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$Sc(OTf)_3$-catalyzed smooth tandem [3+2] cycloaddition/ring opening of donor–acceptor cyclopropane 1,1-diesters with enol silyl ethers

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ABSTRACT

Catalyzed by Lewis acids, donor–acceptor cyclopropane 1,1-diesters reacted with enol silyl ethers to afford 1,6-dicarbonyl compounds in moderate to excellent yields. This supplied a mild carbon–carbon bond-forming method from the ring opening of cyclopropanes. A smooth tandem [3+2] cycloaddition/ring opening process has been clearly proved by an independent experiment.

Carbon–carbon bond formation and cleavage processes are very important in organic synthesis. Combination of carbon–carbon bond formation and cleavage in one reaction would supply synthetic methodologies for efficient construction of complex carbon skeletons.[1] Because of the high efficiency in construction of complex molecular framework, tandem reactions have attracted particular attention over the past few decades.[2]

Functionalized cyclopropanes have found broad applications in modern organic synthesis owing to the unique reactivity of the cyclopropane moiety.[3] Cycloadditions of cyclopropanes are important in this area. Most of the researches have been focused on the [3+2] cycloadditions of electro-withdrawing group (EWG)-activated cyclopropanes, especially the donor–acceptor cyclopropanes (D/A CPs, Scheme 1: **A**, **B** and **C**) with various dienophiles.[3c,d,4] Among these examples, the donor–acceptor cyclopropane 1,1-diesters (D/A CP diesters, Scheme 1: **B**), in which the donors were aryls (at C2-position of cyclopropane moiety), have attracted more attention in recent years, because they were easily available and reactive to a large range of 1, *n*-dipoles including the aforementioned [3+2] cycloadditions, [3+3] cycloadditions with nitrones[5] and azomethine imines,[6] and [4+3] cycloadditions with isobenzofuran[7] to efficiently construct 5 to 7-membered carbocycles or heterocycles. During our study on tandem and cycloaddition reactions of D/A CP 1,1-diesters (Scheme 1: **B**), we found a new tandem [3+2] cycloaddition/ring opening reaction. Catalyzed by Lewis acids, such D/A CP 1,1-diesters reacted with enol silyl ethers to afford 1,6-dicarbonyl compounds under mild conditions in moderate to excellent yields. Mechanism study clearly demonstrated a smooth tandem process. To the best of our knowledge, this is the first [3+2] cycloaddition examples of 1,1-di-EWG-activated cyclopropanes with enol silyl ethers, and the first tandem [3+2] cycloaddition/ring opening process of EWG-activated cyclopropanes with a clear tandem sequence. This reaction can also be thought as a formal homologous Mukaiyama Michael addition. Comparing to the reported nucleophilic ring opening of EWG-activated cyclopropanes,[3,8] this supplied a mild and efficient carbon–carbon bond-forming method with enol silyl ethers as the nucleophiles and $Sc(OTf)_3$ as a Lewis acid. We report herein our recent results.

Several groups have reported the reactions of D/A CP (alkoxyl or siloxyl as the donor) and enol silyl ethers catalyzed by strong Lewis acids or Bronsted acids.[3c,d] Two types of products were obtained in these reactions: the ring ones (5-carbon ring skeleton) by the [3+2] cycloadditions and/or the chain ones. An accepted tandem cyclopropane polarization/intermolecular Mukaiyama Aldol/intramolecular Aldol mechanism was proposed (Scheme 1): under the catalysis of Lewis acids, a separated 1,3-dipole was generated from the polarization of cyclopropane ring and the carbocation could be stabilized by the adjacent oxygen atom to form the oxonium. After the nucleophilic addition of enol silyl ether to the oxonium (a homo Mukaiyama Aldol), the chain product was produced and the ring product was constructed by the subsequent intramolecular Aldol. We noticed that in the aforementioned D/A CP, there was only one EWG as the acceptor and the donor(s) was (were)

