Tetrahedron Letters 52 (2011) 5488–5490

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

DABCO-catalyzed [2+2] cycloaddition reactions of allenoates and trifluoromethylketones: synthesis of 2-alkyleneoxetanes

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ARTICLE INFO

Article history:
Received 22 June 2011
Revised 24 July 2011
Accepted 9 August 2011
Available online 18 August 2011

Keywords:
Lewis base catalysis
Paterno–Buchi reaction
Allenoates
Trifluoromethylketones

ABSTRACT

DABCO was found to be an efficient catalyst for the formal [2+2] cycloaddition reaction of allenoates and trifluoromethylketones (Paterno–Buchi reaction) to give the corresponding 2-alkyleneoxetanes in good yields with good diastereoselectivities.

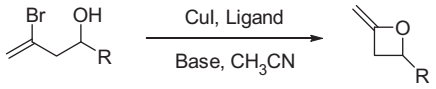
Introduction

Substituted oxetanes present important motifs in a number of natural products and biologically active compounds.[1] In contrast to their homologous heterocycles, such as oxiranes[2], tetrahydrofurans[3] and tetrahydropyrans[4], few methods have been developed for the construction of the strained four-membered ring. Generally, there are two approaches, intra- and intermolecular reactions, for the construction of oxetanes.

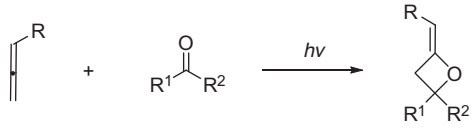
The first intramolecular approach, reported by Hudrlik and Mohtady employed the intramolecular O-alkylation of enolates in 1975.[5] Recently, Li and co-worker reported an efficient 4-*exo*-ring closure of the copper-catalyzed intramolecular coupling of vinyl bromides with alcohols to give 2-methyleneoxetanes (Scheme 1).[6]

The photocycloaddition of allenes and carbonyl compounds is a straightforward intermolecular approach to 2-alkyleneoxetanes (Scheme 2).[7] However, several disadvantages, such as usage of a large excess of allenes, side reaction of further cycloadditions, and poor selectivities, limit its usage in organic synthesis.

Since Lu's pioneering report of the [3+2] cycloaddition of allenoates with olefins,[8] Lewis base-catalyzed [3+2] and [4+2] annulation reactions of allenoates have emerged as powerful tools for the synthesis of cyclic or heterocyclic compounds.[9] In 2003, Shi and co-workers reported an unexpected DABCO-catalyzed [2+2] cycloaddition of allenoates and imines to give azetidine derivatives.[10,11] Recently, we reported the [3+2] and [4+2] annulation of allenoates



Scheme 1. Synthesis of methyloxetanes via copper-catalyzed intramolecular coupling reaction of vinyl bromides with alcohols.



Scheme 2. Synthesis of methyloxenanes via photocycloaddition of allenes and carbonyl compounds.

with trifluoromethyl ketones to give dihydrofurans and dihydropyrans.[12,13] In this Letter, we wish to report a DABCO-catalyzed [2+2] cycloaddition of allenoates and trifluoromethyl ketones to give 2-alkyleneoxetanes. To the best of our knowledge, this is the first example of the Lewis-base-catalyzed [2+2] cycloaddition of allenoates and carbonyl compounds.[14]

Results and discussion

Initially, the model reaction of ethyl allenoate **1a** and trifluoromethyl ketones **2a** was investigated (Table 1). We are happy to find that the [2+2] cycloaddition product of oxetan-2-ylidene **3aa** could

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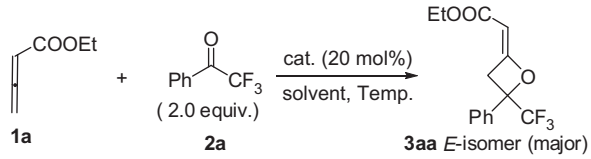
0040-4039/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2011.08.057

