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The first *in situ* synthesis of 1,3-dioxan-5-one derivatives and their direct use in Claisen-Schmidt reactions

(Synthesis of dioxanones and their Claisen-Schmidt reactions)

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Abstract: A method is developed for *in situ* generation of 1,3-dioxan-5-one derivatives **2**. These compounds are simple precursors for accessing carbohydrate structures and previously had to be produced via stepwise procedures using excessive amounts of reagents. In the present work, three different derivatives of **2** were synthesized via the reaction of trialkoxyalkanes with dihydroxyacetone dimer **1** in the presence of acetic acid as the catalyst. In the same pot, derivatives of **2** were reacted with aromatic aldehydes and 30 mol% of pyrrolidine to obtain high yields of the respective bischalcones **3** within short time periods.

Keywords: 1,3-dioxan-5-one; trioses, Claisen-Schmidt reaction; dihydroxyacetone; one-pot reactions.

Introduction

Trioses are among the smallest monosaccharide biomolecules playing important roles in cellular respiration [1]. In the course of glycolysis, fructose-1,6-bisphosphate is cleaved to glyceraldehyde-3-phosphate and dihydroxyacetone phosphate (DHAP) [2]. The latter in turn could convert to lactic acid and pyruvic acid [3]. In the nature, DHAP can lead to more complex carbohydrates stereoselectively via enzyme-catalyzed aldol reactions [4]. The chemical equivalent to DHAP is dihydroxyacetone (**1**, DHA, Scheme 1) which is the only ketotriose and does not exist in enantiomeric forms and is therefore achiral [5]. DHA and its derivatives are successfully employed as C_3 building blocks through synthetic manipulations for asymmetric synthesis of various compounds of interest [6].

The limitation in the chemistry of DHA is that the compound usually exists in relatively inactive dimeric form [7, 8] and researchers have to use its protected heterocyclic synthon, 1,3-dioxan-5-one **2** derivatives instead [9, 10]. In this context, Enders introduced a simple and biomimetic approach for direct proline-catalyzed asymmetric synthesis of several carbohydrate structures and their related compounds through one-step aldol reactions of **2** [11-14]. Majewski reported stereodivergent synthesis of both enantiomers of *glycero-allo*-heptose from similar starting ketone **2** [15] and organocatalyzed synthesis of L-deoxymannojirimycin and L-deoxyidonojirimycin via *syn*-aldol reaction of **2** with (*S*)-isoserinal hydrate [16]. Interestingly, several applications of this chemistry are reported for the synthesis of natural compounds of interest such as total synthesis of (±)-isophellibiline [17], (±)-cortistatin J [18], and (±)-erythroidines [19].

The difficulties associated with the preparation of derivatives of **2** have persuaded synthetic chemists to design and attempt new methods to obtain **2** via more convenient reactions and by performing less synthetic steps [20-23]. In the framework of our studies to develop new synthetic procedures in heterocyclic chemistry [24-27], herein we introduce a new method for *in situ* preparation of three various derivatives of **2** starting from **1** and trialkoxyalkanes (RCR'_3) and acetic acid as catalyst. Then, ketones **2** are reacted in the same pot with aldehydes

