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DABCO-catalyzed formation of 4-methoxy-1,3-dioxolan-2-ones and their synthetic applications in the aromatic electrophilic substitution

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This Letter is dedicated to Professor Chun-Chen Liao for his inspiration and on the occasion of his retirement

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ABSTRACT

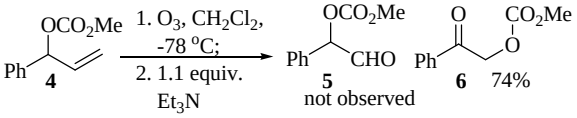
DABCO is a very effective catalyst in the formation of 4-methoxy-1,3-dioxolan-2-ones **10** from the corresponding α-carbonatoaldehydes **8** intermediates. The Friedel–Crafts reaction pathway of the cyclic carbonate **10** is dependent on the electron density of the aromatic nucleophiles.

We have reported that the ozonolysis of 1-substituted allyl silyl ethers or 1-substituted allyl carboxylates **1** followed by treatment with bases gave the corresponding α-silyloxy- or α-acyloxy-ketones **3** in good yields. It is proposed to proceed via a novel ene-diol rearrangement of the corresponding α-silyloxy- or α-acyloxyaldehydes intermediates **2** (Scheme 1).[1] When R is an aryl group in compound **2**, Et_3N is an effective base to promote the rearrangement. Stronger base such as DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) is needed when R of compound **2** is an alkyl group.

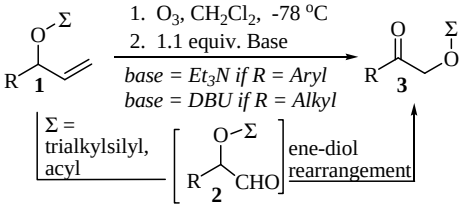
When methyl 1-phenylallyl carbonate (**4**) was sequentially treated with O_3 and Et_3N, the rearranged product **6** was isolated in 74% yield as expected (Eq. 1). To our surprise, no rearranged product **9a** was observed when 1-cyclohexylallyl methyl carbonate (**7a**) was sequentially treated with O_3 and DBU. The crude product ^1H NMR spectrum indicates that aldehyde **8a** was formed instead.

To our surprise, we found that aldehyde **8a** was rearranged to cyclic carbonate **10a** after silica gel column chromatography, albeit in low yield (Eq. 2). It indicates that methoxycarbonyl is a migratory group when α-aryl-aldehyde **5** is treated with base. On the other hand, α-cyclohexyl-aldehyde **7a** prefers the cyclic carbonate formation to the ene-diol rearrangement.

The synthesis and use of cyclic alkylene carbonates in industrial applications have been fully realized.[2] However, to the best of our knowledge, both the synthesis and the synthetic application of the α-methoxy cyclic carbonate **10** are undisclosed in the literature.[3] Therefore, we are interested in improving the preparation of cyclic carbonate **10a** from α-carbonatoaldehyde **8a**. Herein, we want to report our findings that DABCO (1,4-diazabicyclo[2.2.2]octane) is an excellent catalyst in the cyclic carbonates formation, and these cyclic carbonates are demonstrated to be useful in organic synthesis.



(1)



Scheme 1. Synthesis of α-silyloxy- or α-acyloxy-ketones **3** via aldehyde intermediate **2**.

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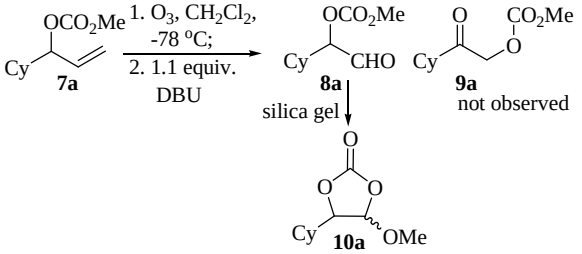