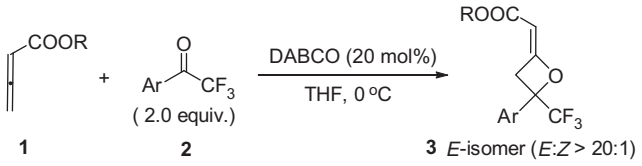
Table 1
Condition screening for the reactions of allenoate **1a** and trifluomethylketone **2a** catalyzed by amines



Entry	Cat.	Solvent	Temp	Time (h)	Yield[a] (%)
1	DMAP	CH_2Cl_2	rt	32	32
2	DABCO	CH_2Cl_2	rt	32	43
3	Qunidine	CH_2Cl_2	rt	52	NP[b]
4	Cinchonine	CH_2Cl_2	rt	52	NP
5	Et_3N	CH_2Cl_2	rt	52	NP
6	DABCO	Toluene	rt	48	Trace
7	DABCO	CH_3CN	rt	48	Trace
8	DABCO	EtOAc	rt	48	29
9	DABCO	THF	rt	48	61
10	DABCO	THF	0 °C	96	78
11	DABCO	THF	Reflux	48	58 (6)[c]

[a] Unless specified, isolated yield of *E*-**3aa** with *E*:*Z* > 20:1.
[b] NP = no product.
[c] Yield of *Z*-**3aa** in parenthesis.

Table 2
Formal [2+2] cycloaddition reaction catalyzed by DABCO



Entry	**1** (R)	**2** (Ar)	Time (d)	**3**	Yield[a] (%)
1	**1a** (Et)	**2a** (Ph)	4	**3aa**	78
2	**1a** (Et)	**2b** (4-MeC_6H_4)	3	**3ab**	74
3	**1a** (Et)	**2c** (4-$MeOC_6H_4$)	3.5	**3ac**	57
4	**1a** (Et)	**2d** (4-ClC_6H_4)	2.5	**3ad**	85
5	**1a** (Et)	**2e** (3-MeC_6H_4)	2.5	**3ae**	73
6	**1a** (Et)	**2f** (2-Thienyl)	3.5	**3af**	47
7	**1b** (Cy)	**2a** (Ph)	3	**3ba**	79
8	**1c** (^{t}Bu)	**2a** (Ph)	3	**3ca**	60

[a] Isolated yield of *E*-isomer with *E*:*Z* > 20:1.

be isolated in reasonable yield with *E*:*Z* > 20:1, when DABCO or DMAP was used as the catalyst for the reaction after 32 h (entries 1 and 2). It is noteworthy that there is no [3+2] cycloaddition or Baylis–Hillmam adduct was observed. Lewis bases screening revealed that qunidine, cinchonine and triethylamine could not catalyze this reaction (entries 3–5). Solvent screening showed that the reaction in THF gave the best yield, while only a trace or low yield was resulted in toluene, acetonitrile or ethyl acetate (entries 6–9). The yield was increased to 78% when the reaction was carried out in 0 °C with prolonged reaction time (entry 10). The reaction in reflux THF gave the *E*-isomer of the cycloadduct in 58% yield along with 6% yield of *Z*-isomer (entry 11).

With the optimized reaction conditions in hand, the reaction scope was then briefly investigated (Table 2). Aryltrifluoromethyl ketones with an electron-withdrawing substituent (Ar = 4-ClC_6H_4) worked better than those with electron-donating substituents (Ar = 4-Me, 4-$MeOC_6H_4$) (entries 2–4). Ketone **2e** with a *m*-methylphenyl group worked to give the corresponding cycloadduct **3ae** in 73% yield (entry 5). Ketone **2f** with a 2-thienyl group also worked well but with low yield (entry 6). When the ethyl group was changed to cyclohexyl or *t*-butyl in substrate **1**, the corresponding [2+2] cycloaddition product could also be isolated in 79% or 60% yield, respectively, (entries 7–8). Unfortunately, no reaction occurred when α-methyl or γ-benzyl allenoate was used, and the reaction with ethyl 3,3,3-trifluoro-2-oxopropanoate gave no desired cycloadduct but a complex.

The structure of the cycloadduct **3ba** was unambiguously established by the X-ray analysis of its crystal (Fig. 1).