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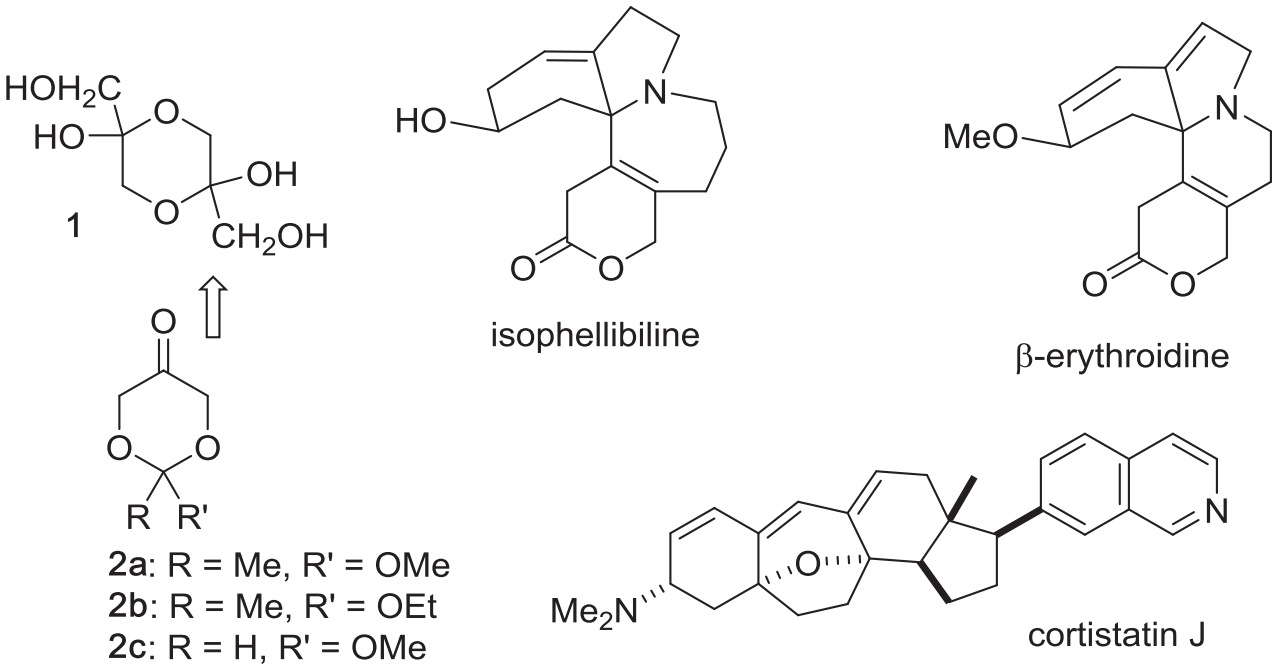


Scheme 1 Important structures derived from ketones **2** (a synthon for **1**).

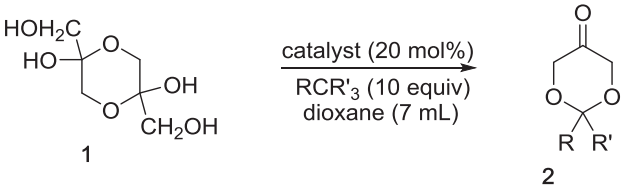
to get the respective bischalcone derivatives **3** via Claisen-Schmidt condensation reactions at room temperature. The importance of chalcone functionalities in heterocyclic chemistry from synthetic [28, 29] and biological points of view is well documented [30, 31].

Results and discussion

We first optimized the conditions for the synthesis of **2a** by reacting **1** with $MeC(OMe)_3$ and various catalysts (Table 1). Under the conditions reported by Müller et al [32], camphor-10-sulfonic acid (CSA) in dioxane caused 81% formation of **2a** after 24 h (entry 1). Use of Lewis acids almost led to minor quantities of the desired product even at a higher temperature or a longer reaction time (entries 2-5). Acetic acid improved the result to give 80% of **2a** at 60 °C and after a much shorter time period (entry 6). Also, less amounts of the solvent (entry 7) or the reagent (entry 8) led to comparable results. Other carboxylic acids did not behave better than CH_3COOH (entries 9-10). These optimum conditions were applied successfully to prepare two other derivatives of **2** in high yields (entries 11-12).

With these results, we were persuaded to use the optimum conditions to prepare derivatives of **2** and subject them to react with an aromatic aldehyde to evaluate the possibility of the synthesis of bischalcone derivatives **3** in the same reaction pot (Table 2). For this purpose, when monitoring of the reaction showed maximum formation of **2a**, the mixture was treated with an alkaline hydroxides followed by addition of $4\text{-}ClC_6H_4CHO$. As a result, use

Table 1 Optimization of the synthesis of **2**.