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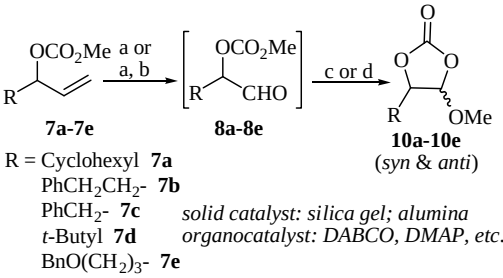


Scheme 2. Reagents and conditions: (a) (i) O_3, CH_2Cl_2, −78 °C; (ii) 0.8 equiv Ph_3P; (b) removed Ph_3PO by filtration; (c) solid catalyst and/or organocatalyst in CH_2Cl_2; (d) solid catalyst and/or organocatalyst in MeOH/CH_2Cl_2.

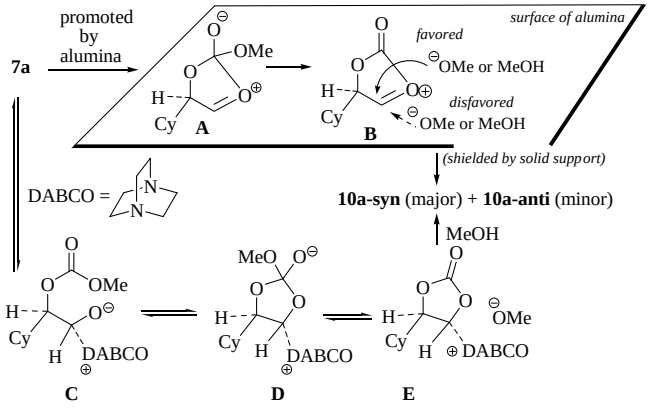


Figure 1. The plausible mechanism of the carbonate **10a** formation from **7a** promoted by either alumina or DABCO.

The aldehyde **8a** was prepared from the ozonolysis of alkene **7a** followed by reduction with Ph_3P. The crude product was triturated with *n*-hexane under sonication, the Ph_3PO was filtered and the filtrate was concentrated to give the crude **8a** (i.e., Procedure A condition). The crude residue was mixed with either silica gel or alumina (5–10 wt equiv) in the solvent as indicated in Table 1, and the slurry was stirred at room temperature until the disappearance of the aldehyde **8a**. The result is shown in Table 1. In CH_2Cl_2, basic alumina is a better catalyst than silica gel to promote the cyclization of aldehyde **8a** (Scheme 2; Table 1, entries 1 and 2). The reaction time is shorter when the weight equivalent of the alumina is increased from 5 to 10 (entries 2 and 3). The basic alumina is the best catalyst among three types of alumina (entries 3–5). When methanol was used as the solvent in the presence of basic alumina, the reaction time is shorter and the yield is improved to 47% (entries 2 and 6). The alumina is not required if DMAP is used as catalyst (entries 7 and 8). The removal of Ph_3PO is not required if DMAP is used as catalyst, and the yield is increased (entries 7, 8, and 10; i.e., Procedure B condition). DABCO is a better catalyst than DMAP to promote the cyclization (entries 8 and 9; 10 and 11). Longer reaction time is needed if the mol equivalent of the DABCO is decreased from 0.1 to 0.05 (entries 12 and 13). The reaction is complete by heating at 50 °C for 5 h when 0.05 mol equiv of the DABCO is used. However, the yield is reduced to 71% (entries 13 and 14). The acidic catalysts, such as PTSA and PPTS, are inferior to the nucleophilic base catalysts in this study (entries 15, 16, and 12). The DABCO-catalyzed cyclization is also applicable to those substrates with phenylethyl, benzyl, *tert*-butyl, and 3-benyzloxypropyl substituents (entries 17–20). In general, the *syn*-iso-

Table 1
The cyclic carbonate **10** formation from allyl carbonate **7** via aldehyde **8** under various catalytic conditions

