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$AlCl_3$-Promoted Highly Regio- and Diastereoselective [3 + 2] Cycloadditions of Activated Cyclopropanes and Aromatic Aldehydes: Construction of 2,5-Diaryl-3,3,4-trisubstituted Tetrahydrofurans

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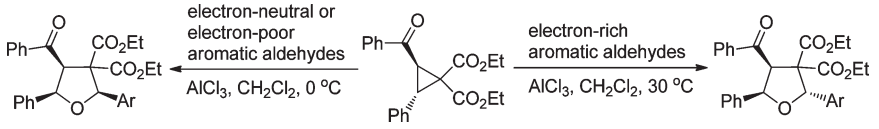

The $AlCl_3$-catalyzed [3 + 2] cycloaddition reaction of diethyl *trans*-2,3-disubstituted cyclopropane-1, 1-dicarboxylates and aromatic aldehydes was carried out under mild conditions to provide a series of diethyl 2,5-diaryl-4-benzoyltetrahydrofuran-3,3-dicarboxylates in moderate to good yields with excellent diastereoselectivities. While common 2,5-*cis* products were obtained with electron-neutral or electron-poor aryl aldehydes, the much less common 2,5-*trans* products were obtained in excellent diastereoselectivities when electron-rich aryl aldehydes were used. The relative configurations of those typical products were confirmed by X-ray crystallographic analyses.

Introduction

Substituted tetrahydrofurans are an important structural motif present in numerous natural products with a wide range of diverse biological and pharmacological activities.[1] Consequently, the synthesis of these substituted tetrahydrofurans has received an intense interest among organic chemists, and plenty of elegant methods have been developed for this purpose.[2] Among those, the Lewis acid-catalyzed [3 + 2] cycloadditions of aldehydes/ketones with activated donor−acceptor (D−A) cyclopropanes are particularly attractive due to their good atomic economy and easy availability of the starting materials.[3−6] Johnson and co-workers have developed highly diastereoselective,[4b,c] enantiospecific,[4a] and enantioselective[4e] Lewis acid-catalyzed intermolecular [3 + 2] cycloadditions of aldehydes with carbon-based donor D−A cyclopropanes, and have applied it for the total synthesis of (+)-Polyanthellin A[7] and (+)-virgatusin.[8] Lately, Wang and co-workers reported a related intramolecular version of this reaction to construct complex oxa-[*n*.2.1]

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(1) (a) Ward, R. S. *Nat. Prod. Rep.* **1997**, *14*, 43–74. (b) Saleem, M.; Kim, H. J.; Ali, M. S.; Lee, Y. S. *Nat. Prod. Rep.* **2005**, *22*, 696–716. (c) Pan, J.-Y.; Chen, S.-L.; Yang, M.-H.; Wu, J.; Sinkkonen, J.; Zou, K. *Nat. Prod. Rep.* **2009**, *26*, 1251–1292. (d) Gautam, R.; Jacbak, S. M. *Med. Res. Rev.* **2009**, *29*, 767–820. (e) Carvalho, A. A. V.; Galdino, P. M.; Nascimento, M. V. M.; Kato, M. J.; Valadares, M. C.; Cunha1, L. C.; Costa, E. A. *Phytother. Res.* **2010**, *24*, 113–118. (f) Seo, C.-S.; Lee, W.-H.; Chung, H.-W.; Chang, E. J.; Lee, S. H.; Jahng, Y.; Hwang, B. Y.; Son1, J.-K.; Han, S.-B.; Kim, Y. *Phytother. Res.* **2009**, *23*, 1531–1536. (g) Nguyen, P. H.; Le, T. V. T.; Kang, H. W.; Chae, J.; Kim, S. K.; Kwon, K.; Seo, D. B.; Lee, S. J.; Oh, W. K. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 4128–4131.