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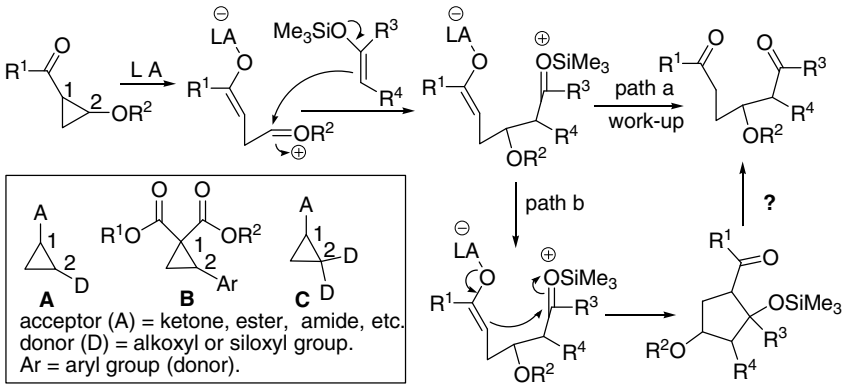
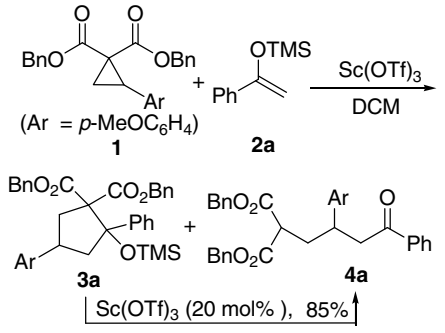


Scheme 1. Some typical examples of D/A CP and the proposed mechanism for [3+2] cycloaddition of D/A CP (A) in references.

one or two alkoxyl (siloxyl) group(s) (Scheme 1: **A** and **C**). There was no distinct evidence for the conversion of ring products to chain products through ring opening process.

We selected the reaction of D/A CP 1,1-diester **1** (1.0 equiv) and enol silyl ether **2a** (1.5 equiv) in our initial investigation (Scheme 2). $Sc(OTf)_3$ (20 mol %) was selected as the Lewis acid and the reaction was run in dichloromethane (DCM). As expected from the aforementioned mechanism, both of the ring product (**3a**) (by a [3+2] cycloaddition) and the chain product **4a**[9] were observed. However, it was noticed that when the reaction time was prolonged, the amount of **3a** was gradually decreased and the amount of **4a** was gradually increased. At the end of the reaction, **4a** was obtained as almost the exclusive product. This phenomenon strongly supported a smooth tandem [3+2] cycloaddition/ring opening process (Scheme 3), which was quite different from the reported one (Scheme 1). In order to confirm this, an independent experiment was carried out and it was found that under the same condition **3a** could be smoothly transformed into **4a** in a yield of 85%.

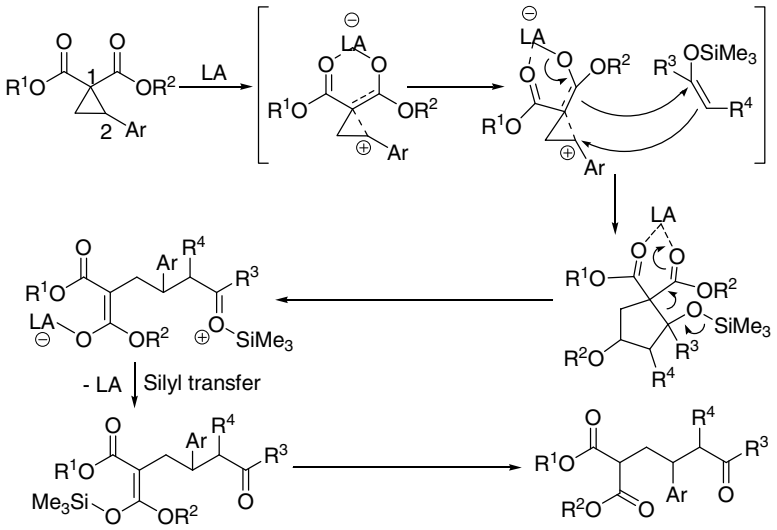


Scheme 2.

Several other Lewis acids (e.g., $Yb(OTf)_3$, $Cu(OTf)_2$, $Zn(OTf)_2$, $Sn(OTf)_2$ and $SnCl_4$) in different solvents (e.g., 1,2-dichloroethane, DMF, toluene, THF and acetonitrile) have been screened (see Supplementary data), and $Sc(OTf)_3$ (20 mol %) in DCM was chosen as the optimized conditon[10] for further investigation.

