Pergamon

Tetrahedron Letters 39 (1998) 8335–8336

TETRAHEDRON LETTERS

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

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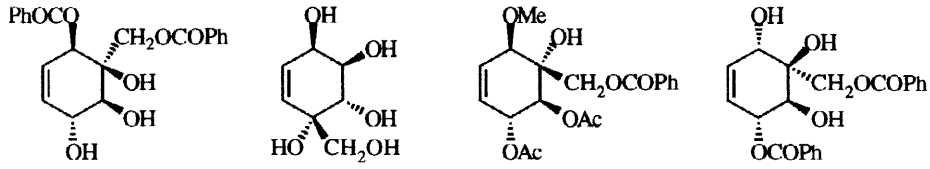
Dedicated to Prof. Joaquín de Pascual Teresa, In Memoriam.

Received 29 May 1998; accepted 14 September 1998

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-oxanorbornenic sulfone using an acidic medium.

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 synthesized[2] (Scheme 1).



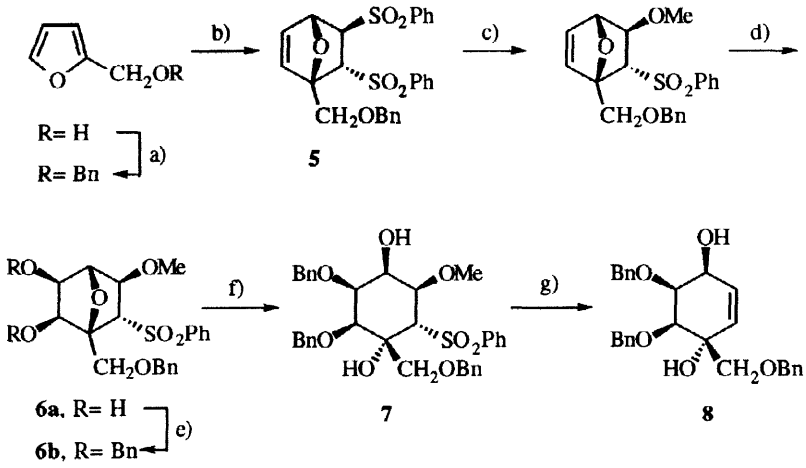
1 **2** **3** **4**

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]

Benzylation of 2-(hydroxymethyl)furan followed by Diels-Alder cycloaddition with *E*-1,2-*bis*-(phenylsulfonyl)ethylene afforded the 7-oxanorbornenic derivative **5**[4] as the sole stereoisomer. Replacement of the *exo*-phenylsulfonyl group by a methoxy functionality[5] followed by bishydroxylation and benzylation gave **6b**. Ring-opening of **6b** using $TiCl_4$[6] yielded stereo- and regioselectively the cyclohexane derivative **7**. The reaction of **7** with Na-Hg in the presence of Na_2HPO_4 (Julia's elimination)[7] afforded protected 1-(hydroxymethyl)conduritol C (Scheme 2).

0040-4039/98/$ - see front matter
PII: S0040-4039(98)01936-4



Reagents and conditions: a) NaH, BnBr, TBAI, THF, 0 °C, 22 h., 96 %. b) *E*-1,2-*bis*-(phenylsulfonyl)ethylene, CH_2Cl_2, 72 h., 78 %. c) KOH, MeOH, CH_3CN, 72 h., 84 %. d) OsO_4, $Me_3NO{\cdot}2H_2O$, acetone:H_2O 8:1, 1.5 h., 88 %. e) NaH, BnBr, TBAI, THF, 3.5 h., 87 %. f) $TiCl_4$ (1.0 M, PhMe), CH_2Cl_2, -78 °C, 10 min., 88 %. g) Na-Hg (6 %, recently prepared), Na_2HPO_4, 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.

Acknowledgements. This work was supported by the DGICYT (Ministerio de Educación y Cultura, Spain, Grant no. 96-0641). F. I. thanks Universidad Complutense de Madrid for a predoctoral fellowship. R. M. thanks Ministerio de Educación y Cultura for a predoctoral fellowship.

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