(2) (a) Wolfe, J. P.; Hay, M. B. *Tetrahedron* **2007**, *63*, 261–290. (b) Yamauchi, S.; Nakato, T.; Tsuchiya, M.; Akiyama, K.; Maruyama, M.; Sugahara, T.; Kishida, T. *Biosci. Biotechnol. Biochem.* **2007**, *71*, 2248–2255. (c) Martinet, S.; Méou, A.; Brun, P. *Eur. J. Org. Chem.* **2009**, 2306–2311. (d) Moinuddin, S. G. A.; Hishiyama, S.; Cho, M.-H.; Davin, L. B.; Lewis, N. G. *Org. Biomol. Chem.* **2003**, *1*, 2307–2313. (e) Yamauchi, S.; Okazaki, M.; Akiyama, K.; Sugahara, T.; Kishida, T.; Kashiwagi, T. *Org. Biomol. Chem.* **2005**, *3*, 1670–1675. (f) Jahn, U.; Rudakov, D. *Org. Lett.* **2006**, *8*, 4481–4484. (g) Kim, H.; Wooten, C. M.; Park, Y.; Hong, J. *Org. Lett.* **2007**, *9*, 3965–3968. (h) Matcha, K.; Ghosh, S. *Tetrahedron Lett.* **2008**, *49*, 3433–3436. (i) Campbell, M. J.; Johnson, J. S.; Parsons, A. T.; Pohlhaus, P. D.; Sanders, S. D. *J. Org. Chem.* **2010**, *75*, 6317–6325. (j) Karadeolian, A.; Kerr, M. A. *J. Org. Chem.* **2010**, *75*, 6830–6841.

(3) Christie, S. D. R.; Davoile, R. J.; Elsegood, M. R. J.; Fryatt, R.; Jones, R. C. F.; Pritchard, G. J. *Chem. Commun.* **2004**, 2474–2475.

(4) (a) Pohlhaus, P. D.; Johnson, J. S. *J. Am. Chem. Soc.* **2005**, *127*, 16014–16015. (b) Pohlhaus, P. D.; Johnson, J. S. *J. Org. Chem.* **2005**, *70*, 1057–1059. (c) Parsons, A. T.; Campbell, M. J.; Johnson, J. S. *Org. Lett.* **2008**, *10*, 2541–2544. (d) Pohlhaus, P. D.; Sanders, S. D.; Parsons, A. T.; Li, W.; Johnson, J. S. *J. Am. Chem. Soc.* **2008**, *130*, 8642–8650. (e) Parsons, A. T.; Johnson, J. S. *J. Am. Chem. Soc.* **2009**, *131*, 3122–3123.

(5) Gupta, A.; Yadav, V. K. *Tetrahedron Lett.* **2006**, *47*, 8043–8047.

(6) (a) Xing, S.; Pan, W.; Liu, C.; Ren, J.; Wang, Z. *Angew. Chem., Int. Ed.* **2010**, *49*, 3215–3218. (b) Hu, B.; Xing, S.; Ren, J.; Wang, Z. *Tetrahedron* **2010**, *66*, 5671–5674.

(7) Campbell, M. J.; Johnson, J. S. *J. Am. Chem. Soc.* **2009**, *131*, 10370–10371.

(8) Sanders, S. D.; Ruiz-Olalla, A.; Johnson, J. S. *Chem. Commun.* **2009**, 5135–5137.

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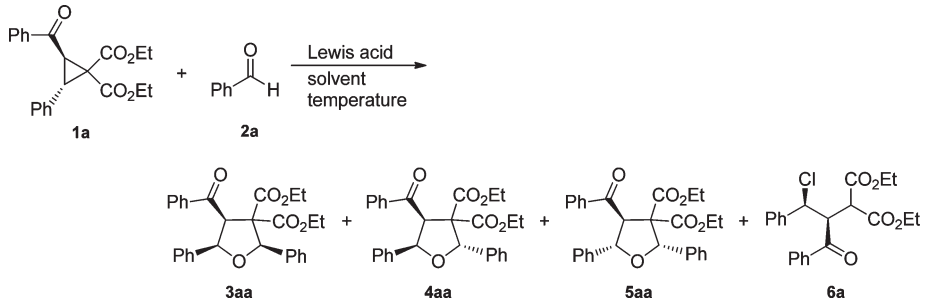
TABLE 1. Optimization of Reaction Conditions for the [3 + 2] Addition of 1a and 2a[a]