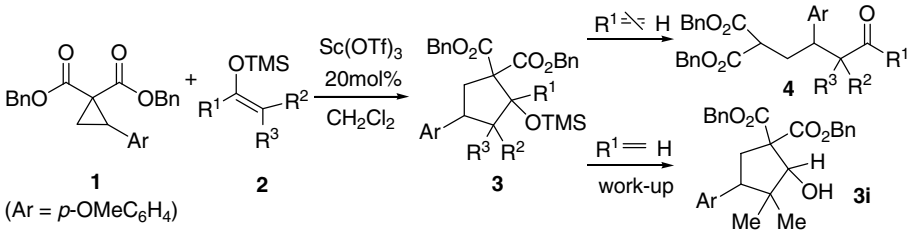
Scope of the substrates was studied next. Reactions of cyclopropane **1** (1.0 equiv) and various enol silyl ethers **2** (1.5 equiv)[11] were carried out, and the results are summarized in Table 1. It was found that except the ketene acetal **2e,** most of the products were formed in moderate to excellent yields. The result of **2j** was complex. In order to determine the stereochemistries of the [3+2] cycloaddition products, reaction of **1** and **2a** was stopped midway and **3a** was separated. NOESY experiment confirmed **3a** as a sole cis-isomer (Fig. 1). Compounds **4b**, **4g**, **4h**, and **3i** were mixtures of two stereomers which were unable to be separated.

It was worth to note that reaction of **2i** (R^1 = H) and **1** afforded the product **3i** that was supposed to be obtained by the hydrolysis



Scheme 3. Proposed mechanism for the smooth tandem [3+2]/ring opening reaction.

Table 1
$Sc(OTf)_3$-catalyzed tandem [3+2]/ring opening reactions of **1** and various enol silyl ethers **2**



Entry	Substrate	R^1	R^2	R^3	Product	Yield[a] (%)
1	**2a**	C_6H_5	H	H	**4a**	94
2	**2b**	C_6H_5	CH_3	H	**4b**	99[b]
3	**2c**	CH_3	H	H	**4c**	92
4	**2d**	*i*-butyl	H	H	**4d**	90
5	**2e**	OEt	H	H	**4e**	22
6	**2f**	styryl	H	H	**4f**	87
7	**2g**	R^1R^3 C_4H_8	H		**4g**	60[b]
8	**2h**	R^1R^3 C_3H_6	H		**4h**	95[b]
9	**2i**	H	CH_3	CH_3	**3i**	78
10	**2j**	CH_3	CO_2Et	H	**4j**	Complex

[a] Yields of the isolated products.
[b] A mixture of two stereomers.

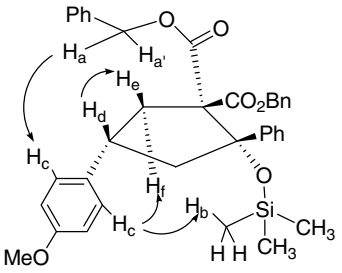
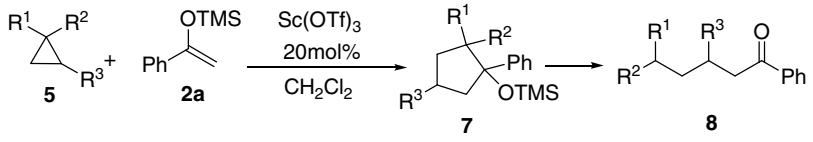


Figure 1. 2DNOESY correlation for compound **3a**.

of the [3+2] cycloaddition product in the work-up process. This is the only example of cyclopropane 1,1-diester **1** and enol silyl ethers, in which the reaction stopped in the [3+2] stage.

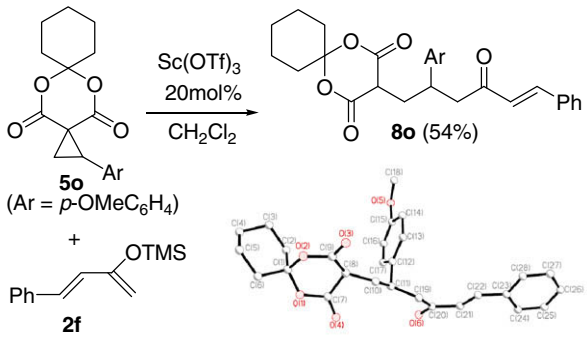
Further investigations were expanded for reactions of substrate **2a** and various EWG-activated cyclopropanes **5**[12] (Table 2). When the donors were substituted phenyl groups, reactions of the cyclopropane 1,1-diesters (**1** and **5b**–**h**) gave moderate to excellent yields. In these examples, electron-donating-group-substituted phenyls gave relatively higher yields, and electron-withdrawing-group-substituted phenyls gave relatively lower yields. In case of strong electron-withdrawing group (nitro group), 40 mol % of $Sc(OTf)_3$ and higher reaction temperature were needed to promote the reaction. Reaction between **2a** and vinyl cyclopropane diester (**5i**) gave complex result and only 29% of the product was obtained. When the donor was isopropyl or hydrogen, the desired products were not observed. Different from the case of the D/A CP 1,1-diesters, cyclopropane β-keto esters (**5l** and **5m**) afforded only [3+2] cycloaddition products in lower yields. It should also be noted that the reaction of mono-EWG-activated D/A CP ketone (**5n**) with **2a** still proceeded successfully to afford the chain product (61%).