Entry	Catalyst	Temperature (°C)	Time (h)	Product	Yield (%)[a]
1	CSA	60	24	**2a** (R = Me, R' = OMe)	81
2	$MgBr_2$	60	48	**2a**	< 5
3	$MgBr_2$	80	72	**2a**	< 5
4	LiBr	60	48	**2a**	< 5
5	LiBr	80	72	**2a**	< 5
6	CH_3CO_2H	60	8	**2a**	80
7	CH_3CO_2H[b]	60	8	**2a**	83
8	CH_3CO_2H[b,c]	60	8	**2a**	83
9	$H_2C_2O_4$[b,c]	80	72	**2a**	< 5
10	$PhCO_2H$[b,c]	80	72	**2a**	< 5
11	CH_3CO_2H[b,c]	60	8	**2b** (R = Me, R' = OEt)	85
12	CH_3CO_2H[b,c]	60	8	**2c** (R = H, R' = OMe)	80[d]

[a]Isolated yields. [b]Dioxane (2 mL). [c]$MeC(OMe)_3$ (2.0 equiv). [d]GC yield.

of NaOH (entries 1-2) or KOH (entries 3-4) in aqueous or solvent-free conditions gave no minor amounts of **3a**. However, when organocatalysts were used, pyrrolidine (entry 5) gave **3a** in 83% yield after 15 min, while Et_2NH (entry 6) or Et_3N (entry 7) produced 63% or 41% of the same product after similar time period.

To show the generality of the process, we synthesized various derivatives of **3** by subjecting **2a** to react with different aldehydes bearing electron withdrawing groups (Scheme 2). Thus **3a**-**f** were obtained in high yields. Also, the reaction with benzaldehyde itself led to the same observations and **3g** was obtained in 80%. Similarly, use of **2b** or **2c** produced the target products (**3h**-**3n**) in 85-95% yields. The condensation step for all reactions occurred within 15-20 min and products precipitated in the mixtures spontaneously.

Table 2 Optimization of the synthesis of **3a**.

Entry	Conditions (30 mol%)	Solvent	Time (min)	Yield (%)[a]
1	NaOH	none	24	< 5
2	NaOH	H_2O	24	< 5
3	KOH	none	24	< 5
4	KOH	H_2O	24	< 5
5	pyrrolidine	none	15	83
6	Et_2NH	none	15	63
7	Et_3N	none	15	41

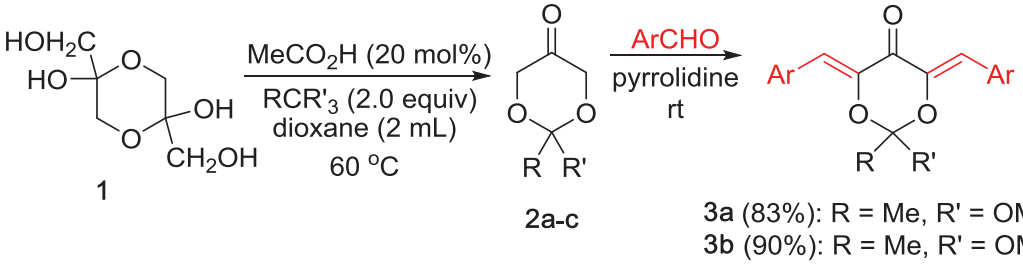
[a]Isolated yields.

Conclusion

In summary, we succeeded to prepare derivatives of **2**, which could be either isolated from the reaction mixtures or further subjected to Claisen-Schmidt reactions in the same pot. Thus various derivatives of **2** and **3** could be prepared efficiently. After the prevailing reaction conditions, the products were solidified in the reaction vessels and required no expensive and time consuming chromatographic separations. In addition, synthesis of **2** succeeded by using much less amounts of solvent and the required orthoesters.

