



## Mild, aprotic synthesis of 1,2-diacetals

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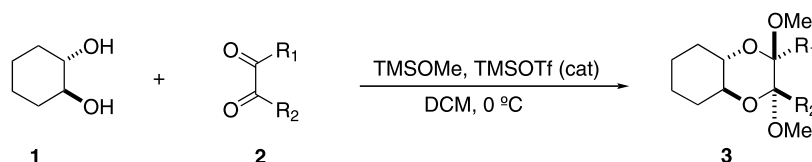
**Abstract**—A new, efficient and mild method for the formation of 1,2-diacetals is described. © 2002 Elsevier Science Ltd. All rights reserved.

The primary driving force behind the development of 1,2-diacetals for organic synthesis was their potential application in carbohydrate chemistry.<sup>1</sup> Their main utility is for the selective protection of diequatorial 1,2-diols due to the anomeric effect at the newly formed spirocenters. They are usually prepared from an  $\alpha$ -diketone and a *trans*-1,2-diol in refluxing methanol containing sulfuric or camphorsulfonic acid (CSA) as catalysts and four equivalents of trimethyl orthoformate, but not all can be synthesized in this way.<sup>1</sup> Here we describe a new procedure allowing the formation of a range of 1,2-diacetals under mild aprotic conditions directly from the corresponding  $\alpha$ -diketones.

The new method uses methoxytrimethylsilane (TMSOMe) and trimethylsilyl trifluoromethanesulfonate (TMSOTf) as acetalizing agent and catalyst, respectively. The reaction of  $\alpha$ -diketones with *trans*-1,2-cyclohexanediol (**1**) in the presence of TMSOMe and TMSOTf in dichloromethane proceeds smoothly at 0°C to give 1,2-diacetals in high yields (Scheme 1 and Table

1). Using the conventional protic method (MeOH/CH(OMe)<sub>3</sub>/H<sup>+</sup>), ketones **2b**, **2e** and **2f** (entries 2, 5 and 6) undergo monoacetalization of the more external ketone; ketones **2c** and **2d** (entries 3 and 4) undergo monoacetalization with concomitant  $\beta$ -elimination and intramolecular cyclization, respectively; and ketones **2g** and **2h** do not react. Using the new TMSOMe/TMSOTf method the corresponding 1,2-diacetals were in all cases obtained in high yields (Table 1).<sup>2</sup>

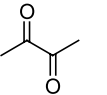
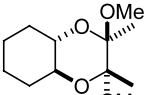
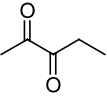
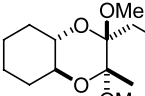
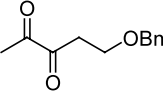
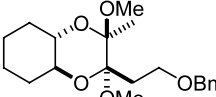
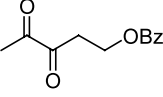
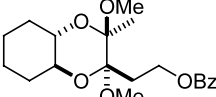
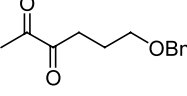
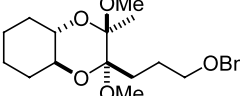
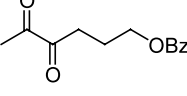
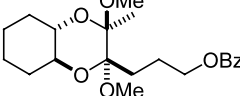
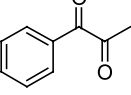
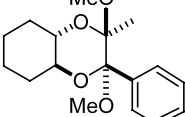
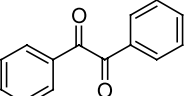
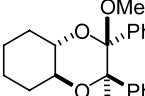

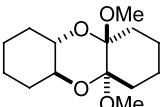
The general procedure is as follows: to a stirred 1 M solution of  $\alpha$ -diketone in dry dichloromethane at 0°C were successively added, under an inert atmosphere, 1.3 equiv. of *trans*-1,2-cyclohexanediol, 8 equiv. of TMSOMe and 0.1 equiv. of TMSOTf. The mixture was stirred at 0°C for 3 h and quenched by pouring into saturated sodium bicarbonate. The aqueous layer was extracted three times with diethyl ether; the combined extracts were dried (anhyd. Na<sub>2</sub>SO<sub>4</sub>), filtered and evaporated; and the residue was purified by flash chromatography.



Scheme 1.

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**Table 1.** The TMSOTf-catalyzed formation of 1,2-diacetals from  $\alpha$ -diketones

Entry	Ketone 2	1,2-diacetals 3	Yield (%)
1	2a 	3a 	97
2	2b 	3b <sup>2</sup> 	97
3	2c 	3c <sup>2</sup> 	83
4	2d 	3d <sup>2</sup> 	95
5	2e 	3e <sup>2</sup> 	93
6	2f 	3f <sup>2</sup> 	85
7	2g 	3g <sup>2</sup> 	86
8	2h 	3h <sup>2</sup> 	99
9	2i 	3i 	70

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- All new compounds gave satisfactory spectroscopic and analytical data.