entry	**2a**/equiv	Lewis acid/equiv	solvent	temp (°C)	time (h)	product/yield[b] (%)	product ratio[c] **3aa**:**4aa**:**5aa**:**6a**
1	5.0	$AlCl_3$/0.5	CH_2Cl_2	20	22	**3aa**/41	66:8:8:18
2	5.0	$AlCl_3$/0.5	CH_2Cl_2	30	18	**3aa**/19 **4aa**/19 **5aa**/21	21:22:23:34
3	5.0	$AlCl_3$/0.5	CH_2Cl_2	0	19	**3aa**/87	88:3:2:7
4	5.0	$AlCl_3$/0.5	CH_2Cl_2	−15	75	**3aa**/88	93:2:0:5
5	5.0	$AlCl_3$/1.0	CH_2Cl_2	0	19	**3aa**/38	38:15:6:41
6	5.0	$AlCl_3$/0.3	CH_2Cl_2	0	40	**3aa**/59	93:1:1:5
7	3.0	$AlCl_3$/0.5	CH_2Cl_2	0	25	**3aa**/65	73:6:3:18
8	2.0	$AlCl_3$/0.5	CH_2Cl_2	0	45	**3aa**/51	81:2:2:15
9	5.0	$AlCl_3$/0.5	DCE	0	19	**3aa**/79	83:5:3:9
10	5.0	$AlCl_3$/0.5	toluene	0	19	**3aa**/62	78:2:1:19
11	5.0	$AlCl_3$/0.5	benzene	10	19	**3aa**/12	57:7:3:33
12	5.0	$AlCl_3$/0.5	CH_2Cl_2	10	9	**3aa**/59	79:10:1:10
13	5.0	$Cu(OTf)_2$[d]/0.5	CH_2Cl_2	0−30	26	NR	
14	5.0	$Yb(OTf)_3$/0.5	CH_2Cl_2	0−30	26	NR	
15	5.0	$ZnCl_2$/0.5	CH_2Cl_2	0−30	26	NR	
16	5.0	$BF_3 \cdot Et_2O$/0.5	CH_2Cl_2	0−30	26	NR	
17	5.0	$TiCl_4$/0.5	CH_2Cl_2	0	57	**6a**/90	2:0:0:98
18	5.0	$Al_2(SO_4)_3$/0.5	CH_2Cl_2	0−30	120	NR	
19	5.0	$Al(OTf)_3$/0.5	CH_2Cl_2	30	20	complicated	–[e]

[a]The reaction was conducted with 0.3 mmol of **1a**. [b]Isolated yield. [c]Determined by ^{1}H NMR. [d]Tf refers to trifluoromethanesulfonyl. [e]No formation of **3aa** and **5aa** and only a trace of **4aa** were observed by crude ^{1}H NMR analysis along with other unidentifiable signals.

skeletons, in which there is no strict requirement for the presence of a typical donor group in cyclopropane 1,1-diesters.[6]

Most of the above examples are focused on the [3 + 2] cycloadditions of 2-substituted cyclopropane-1,1-diesters with aldehydes to afford 2,3,3,5-tetrasubstituted tetrahydrofurans with 2,5-*cis* diastereoselectivity. On the other hand, the corresponding reaction of 2,3-disubstituted cyclopropane-1,1-diesters, especially those with an electron-withdrawing group at the 3-position, with aldehydes to provide 2,3,3,4,5-pentasubstituted tetrahydrofurans, has rarely been studied.[4d,7,8] Moreover, to the best of our knowledge, this kind of cycloaddition with a high 2,5-*trans* diastereoselectivity has so far not been reported.

Our group has recently developed a method for the facile synthesis of 2,3-disubstituted cyclopropane-1,1-diesters like **1a**,[9] which have an aryl carbonyl group at the 3-position of the cyclopropane ring. As an effort to extend the synthetic utility of these resultant products in this work, we investigated the application of 2,3-*trans*-disubstituted cyclopropane-1,1-diesters **1** in the cycloaddition reactions with aromatic aldehydes. Some interesting results were obtained and were compared with those well-studied 2-substituted cyclopropane-1,1-diesters.