Experimental

Melting points are uncorrected. FT-IR spectra were recorded using KBr disks on a Bruker Vector-22 spectrometer. NMR spectra were obtained on a FT-NMR Bruker Ultra Shield™ (500 MHz for ^1H and 125 MHz for ^{13}C) as DMSO-d_6 solutions using TMS as internal standard reference. Elemental analyses were performed using a Thermo Finnigan Flash EA 1112 instrument. MS spectra were obtained on a Finnigan Mat 8430 instrument at ionization potential of 70 eV. TLC experiments were carried out on pre-coated silica gel plates using petroleum ether/EtOAc as the eluent. Chemicals and starting materials were purchased from commercial sources. Aldehydes were redistilled or recrystallized before being used. Products **3a**, **3f**, **3g**, and



3a (83%): R = Me, R' = OMe, Ar = 4-ClC_6H_4
3b (90%): R = Me, R' = OMe, Ar = 4-BrC_6H_4
3c (71%): R = Me, R' = OMe, Ar = 3-$O_2NC_6H_4$
3d (70%): R = Me, R' = OMe, Ar = 4-NCC_6H_4
3e (87%): R = Me, R' = OMe, Ar = 2,4-$Cl_2C_6H_3$
3f (81%): R = Me, R' = OMe, Ar = 4-$Me_2NC_6H_4$
3g (80%): R = Me, R' = OMe, Ar = C_6H_5
3h(95%): R = Me, R' = OEt, Ar = 4-ClC_6H_4
3i (86%): R = Me, R' = OEt, Ar = 4-BrC_6H_4
3j (87%): R = Me, R' = OEt, Ar = 2,4-$Cl_2C_6H_3$
3k (81%): R = Me, R' = OEt, Ar = 4-$MeOC_6H_4$
3l (90%): R = Me, R' = OEt, Ar = 4-$Me_2NC_6H_4$
3m (85%): R = H, R' = OMe, Ar = 4-ClC_6H_4
3n (87%): R = H, R' = OMe, Ar = 2,4-$Cl_2C_6H_3$

Scheme 2 One-pot synthesis of various derivatives of 3.

3k were known [33, 34]. All other products were new and were characterized by analyzing their ^{1}H NMR, ^{13}C NMR, IR, and mass spectra.

General procedure for the synthesis of 2

Acetic acid (125 µl, 20 mol%) was added dropwise to a mixture of dihydroxyacetone dimer **1** (1.01 g, 5.6 mmol) in dioxane (2 mL), while being heated at 60 °C under argon atmosphere. After 10 min, a trialkyl orthoacetate (23 mmol) was added to the mixture and was stirred for another 8 h. The mixture was concentrated under reduced pressure and the residue was distilled to obtain derivatives of **2**. Products **2a**-**b** are known [32, 34].The structure of **2c** is inferred from the final products (**3m** and **3n**) containing this central ring.

General procedure for one-pot synthesis of 3

Acetic acid (125 µl, 20 mol%) was added dropwise to a mixture of dihydroxyacetone dimer **1** (1.01 g, 5.6 mmol) in dioxane (2 mL), while being heated at 60 °C under argon atmosphere. After 10 min, trialkyl orthoacetate (23 mmol) was added to the mixture and the mixture was stirred for another 8 h. TLC (petroleum ether/EtOAc 4:1) showed complete conversion of the starting materials to **2** after 8 h. The heating source was removed and an aldehyde (18.6 mmol) and pyrrolidine (3.36 mmol, 277 µl, 30 mol%) were added and mixing was continued at room temperature for 10-15 min. The completion of the reaction was monitored with TLC (petroleum ether/EtOAc:10:1). The product precipitated in the mixture. The crude solid product was purified by recrystallization from EtOH and solid products **3** were obtained.

Spectral data of new products

4,6-Bis((Z)-4-bromobenzylidene)-2-methoxy-2-methyl-1,3-dioxan-5-one (3b) Mp: 224-225 °C; IR (KBr) ν 2940, 1578, 1464 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d$_6$) δ 7.79 (d, *J* = 8.5 Hz, 4H), 7.62 (d, *J* = 8.5 Hz, 4H), 6.87 (s, 2H), 3.30 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d$_6$) δ 176.6, 144.5, 133.0, 132.9, 132.5, 123.4, 114.6, 113.7, 52.7, 21.1; MS (70 eV) m/z 480 (M$^+$), 404, 325, 196, 89; Anal. Calcd for $C_{20}H_{16}Br_2O_4$: C, 50.03; H, 3.36. Found: C, 50.16; H, 3.27.

