheme 1

In this paper, we wish to report a new, general approach to obtaining 1-(hydroxymethyl)conduritols taking the hitherto unknown (±)-1-(hydroxymethyl)conduritol C as a model and using commercially available 2-(hydroxymethyl)furan and *E*-1,2-bis-(phenylsulfonyl)ethylene as starting materials.³

Benzoylation of 2-(hydroxymethyl)furan followed by Diels-Alder cycloaddition with *E*-1,2-bis-(phenylsulfonyl)ethylene afforded the 7-oxanorbomenic derivative **5**⁴ as the sole stereoisomer. Replacement of the *exo*-phenylsulfonyl group by a methoxy functionality⁵ followed by bishydroxylation and benzoylation gave **6b**. Ring-opening of **6b** using TiCl₄⁶ yielded stereo- and regioselectively the cyclohexane derivative **7**. The reaction of **7** with Na-Hg in the presence of Na₂HPO₄ (Julia's elimination)⁷ afforded protected 1-(hydroxymethyl)conduritol C (Scheme 2).



Reagents and conditions: a) NaH, BnBr, TBAI, THF, 0 °C, 22 h., 96 %. b) *E*-1,2-bis-(phenylsulfonyl)ethylene, CH₂Cl₂, 72 h., 78 %. c) KOH, MeOH, CH₃CN, 72 h., 84 %. d) OsO₄, Me₃NO·2H₂O, acetone:H₂O 8:1, 1.5 h., 88 %. e) NaH, BnBr, TBAI, THF, 3.5 h., 87 %. f) TiCl₄ (1.0 M, PhMe), CH₂Cl₂, -78 °C, 10 min., 88 %. g) Na-Hg (6 %, recently prepared), Na₂HPO₄, MeOH, from -20 °C to rt, 5 h., 60 %.

Scheme 2

In summary, an efficient synthesis of a protected derivative of 1-(hydroxymethyl)conduritol C starting from 2-(hydroxymethyl)furan has been achieved. The sequential introduction of the hydroxy functionality makes the procedure versatile in order to prepare other conduritol derivatives. On the other hand, research for the synthesis of **5** in optically pure form, currently performed in our laboratory, should permit the synthesis of these compounds in non-racemic form. Further details will be presented in due course.

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