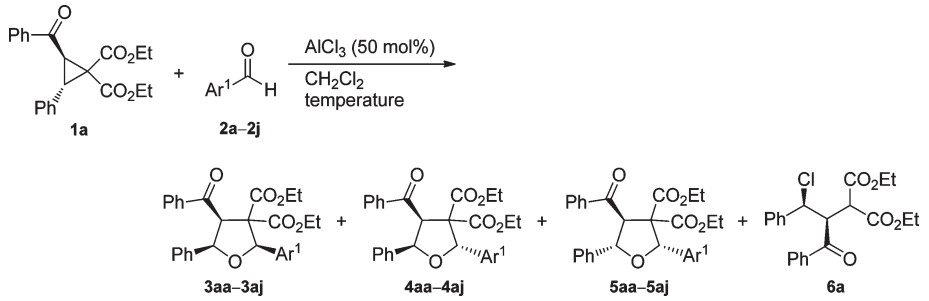
Results and Discussion

The reaction of diethyl *trans*-2-benzoyl-3-phenylcyclopropane-1,1-dicarboxylate **1a**[9] with benzaldehyde **2a** was selected as a model reaction to screen the reaction conditions. Table 1 summarizes the results. Initially, the reaction of **1a** (1.0 equiv) and **2a** (5.0 equiv) in the presence of $AlCl_3$ (50 mol %) was performed in dichloromethane (CH_2Cl_2) at room temperature (about 20 °C) (Table 1, entry 1). Three [3 + 2] cycloaddition products **3aa** (2,4,5-*cis*-isomer), **4aa** (2,4-*trans*-2,5-*trans*-isomer), and **5aa** (2,4-*trans*-2,5-*cis*-isomer) were isolated with a byproduct **6a** resulting from the chloride addition to the cyclopropane. The structure of these compounds was characterized by spectral analyses and confirmed by X-ray crystallographic analyses.[10] It is worth mentioning that the isolation and characterization of **6a** corroborated a presumption for the formation of this kind of byproducts in related reactions in literature.[4d] In comparison with Johnson's result (81% NMR yield, 2:1 dr),[4d] in which the 2-benzoyl group was absent, the diastereoselectivity (*cis* vs *trans* at the 2,5-positions) for the major product 2,4,5-*cis*-isomer **3aa** was significantly improved in our system under extremely similar conditions, although the isolated yield was lower (41%). Raising the reaction temperature (30 °C) decreased the selectivity of this reaction

(9) Yang, G. S.; Hua, Y. Y.; Shen, Y. *Chin. J. Chem.* **2009**, *27*, 1811–1819.

(10) See the Supporting Information. The crystal structures have been deposited with the Cambridge Crystallographic Data Centre; deposition nos. CCDC 795516, 795517, 795518, and 795519 for **3aa**, **4aa**, **5aa**, and **6a**, respectively. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre, 12 Union Rd., Cambridge CB2 1EZ, UK or via www.ccdc.cam.ac.uk/conts/retrieving.html.

TABLE 2. Aldehyde Scope in $AlCl_3$-Catalyzed [3 + 2] Cycloaddition of 1a [a]



entry	Ar^1	temp (°C)	time (h)	product/yield[b] (%)	product ratio[c] **3**:**4**:**5**:**6**
1	C_6H_5 **2a**	0	19	**3aa**/87	88:3:2:7
2	4-ClC_6H_4 **2b**	0	26	**3ab**/77	85:1:2:12
3[d]	2,4-$Cl_2C_6H_3$ **2c**	0	20	**3ac**/88	90:0:0:10
4	4-BrC_6H_4 **2d**	0	29	**3ad**/77	88:1:1:10
5	4-$NO_2C_6H_4$ **2e**	0	29	**3ae**/37	43:0:1:56
6	4-MeC_6H_4 **2f**	0	44	**3af**/57	75:16:1:8
7	4-MeC_6H_4 **2f**	30	29	**4af**/51	4:65:10:21
8[d]	4-$MeOC_6H_4$ **2g**	30	6d	**4ag**/67	4:81:3:12
9	3,4-$(MeO)_2C_6H_3$ **2h**	30	55	**4ah**/81	0:82:2:16
10	4-$BnOC_6H_4$ **2i**	30	90	**4ai**/50	3:62:2:33
11	3-MeO-4-$BnOC_6H_3$ **2j**	30	90	**4aj**/47	0:77:2:21

[a]The reaction was conducted with 0.3 mmol of **1a**. [b]Isolated yield. [c]Determined by ^1H NMR. [d]The structures of **3ac** and **4ag** were confirmed by X-ray crystallographic analyses.[11]

(Table 1, entry 2), while the decreasing of the reaction temperature to 0 °C led to the improvements of both the yield and the selectivity of **3aa** (87%) (Table 1, entry 3). Further decreasing the reaction temperature to −15 °C brought in a negligible improvement even with a much longer reaction time (Table 1, entry 4). Screening of other conditions including the loading of $AlCl_3$, the ratio of the aldehyde **2a**, the variation of solvents (e.g., 1,2-dichloroethane, toluene, and benzene), and Lewis acids (e.g., $Cu(OTf)_2$, $Yb(OTf)_3$, $ZnCl_2$, $BF_3 \cdot Et_2O$, $TiCl_4$, and other aluminum salts such as $Al_2(SO_4)_3$ and $Al(OTf)_3$) all failed to improve the results (Table 1, entries 5−19). Thus, 5 equiv of aldehyde and 50 mol % of $AlCl_3$ in CH_2Cl_2 at 0 °C were chosen as the optimal conditions for further investigation.