2-Methoxy-2-methyl-4,6-bis((Z)-3-nitrobenzylidene)-1,3-dioxan-5-one (3c). Mp: > 250 °C; IR (KBr) ν 2920, 1701, 1615, 1528, 1345 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d$_6$) δ 8.71 (s, 2H), 8.26 (d, *J* = 8.0 Hz, 2H), 8.21 (d, *J* = 8.0 Hz, 2H), 7.74 (dd, *J* = 8.0, 8.0 Hz, 2H), 7.07 (s, 2H), 3.35 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d$_6$) δ 176.4, 148.6, 145.3, 137.2, 134.6, 130.9, 125.2, 124.2, 114.0, 113.7, 52.9, 21.0; MS (70 eV) m/z 412 (M$^+$), 381, 337, 163, 129; Anal. Calcd for $C_{20}H_{16}N_2O_8$: C, 58.26; H, 3.91; N, 6.79. Found: C, 58.33; H, 3.79; N, 6.90.

4,4'-((1Z,1'Z)-(2-Methoxy-2-methyl-5-oxo-1,3-dioxane-4,6-diylidene)bis(methanylylidene))dibenzonitrile (3d). Mp: 248-249 °C; IR (KBr) ν 3053, 2228, 1603, 1279 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d$_6$) δ 8.02 (d, *J* = 8.0 Hz, 4H), 7.90 (d, *J* = 8.0 Hz, 4H), 6.97 (s, 2H), 3.34 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d$_6$) δ 176.6, 145.6, 137.6, 133.2, 131.7, 119.3, 114.1, 113.9, 111.7, 52.9, 20.9; MS (70 eV) m/z 372 (M$^+$), 341, 297, 173, 143; Anal. Calcd for $C_{22}H_{16}N_2O_4$: C, 70.96; H, 4.33; N, 7.52. Found: C, 70.77; H, 4.60; N, 7.59.

4,6-Bis((Z)-2,4-dichlorobenzylidene)-2-methoxy-2-methyl-1,3-dioxan-5-one (3e). Mp: 195-196 °C; IR (KBr) ν 1739, 1577, 1466, 1281, 826 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d$_6$) δ 8.12 (d, *J* = 8.0 Hz, 2H), 7.73 (s, 2H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.08 (s, 2H), 3.32 (s, 3H), 1.96 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d$_6$) δ 176.2, 145.0, 135.3, 134.9, 132.3, 129.9, 129.3, 128.3, 113.9, 109.2, 52.8, 20.7; MS (70 eV) m/z 460 (M$^+$), 427, 349, 186, 123; Anal. Calcd for $C_{20}H_{14}Cl_4O_2$: C, 52.21; H, 3.07. Found: C, 52.16; H, 3.28.

4,6-Bis((Z)-4-chlorobenzylidene)-2-ethoxy-2-methyl-1,3-dioxan-5-one (3h). Mp: 176-177 °C; IR (KBr) ν 2965, 1595, 1485, 802 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d$_6$) δ 7.85 (d, *J* = 8.5 Hz, 4H), 7.50 (d, *J* = 8.5 Hz, 4H), 6.87 (s, 2H), 3.61 (q, *J* = 7.0 Hz, 2H), 2.0 (s, 3H), 1.03 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d$_6$) δ 176.6, 144.4, 134.3, 132.6, 132.0, 129.3, 114.0, 113.2, 60.9, 21.7, 15.1; MS (70 eV) m/z 404 (M$^+$), 334, 281, 181, 152; Anal. Calcd for $C_{21}H_{18}Cl_2O_4$: C, 62.24; H, 4.48. Found: C, 62.03; H, 4.59.

4,6-Bis((Z)-4-bromobenzylidene)-2-ethoxy-2-methyl-1,3-dioxan-5-one (3i). Mp: 234-235 °C; IR (KBr) ν 2923, 1597, 1481, 1283, 812 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d$_6$) δ 7.79 (d, *J* = 8.5 Hz, 4H), 7.64 (d, *J* = 8.5 Hz, 4H), 6.85 (s, 2H), 3.60 (q, *J* = 7.0 Hz, 2H), 1.99 (s, 3H), 1.02 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d$_6$) δ 176.6, 144.5, 132.9, 132.3, 123.1, 114.1, 113.2, 112.9, 61.0, 21.6, 15.1; MS (70 eV) m/z 494 (M$^+$), 424, 269, 198, 149; Anal. Calcd for $C_{21}H_{18}Br_2O_4$: C, 51.04; H, 3.67. Found: C, 50.92; H, 3.77.