Entry	Starting material R =	Procedure[a]	Solid support (wt equiv)	Catalyst (equiv)	Solvent[b]	Time (h)	Yield (%) (*syn*:*anti*)
1	Cyclohexyl **7a**	A	SiO_2 (10)	—	CH_2Cl_2	48	**10a** —[c] (1:0)
2	Cyclohexyl **7a**	A	Basic Al_2O_3 (5)	—	CH_2Cl_2	28	**10a** 29 (8.3:1)
3	Cyclohexyl **7a**	A	Basic Al_2O_3 (10)	—	CH_2Cl_2	6	**10a** 32 (8.3:1)
4	Cyclohexyl **7a**	A	Acidic Al_2O_3 (10)	—	CH_2Cl_2	6	**10a** 29 (6:1)
5	Cyclohexyl **7a**	A	Neutral Al_2O_3 (10)	—	CH_2Cl_2	6	**10a** 23 (6:1)
6	Cyclohexyl **7a**	A	Basic Al_2O_3 (10)	—	MeOH	6	**10a** 47 (6:1)
7	Cyclohexyl **7a**	A	Basic Al_2O_3 (10)	DMAP (0.2)	MeOH	6	**10a** 59 (5.9:1)
8	Cyclohexyl **7a**	A	—	DMAP (0.2)	MeOH	6	**10a** 60 (6.2:1)
9	Cyclohexyl **7a**	A	—	DABCO (0.2)	MeOH	6	**10a** 70 (6.5:1)
10	Cyclohexyl **7a**	B	—	DMAP (0.2)	MeOH	8	**10a** 71 (5.8:1)
11	Cyclohexyl **7a**	B	—	DABCO (0.2)	MeOH	6	**10a** 91 (5.6:1)
12	Cyclohexyl **7a**	B	—	DABCO (0.1)	MeOH	8	**10a** 91 (6.3:1)
13	Cyclohexyl **7a**	B	—	DABCO (0.05)	MeOH	20	**10a** 87 (6.3:1)
14	Cyclohexyl **7a**	B	—	DABCO (0.05)	MeOH	5	**10a** 71[d] (6.2:1)
15	Cyclohexyl **7a**	B	—	PPTS (0.2)	MeOH	12	**10a** 0[e]
16	Cyclohexyl **7a**	B	—	PTSA (0.2)	MeOH	12	**10a** 34[f] (2.4:1)
17	$Ph(CH_2)_2$-**7b**	B	—	DABCO (0.1)	MeOH	8	**10b** 93 (2.5:1)
18	$PhCH_2$-**7c**	B	—	DABCO (0.1)	MeOH	8	**10c** 83 (2.9:1)
19	*t*-Butyl **7d**	B	—	DABCO (0.1)	MeOH	8	**10d** 76 (1:0)
20	$BnO(CH_2)_3$-**7e**	B	—	DABCO (0.1)	MeOH	10	**10e** 84 (3.5:1)

[a] To carry out the cyclization after removal of Ph_3PO is termed as Procedure A condition. To carry out the cyclization in the presence of Ph_3PO is termed as Procedure B condition.
[b] Anhydrous solvent.
[c] 10% conversion and **10a**:**8a** = 1:8 by ^1H NMR integration.
[d] Reaction temperature is 50 °C.
[e] Recovered aldehyde **8a**.
[f] 60% conversion.