With the optimized reaction conditions in hand, the scope of this reaction was then probed with a range of different aromatic aldehydes (Table 2). In general, most of the electron-neutral and electron-poor aldehydes were suitable for this reaction and smoothly generated the desired 2,4,5-*cis*-pentasubstituted tetrahydrofuran derivatives **3aa**−**3ad** in good yields with high diastereoselectivities (Table 2, entries 1−4). Although excellent diastereoselectivity was obtained for *p*-nitrobenzaldehyde **2e**, the yield was low (Table 2, entry 5), which may be attributed to the significant decomposition of **1a** as observed in some related studies.[4] In contrast to the better reactivities observed for highly electron-rich aldehydes in Johnson's system,[4] these substrates are less reactive here and a higher temperature (30 °C) was required to react with **1a** (Table 2, entries 8−11). This may be due to the preferential coordination of $AlCl_3$ with electron-rich aldehydes than with **1a**. In addition, the 2,4-*trans*-2,5-*trans*-pentasubstituted tetrahydrofurans **4ag**−**4aj** were obtained here as the major products in moderate to good yields with excellent diastereoselectivity. Such an inversion of the 2,5-diastereoselectivity seemed to be favored at a high reaction temperature as in the case of the slightly electron-rich *p*-methylbenzaldehyde **2f** (Table 2, entries 6 and 7). It is also worth mentioning that only one regioisomer of the cycloaddition products was isolated in all the cases described above.

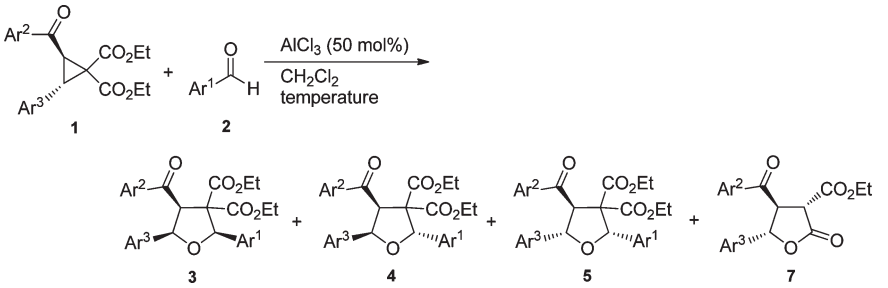
Furthermore, several other diethyl cyclopropane-1,1-dicarboxylates were also examined in the reaction (Table 3). It was found that the presence of electron-donating groups on the phenyl ring (Ar^2 or Ar^3) lead to a rather messy system (Table 3, entries 5, 6, and 10−12). The electron-donating groups on Ar^3 in **1** may inhibit the nucleophilic attack of an electron-deficient or electron-neutral aldehyde, facilitating an intramolecular attack of the oxygen atom of the ester group in **1f**, and lead to the formation of lactone **7f** as the major product similar to that described in literature (Table 3, entries 10 and 11).[12]

A reaction mechanism similar to that of Johnson's was proposed for this reaction (Scheme 1). Compound **1a** was activated through the coordination of the diester group with $AlCl_3$. Subsequently, a nucleophilic attack of an aldehyde was performed to form a zwitterion (**I**), which then underwent a bond rotation and an ensuing intramolecular nucleophilic attack to form the product **3**.[4d] For those electron-rich aromatic aldehydes, two pathways may be used to explain the inversion of the diastereoselectivity. One is similar to that proposed in literature: the initially formed *cis* product **3** undergoes the isomerization via a carbenium ion (**III**), which

(11) See the Supporting Information. The crystal structures have been deposited with the Cambridge Crystallographic Data Centre; deposition numbers: CCDC 795520 and 795521 for **3ac** and **4ag**, respectively. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre, 12 Union Rd., Cambridge CB2 1EZ, UK or via www.ccdc.cam.ac.uk/conts/retrieving.html.