4,6-Bis((Z)-2,4-dichlorobenzylidene)-2-ethoxy-2-methyl-1,3-dioxan-5-one (3j). Mp: 205-206 °C; IR (KBr) ν 2923, 1577, 1464, 1126 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d$_6$) δ 8.11 (d, *J* = 8.5 Hz, 2H), 7.70 (s, 2H), 7.50 (d, *J* = 8.5 Hz, 2H), 7.06 (s, 2H), 3.61 (q, *J* = 7.0 Hz, 2H), 1.96 (s, 3H), 1.04 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d$_6$) δ 176.4, 145.2, 135.3, 134.8, 132.3, 129.9, 129.4, 128.4, 113.6, 108.9, 61.3, 21.5, 15.3;

MS (70 eV) m/z 474 (M^+), 404, 217, 186, 123; Anal. Calcd for $C_{21}H_{16}Cl_4O_4$: C, 53.20; H, 3.40. Found: C, 53.36; H, 3.38.

4,6-Bis((Z)-4-(dimethylamino)benzylidene)-2-ethoxy-2-methyl-1,3-dioxan-5-one (3l). Mp: 230-231 °C; IR (KBr) ν 1591, 1527, 1127 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 7.69 (d, *J* = 9.0 Hz, 4H), 6.76 (d, *J* = 9.0 Hz, 4H), 6.75 (s, 2H), 3.58 (q, *J* = 7.0 Hz, 2H), 2.98 (s, 12H), 1.94 (s, 3H), 1.02 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 175.7, 151.0, 141.9, 132.6, 121.0, 116.1, 112.5, 112.3, 60.2, 40.1, 22.1, 15.3; MS (70 eV) m/z 422 (M^+), 306, 266, 205, 161; Anal. Calcd for $C_{25}H_{30}N_2O_4$: C, 71.07; H, 7.16; N, 6.63. Found: C, 71.15; H, 7.27; N, 6.52.

4,6-Bis((Z)-4-chlorobenzylidene)-2-methoxy-1,3-dioxan-5-one (3m). Mp: 155-156 °C; IR (KBr) ν 2934, 1606, 1578, 1464, 825 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 7.87 (d, *J* = 8.5 Hz, 4H), 7.50 (d, *J* = 8.5 Hz, 4H), 6.93 (s, 2H), 6.55 (s, 1H), 3.43 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 176.4, 144.1, 134.5, 132.7, 131.8, 129.3, 114.9, 107.2, 54.3; MS (70 eV) m/z 376 (M^+), 315, 281, 225, 152; Anal. Calcd for $C_{19}H_{14}Cl_2O_4$: C, 60.50; H, 3.74. Found: C, 60.66; H, 3.85.

4,6-Bis((Z)-2,4-dichlorobenzylidene)-2-methoxy-1,3-dioxan-5-one (3n). Mp: 186-187 °C; IR (KBr) ν 2897, 1577, 1464, 1268, 824 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 8.12 (d, *J* = 8.5 Hz, 2H), 7.72 (s, 2H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.11 (s, 2H), 6.58 (s, 1H), 3.43 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 176.2, 144.9, 135.3, 135.0, 132.3, 129.9, 129.3, 128.3, 109.9, 107.3, 54.5; MS (70 eV) m/z 446 (M^+), 409, 349, 186, 123; Anal. Calcd for $C_{19}H_{12}Cl_4O_4$: C, 51.16; H, 2.71. Found: C, 51.27; H, 2.86.

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References

[1] Jeremy, M. B.; Tymoczko, J. L.; Stryer, L. Biochemistry; 5th ed., Freemanm: New York, 2002.