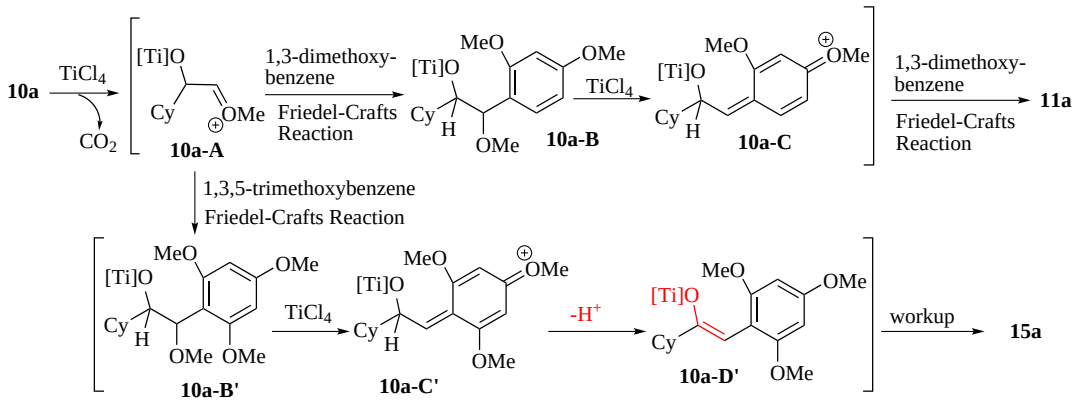
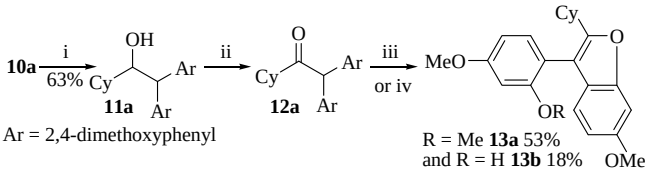
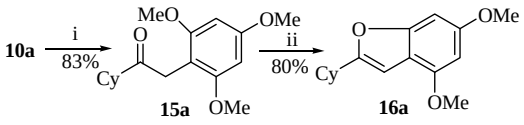


Figure 2. The plausible mechanisms for the formation of compounds **11a** and **15a** from cyclic carbonate **10a** via Friedel–Crafts reaction.



Scheme 3. Reagents and conditions: (i) 2.0 equiv $TiCl_4$, 2.2 equiv 1,3-dimethoxybenzene, CH_2Cl_2, −50 °C to rt; (ii) 1.5 equiv Dess–Martin periodinane; (iii) 1 equiv BBr_3, EtOAc, 0 °C to rt, 12 h; (iv) 3 equiv BBr_3, EtOAc, 0 °C to rt, 4 h.

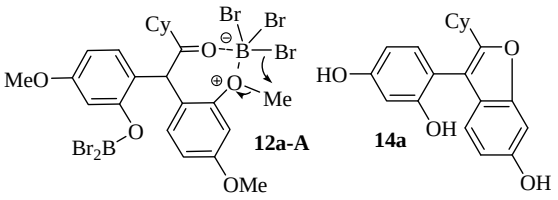


Scheme 4. Reagents and conditions: (i) 2.0 equiv $TiCl_4$, 1.5 equiv 1,3,5-trimethoxybenzene, CH_2Cl_2, −50 °C to rt; (ii) 1 equiv BBr_3, EtOAc, 0 °C, 12 h.

mer is formed preferentially in each case (Table 1). Their *syn*- and *anti*-stereochemistry are confirmed by their 2D-NOESY technique.

The rationale of the stereoselectivity of the ring formation is described as follows. The basic alumina promotes the cyclization of compound **8a** to give intermediate **A** which undergoes elimination to give oxonium ion **B**, where the cyclohexyl group is oriented in the opposite side of the alumina surface due to the steric hindrance. Either methoxide or methanol will attack the oxonium ion **B** from the less hindered β-face preferentially to give **10a-syn** predominately as shown in Figure 1. DABCO is known to be the effective catalyst in Morita–Baylis–Hillman reaction.[4] In the present reaction, the nucleophilic attack of aldehyde **7a** by DABCO followed by elimination to give the intermediate **E**. Nucleophilic substitution of intermediate **E** with methanol gives **10a-syn** as the major product (Fig. 1). Interestingly, the formation of 4-alkyl-1,3-dioxol-2-one via a proton elimination is not observed.