(12) For examples of the formation of similar products in related reactions, see: (a) Wu, X.; Cao, W.; Zhang, H.; Chen, J.; Jiang, H.; Deng, H.; Shao, M.; Zhang, J.; Chen, H. *Tetrahedron* **2008**, *64*, 10331–10338. (b) Kolsaker, P.; Jensen, A. K. *Acta Chem. Scand., Ser. B* **1988**, *42*, 345–353.

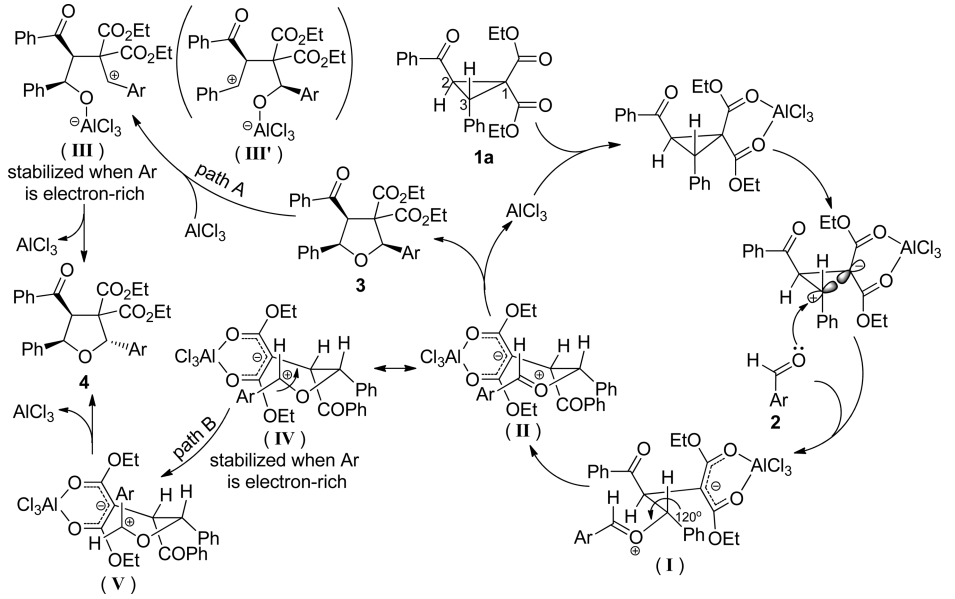
TABLE 3. Cyclopropane Scope in $AlCl_3$-Catalyzed [3 + 2] Cycloaddition of Ar^1CHO[a]



		1					
entry	Ar^1	Ar^2	Ar^3	temp (°C)	time (h)	product[b]	yield[c] (%)
1	C_6H_5 **2a**	C_6H_5	C_6H_5 **1a**	0	19	**3aa**	87
2	C_6H_5 **2a**	4-BrC_6H_4	C_6H_5 **1b**	0	55	**3ba**	60
3	C_6H_5 **2a**	4-MeC_6H_4	C_6H_5 **1c**	0	80	**3ca**	56
4	4-ClC_6H_4 **2b**	4-MeC_6H_4	C_6H_5 **1c**	0	84	**3cb**	55
5	3,4-$(MeO)_2C_6H_3$ **2h**	4-MeC_6H_4	C_6H_5 **1c**	30	120	**4ch**	29
6	C_6H_5 **2a**	4-$MeOC_6H_4$	C_6H_5 **1d**	0	60	**3da**	21
7	C_6H_5 **2a**	C_6H_5	4-ClC_6H_4 **1e**	0	60	**3ea**	45
8	C_6H_5 **2a**	C_6H_5	4-ClC_6H_4 **1e**	30	46	**3ea**	33
9	4-ClC_6H_4 **2b**	C_6H_5	4-ClC_6H_4 **1e**	0	100	**3eb**	67
10	C_6H_5 **2a**	C_6H_5	3,4-$(MeO)_2C_6H_3$ **1f**	0	53	**7f**	18
11	4-ClC_6H_4 **2b**	C_6H_5	3,4-$(MeO)_2C_6H_3$ **1f**	0	50	**7f**	32
12	3,4-$(MeO)_2C_6H_3$ **2h**	C_6H_5	3,4-$(MeO)_2C_6H_3$ **1f**	30	100	**5fh**	19

[a]The reaction was conducted with 0.3 mmol of **1**. [b]Only the major product was shown. [c]Isolated yield.