The mechanism for this reaction is believed to go with a similar catalytic cycle as the reaction with imines proposed by Shi and coworkers (Fig. 2).[10] The nucleophilic addition of DABCO to allenoate **1** produces the enolate intermediate **A**, which is in resonance with the allylic carbanion **A′**. The γ-addition of **A′** to trifluoromethyl ketone gives the α,β-unsaturated ester **B**, which undergoes an intramolecular Michael addition to give the ring-closed zwitterion **C**. The elimination of catalyst from **C** affords the product and regenerates DABCO.

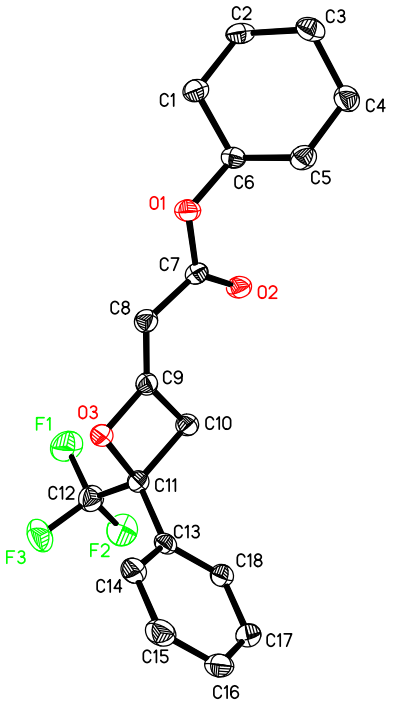


Figure 1. X-ray structure of cycloadduct **3ba**.

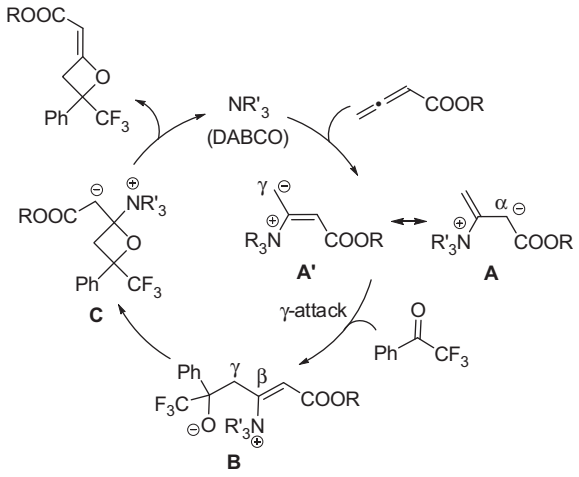


Figure 2. Proposed catalytic cycle.

In conclusion, the DABCO-catalyzed [2+2] cycloaddition of allenoates with trifluoromethylketones was reported, which provides a new catalytic approach to 2-alkyleneoxetanes in good yields with high diastereoselectivities.

Experimental section

Typical procedure for the [2+2] cycloaddition of allenoates with trifluoromethylketones

To a stirred solution of allenoate **1a** (0.5 mmol) and trifluomethylketone **2a** (1.0 mmol) in THF (5 mL) was added DABCO (0.1 mmol). The solution was stirred at 0 °C until the full consumption of the allenoate (2.5–4 days). The reaction mixture was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, typically 50:1–20:1) to furnish the corresponding cycloaddtion product **3aa** in 78% yield. White solid, m.p. 53–54 °C; R_f = 0.3 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.33 (m, 5H), 5.30 (s, 1H), 4.06–4.00 (m, 3H), 3.71–3.65 (m, 1H), 1.14 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.6, 166.8, 133.3, 129.7, 128.6, 126.0, 123.5 (q, J = 282 Hz), 93.5, 86.5 (q, J = 33 Hz), 60.0, 39.2 (q, J = 1.5 Hz), 14.3; IR (KBr): ν 2939, 1720, 1677, 1373, 1273, 1177, 1039, 821, 761, 697 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{13}F_3O_3$ $[M]^+$ 286.0817, found 286.0821.

Acknowledgments

Financial support from the National Science Foundation of China (20932008), the Ministry of Science and Technology of China (2011CB808600) and the Chinese Academy of Sciences are greatly acknowledged.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.08.057.

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