[2] Robina, I.; Vogel, P. Synthesis of monosaccharides and analogues. part 1. applications of chemoenzymatic methods and organocatalysis. *Chim. Oggi* **2007**, *25*, 65–71.

[3] Lux, S.; Siebenhofer, M. Synthesis of lactic acid from dihydroxyacetone: use of alkaline-earth metal hydroxides. *Catal. Sci. Technol.* **2013**, *3*, 1380–1385.

[4] Suri, J. T.; Ramachary, D. B.; Barbas, C. F. Mimicking dihydroxyacetone phosphate-utilizing aldolases through organocatalysis: a facile route to carbohydrates and aminosugars. *Org. Lett.* **2005**, *7*, 1383–1385.

[5] Rao, V. S. R.; Qasba, P. K.; Balaji, P. V.; Chandrasekaran, R. Conformation of carbohydrates; Harwood Academic Publishers: Amsterdam, 1998.

[6] Enders, D.; Voith, M.; Lenzen, A. The dihydroxyacetone unit-a versatile C(3) building block in organic synthesis. *Angew. Chem. Int. Ed. Engl.* **2005**, *44*, 1304–1325.

[7] Gardiner, D. The dimeric forms of some α-hydroxycarbonyl compounds. *Carbohydr. Res.* **1966**, *2*, 234–239.

[8] Kobayashi, Y.; Igarashi, T.; Takahashi, H.; Higasi, K. Infrared and raman studies of the dimeric structures of 1,3-dihydroxyacetone, d(+)- and dl-glyceraldehyde. *J. Mol. Struct.* **1976**, *35*, 85–99.

[9] Feng, J.; Liu, B. Formal carbo [3+3] annulation and its application in organic synthesis. *Tetrahedron Lett.* **2015**, *56*, 1474–1485.

[10] Carlsen, P. H. J.; Søerbye, K.; Ulven, T. Aasbøe, K. Synthesis of benzylidene-protected dihydroxyacetone. *Acta. Chem. Scand.* **1996**, *50*, 185–187.

[11] Grondal, C.; Enders, D. Direct asymmetric organocatalytic de novo synthesis of carbohydrates. *Tetrahedron* **2006**, *62*, 329–337.

[12] Enders, D.; Grondal, C. Direct organocatalytic de novo synthesis of carbohydrates. *Angew. Chem. Int. Ed. Engl.* **2005**, *44*, 1210–1212.

[13] Enders, D.; Jegelka, U. 1,3-Dioxan-5-one as C3-building block for the diastereo- and enantioselective synthesis of C5- to C9-deoxy sugars using the SAMP-/RAMP-hydrazone method. *Tetrahedron Lett.* **1993**, *34*, 2453–2456.

[14] Enders, D.; Narine, A. A. Lessons from nature: biomimetic organocatalytic carbon–carbon bond formations. *J. Org. Chem.* **2008**, *73*, 7857–7870.

[15] Palyam, N.; Niewczas, I.; Majewski, M. Stereodivergent synthesis of d,d-and l,l-glycero-β-allo-heptopyranoses on a dioxanone scaffold. *Synlett* **2012**, *23*, 2367–2370.

[16] Palyam, N.; Majewski, M. Organocatalytic syn-aldol reactions of dioxanones with (*S*)-isoserinal hydrate: synthesis of l-deoxymannojirimycin and l-deoxyidonojirimycin. *J. Org. Chem.* **2009**, *74*, 4390–4392.

[17] Funk, R. L.; Belmar, J. Total synthesis of (±)-isophellibiline. *Tetrahedron Lett.* **2012**, *53*, 176–178.

[18] Nilson, M. G.; Funk, R. L. Total synthesis of (±)-cortistatin J from furan. *J. Am. Chem. Soc.* **2011**, *133*, 12451–12453.

[19] He Y.; Funk, R. L. Total syntheses of (±)-β-erythroidine and (±)-8-oxo-β-erythroidine by an intramolecular Diels–Alder cycloaddition of a 2-amidoacrolein. *Org. Lett.* **2006**, *8*, 3689–3692.