SCHEME 1. Possible Mechanism for the Reaction



is stabilized by the strong electron-donating substituents (Scheme 1, path A),[8,4d,13] with the assistance of $AlCl_3$ to generate the thermodynamically more stable *trans* product **4**. However, the complete absence of the product derived from (**III′**) indicates the possibility of an alterative pathway for this reaction. This latter one[14] involves the bond rotation of the resonance structure (**IV**) of the intermediate (**II**) favored by electron-rich Ar groups, and the subsequent cyclization to give **4** (Scheme 1, path B).

Conclusion

In summary, we have developed a $AlCl_3$-catalyzed [3 + 2] cycloaddition reaction of 2,3-disubstituted D−A cyclopropane 1,1-diesters with aromatic aldehydes. The facile synthesis of 2,5-diaryl-3,3,4-trisubstituted tetrahydrofurans from

(13) In a control experiment, the 2,5-*cis* product **3af** was subjected to the similar reaction conditions (30 °C, 0.5 equiv of $AlCl_3$, 5 equiv of 4-methylbenzaldehyde, in CD_2Cl_2), and it was converted to the desired 2,5-*trans* product **4af** as the major product along with a small amount of **5af** (**4af**: **5af** = 4:1) as monitored by ^1H NMR analyses (4 h, >90% conversion). For detailed information see the Supporting Information (S58−S59).

(14) We thank one of the reviewers for proposing this mechanism.

easily available reactants and inexpensive catalyst has been achieved in moderate to good yield with excellent regioselectivity and diastereoselectivity.

Experimental Section

General Procedure for the Cycloaddition Reaction. To a solution of 2,3-*trans*-disubstituted cyclopropane-1,1-diesters **1** (0.3 mmol) and aromatic aldehydes (1.5 mmol) in 10.0 mL of dichloromethane was added $AlCl_3$ (0.15 mmol) at 0 or 30 °C. The reaction mixture was stirred at 0 or 30 °C and monitored by TLC. Upon completion, the reaction mixture was passed through a small plug of silica, eluting with 20 mL of CH_2Cl_2, and the solvent was removed under vacuum. ^{1}H NMR analyses of the unpurified products gave the diastereomeric ratio. The crude products were purified by flash chromatography (silica gel, petroleum ether/ethyl acetate = 20/1 to 10/1, v/v) to give the pure products.

Diethyl *r*-4-benzoyl-*c*-2,*c*-5-diphenyltetrahydrofuran-3,3-dicarboxylate (3aa): white solid; mp 103−104 °C; IR (KBr, cm^{-1}) ν 1728, 1695, 1595, 1580, 1497, 1449, 1099, 1020, 764, 698; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.85 (d, J = 7.4 Hz, 2H), 7.55 (d, J = 8.2 Hz, 2H), 7.45−7.30 (m, 6H), 7.26−7.18 (m, 2H), 7.14−7.00 (m, 3H), 5.53 (s, 1H), 5.39 (d, J = 6.4 Hz, 1H), 5.19 (d, J = 6.4 Hz, 1H), 4.50−4.31 (m, 2H), 3.73−3.57 (m, 2H), 1.36 (t, J = 7.2 Hz, 3H), 0.71 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 197.1, 170.5, 166.2, 138.3, 137.2, 135.9, 132.2, 128.5, 128.0, 127.9, 127.7, 127.6, 127.5, 126.7, 84.9, 81.5, 68.8, 62.6, 61.1, 58.0, 14.0, 13.2; HRMS (ESI) calcd for $C_{29}H_{29}O_6$ ($[M + H]^+$) 473.1964, found 473.1965. Anal. Calcd for $C_{29}H_{28}O_6$ (472.53): C, 73.71; H, 5.97. Found: C, 73.49; H, 5.99.