A mixture of cyclic carbonate **10a** and 2.2 equiv of 1,3-dimethoxybenzene in CH_2Cl_2 was treated with 2.0 equiv of $TiCl_4$ at −50 °C to give the diarylated product **11a** in 63% yield (Scheme 4). Presumably, the Friedel–Crafts reaction of 1,3-dimethoxybenzene with intermediate **10a-A** gave the intermediate **10a-B**. The leaving of the benzylic methoxy group was promoted by $TiCl_4$ to give intermediate **10a-C,** which then underwent the second Friedel–Crafts reaction with 1,3-dimethoxybenzene to give diaryl compound **11a** (Fig. 2). Alcohol **11a** was oxidized with Dess–Martin periodinane to give ketone **12a**, which was then treated with BBr_3 (1 or 3 equiv) in ethyl acetate to give the benzofuran **13a** and **13b** in good yield (Scheme 3). Presumably, the carbonyl group-directed demethylation of compound **12a** at *ortho*-position selectively (i.e., via intermediate **12a-A**) occurred before the benzofuran ring formation. When the demethylation reaction was carried out with 3 equiv of BBr_3 in CH_2Cl_2, the benzofuran **14a** was formed in 58% yield. It is interesting to point out that BBr_3 in EtOAc is less reactive and more selective in the demethylation of compound **12a** in comparison with the reaction in CH_2Cl_2.



Under similar condition, the cyclic carbonate **10a** reacted with 1,3,5-trimethoxybenzene in the presence of $TiCl_4$ at −50 °C in CH_2Cl_2 to give mono-arylated ketone **15a** in 83% yield, and no diarylated product was observed (Scheme 4). Ketone **15a** was then treated with BBr_3 in ethyl acetate to give the benzofuran **16a** in 80% yield. The carbonyl group-directed demethylation of compound **15a** at the *ortho*-position selectively occurred before the benzofuran ring formation.

The rationale for formation of compounds **11a** and **15a** from cyclic carbonate **10a** was described in Figure 2. The cyclic carbonate **10a** was decomposed by the first equivalent of TiCl4 to give oxonium intermediate **10a-A**. When 1,3-dimethoxybenzene was used as nucleophile, **10a-A** undergoes Friedel–Crafts reaction to give intermediate **10a-B**. The benzylic methoxy group of **10a-B** is removed by the help of the second equivalent of TiCl4 to give the intermediate **10a-C**. It then undergoes the second Friedel–Crafts reaction to give the diarylated product **11a**. Interestingly, when the more electron-rich nucleophile such as 1,3,5-trimethoxybenzene was used as nucleophile in the reaction, its reaction pathway is different from that of using 1,3-dimethoxybenzene. The intermediate **10a-C′** undergoes deprotonation instead of second arylation to give mono-arylated product **15a**. In conclusion, DABCO is a very efficient organocatalyst in the formation of 4-methoxy-1,3-dioxolan-2-ones **10** from the corresponding α-carbonatoaldehydes **8**. The cyclic carbonate **10** reacts with TiCl4 to give the intermediate **10a-A**. This intermediate reacts with 1,3-dimethoxybenzene to give the β,β-diaryl ethanol **11a**. The cyclic carbonate **10** is considered to be the synthetic equivalent of the synthon-*I* (Fig. 3). When 1,3,5-trimethoxybenzene was used as the nucleophile, the α-arylated ketone **15a** was formed. The cyclic carbonate **10** is considered

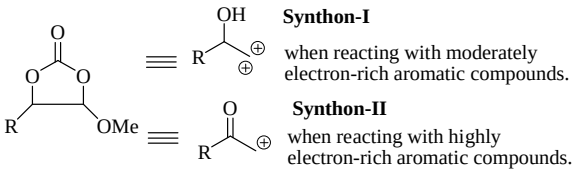


Figure 3. 4-Methoxy-1,3-dioxolan-2-ones can be considered as either Synthon **I** or **II** depending on the nucleophiles.

to be the synthetic equivalent of the synthon-**II** (Fig. 3). The α-arylation of ketone is extensively studied in past decade.[5] Most importantly, the reversed polarity disconnection of the α-arylation in this study is discovered in comparison with the approaches in the literature.[5]

Further studies are in progress in order to investigate the further synthetic applications of the cyclic carbonates **10** with different nucleophiles in the presence of Lewis acids.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.09.173.

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