[20] Enders, D.; Voith, M.; Ince, S. J. Preparation and reactions of 2,2-dimethyl-1,3-dioxan-5-one-SAMP-hydrazone: a versatile chiral dihydroxyacetone equivalent. *Synthesis* **2002**, *34*, 1775–1779.

[21] Peukert, S.; Giese, B. The pivaloylglycol anchor group: a new platform for a photolabile linker in solid-phase synthesis. *J. Org. Chem.* **1998**, *63*, 9045–9051.

[22] Majewski, M.; Gleave, D. M.; Nowak, P. 1,3-Dioxan-5-ones: synthesis, deprotonation, and reactions of their lithium enolates. *Can. J. Chem.* **1995**, *73*, 1616–1626.

[23] Smithson, T. L.; Ibrahim, N.; Wieser, H. Cyclohexanones: evidence of chair inversion and estimate for barriers to planarity from the far-infrared spectra. *Can. J. Chem.* **1983**, *61*, 1924–1932.

[24] Abaee, M. S.; Mojtahedi, M. M.; Hamidi, V.; Mesbah, A. W.; Massa, W. The first synthesis of bis (arylmethylidene) dioxan-5-ones: potential scaffolds to access vicinal tricarbonyl derivatives. *Synthesis* **2008**, *40*, 2122–2126.

[25] Mojtahedi, M. M.; Mehraban, M.; Darvishi, K.; Abaee, M. S. Ultrasound mediated synthesis of dihydropyrano [3, 2-*d*] [1, 3] dioxin-7-carbonitrile derivatives in H_2O/EtOH medium. *Heterocycl. Commun*. **2017**, *23*, 91–95.
[26] Abaee, M. S.; Akbarzadeh, E.; Shockravi, A.; Mojtahedi, M. M.; Mehraki, E.; Khavasi, H. R. Three-component anti selective Mannich reactions in a tetrahydro-4-pyranone system by using PDAG-Co catalyst. *Heterocycl. Commun*. **2014**, *20*, 123–128.
[27] Mojtahedi, M. M.; Pourabdi, L.; Abaee, M. S.; Jami, H.; Dini, M.; Halvagar, M. R. Facile one-pot synthesis of novel *ortho*-aminocarbonitriles and dicyanoanilines fused to heterocycles via pseudo four-component reactions. *Tetrahedron* **2016**, *72*, 1699–1705.
[28] Li, Z.; Song, W.; He, J.; Du, Y.; Yang, J. Synthesis of 4-arylethyl-6-arylpyrimidine-2-thiols through aza-Michael addition/nucleophilic addition/aromatization tandem reactions. *Heterocycl. Commun.* **2018**, *24*, 23–26.
[29] El-Hussieny, M.; Yosef, H. A. A.; Mahran, M. R. H.; Ibrahim, N. M. Reactions of ferrocenyl chalcones with hydrazines and active methylene compounds. *Heterocycl. Commun*. **2016**, *22*, 69–77.
[30] Singh, P.; Anand, A.; Kumar, V. Recent developments in biological activities of chalcones: a mini review. *Eur. J. Med. Chem*. **2014**, *85*, 758–777.
[31] Arasavelli, A. M.; Ganapavarapu, V.; S. Vidavalur, S. Design, synthesis, and anticancer activity of novel aryl/heteroaryl chalcone derivatives. *Heterocycl. Commun*. **2016**, *22*, 1–5.
[32] Müeller, S. N.; Batra, R.; Senn, M.; Giese, B.; Kisel, M.; Shadyro, O. Chemistry of C-2 glyceryl radicals: indications for a new mechanism of lipid damage. *J. Am. Chem. Soc*. **1997**, *119*, 2795–2803.
[33] Mojtahedi, M. M.; Darvishi, K.; Abaee, M. S.; Halvagar, M. R. Synthesis and fluorescence studies of novel bisarylmethylidene derivatives of 2-methoxy-2-methyl-1, 3-dioxan-5-one. *Can. J. Chem*. **2017**, *95*, 785–791.
[34] Rudolph, T.; Buehle, P.; Rosskopf, R. US Patent 2013/0309184 A1, 2013.