Diethyl *r*-4-benzoyl-*t*-2,*c*-5-diphenyltetrahydrofuran-3,3-dicarboxylate (4aa): white solid; mp 146−147 °C; IR (KBr, cm^{-1}) ν 1753, 1732, 1672, 1593, 1495, 1454, 1447, 1092, 1045, 773, 700; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.64 (d, J = 7.2 Hz, 2H), 7.48−7.43 (m, 2H), 7.38−7.23 (m, 6H), 7.22−7.15 (m, 2H), 7.06−6.93 (m, 3H), 6.56 (s, 1H), 6.28 (d, J = 6.3 Hz, 1H), 5.18 (d, J = 6.3 Hz, 1H), 4.04 (q, J = 7.2 Hz, 2H), 3.79 (dq, J = 7.1, 3.5 Hz, 1H), 3.48 (dq, J = 7.1, 3.5 Hz, 1H), 0.97 (t, J = 7.1 Hz, 3H), 0.77 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 199.2, 169.0, 168.3, 139.2, 137.7, 137.1, 132.6, 128.0, 127.95, 127.9, 127.8, 126.9, 126.6, 84.8, 84.75, 70.3, 62.0, 61.6, 59.0, 13.6, 13.3; HRMS (ESI) calcd for $C_{29}H_{29}O_6$ ($[M + H]^+$) 473.1964, found 473.1960. Anal. Calcd for $C_{29}H_{28}O_6$ (472.53): C, 73.71; H, 5.97. Found: C, 73.62; H, 5.99.

Diethyl *r*-4-benzoyl-*t*-2,*t*-5-diphenyltetrahydrofuran-3,3-dicarboxylate (5aa): white solid; mp 106−107 °C; IR (KBr, cm^{-1}) ν 1751, 1720, 1678, 1597, 1582, 1495, 1472, 1450, 1082, 1055, 1030, 770, 750, 696; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.85−7.79 (m, 2H), 7.65−7.60 (m, 2H), 7.54−7.47 (m, 3H), 7.40−7.24 (m, 8H), 6.01 (s, 1H), 5.31 (d, J = 8.9 Hz, 1H), 5.23 (d, J = 8.9 Hz, 1H), 4.04 (dq, J = 7.2, 3.5 Hz, 1H), 3.86 (dq, J = 7.2, 3.6 Hz, 1H), 3.79 (dq, J = 7.2, 3.5 Hz, 1H), 3.32 (dq, J = 7.2, 3.5 Hz, 1H), 0.82 (t, J = 7.2 Hz, 3H), 0.70 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 199.4, 168.9, 168.0, 138.7, 137.5, 136.9, 133.6, 128.7, 128.62, 128.59, 128.5, 128.3, 127.9, 127.3, 126.7, 85.5, 85.1, 70.8, 62.0, 61.5, 59.6, 13.2; HRMS (ESI) calcd for $C_{29}H_{29}O_6$ ($[M + H]^+$) 473.1964, found 473.1961. Anal. Calcd for $C_{29}H_{28}O_6$ (472.53): C, 73.71; H, 5.97. Found: C, 73.73; H, 5.94.

Diethyl 2-(1-benzoyl-2-chloro-2-phenylethyl)malonate (6a): white solid; mp 104−105 °C; IR (KBr, cm^{-1}) ν 1740, 1719, 1678, 1597, 1495, 1452, 1022, 758, 696; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (d, J = 7.5 Hz, 2H), 7.56−7.22 (m, 8H), 5.33 (d, J = 8.1 Hz, 1H), 4.989 (t, J = 8.1 Hz, 1H), 4.15−3.82 (m, 5H), 1.20−1.10 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.7, 167.6, 167.4, 138.0, 133.0, 128.9, 128.7, 128.6, 128.5, 128.3, 128.1, 62.1, 61.9, 53.9, 51.4, 13.8; HRMS (ESI) calcd for $C_{22}H_{24}ClO_5$ ($[M + H]^+$) 403.1312, found 403.1314. Anal. Calcd for $C_{22}H_{23}ClO_5$ (402.87): C, 65.59; H, 5.75. Found: C, 65.44; H, 5.78.

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Supporting Information Available: X-ray structures of **3aa**, **4aa**, **5aa**, **6a**, **3ac**, and **4ag**; characterization data for **3ab**−**3af**, **4af**−**4aj**, **3ba**−**3ea**, **3cb**, **3eb**, **4ch**, **7f**, and **5fh**; copies of ^{1}H, ^{13}C, COSY, and NOESY NMR spectra for all compounds; and crystal data of **3aa**, **4aa**, **5aa**, **6a**, **3ac**, and **4ag** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.