Table 2
$Sc(OTf)_3$-catalyzed ring opening reactions of **2a** and substituted cyclopropanes **5**



Entry	Substrate	R^1	R^2	R^3	Product	Yield[a] (%)
1	**1**	CO_2Bn	CO_2Bn	4-$MeOC_6H_4$	**4a**	94
2	**5b**	CO_2Bn	CO_2Bn	4-MeC_6H_4	**8b**	92
3	**5c**	CO_2Bn	CO_2Bn	C_6H_5	**8c**	87
4[c]	**5d**	CO_2Bn	CO_2Bn	4-$NO_2C_6H_4$	**8d**	73 (95)[b]
5	**5e**	CO_2Bn	CO_2Bn	3-$MeOC_6H_4$	**8e**	87
6	**5f**	CO_2Bn	CO_2Bn	2-ClC_6H_4	**8f**	64
7	**5g**	CO_2Me	CO_2Me	4-$MeOC_6H_4$	**8g**	85
8	**5h**	CO_2Et	CO_2Et	4-$MeOC_6H_4$	**8h**	78
9	**5i**	CO_2Et	CO_2Et	Vinyl	**8i**	29
10	**5j**	CO_2Bn	CO_2Bn	*i*-Propyl	**NR**	0
11	**5k**	CO_2Bn	CO_2Bn	H	**NR**	0
12	**5l**	CO_2Et	$COCH_3$	C_6H_5	**7l**	19
13	**5m**	CO_2Et	COC_6H_5	C_6H_5	**7m**	24
14[c]	**5n**	H	COC_6H_5	4-$MeOC_6H_4$	**8n**	61

[a] Yields of the isolated products.
[b] Isolated yield based on the conversion of **5d**.
[c] 40 mol % of $Sc(OTf)_3$, 1,2-dichloroethane, 2.0 equiv of **2**: 0 °C for 10 min, 40–45 °C for 4 h, room temperature overnight.



Scheme 4. Preparation of compound **8o** and its X-ray structure.

In order to identify the structure of the final chain products, compound **8o** was prepared by the reaction of **5o** and diene **2f**. The structure of **8o** was confirmed by single-crystal X-ray diffraction analysis[13] (Scheme 4).

In conclusion, we have developed a smooth tandem [3+2]/ring opening reaction between D/A CP 1,1-diesters and enol silyl ethers to afford 1,6-dicarbonyl compounds under the catalysis of $Sc(OTf)_3$. This is the first [3+2] cycloaddition reaction of cyclopropane 1,1-diesters with enol silyl ethers and supplied a mild carbon–carbon bond-forming method by a formal homologous Mukaiyama Michael addition. Mechanism study has proved for the first time a tandem cycloaddition sequence of EWG-activated cyclopropane.

Acknowledgements

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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.2008.09.028.

References and notes

1. (a) Trost, B. M.; Fleming, I. In *Comprehensive Organic Synthesis*; Pergamon: Oxford, 1991; Vol. 3. pp 705–1014; (b) Trost, B. M.; Fleming, I. In *Comprehensive Organic Synthesis*; Pergamon: Oxford, 1991; Vol. 3. pp 785–1035; Intermolecular reaction including carbon–carbon bond formation and ring cleavage: c Karim, M. R.; Sampson, P. *Tetrahedron Lett.* **1988**, *29*, 6897.
2. For some reviews of tandem domino reactions, please see: (a) Tietze, L. F.; Beifuss, U. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 131; (b) Tieze, L. F. *Chem. Rev.* **1996**, *96*, 115; (c) Parsons, P. J.; Penkett, C. S.; Shell, A. J. *Chem. Rev.* **1996**, *96*, 195; (d) Bunce, R. A. *Tetrahedron* **1995**, *51*, 13103; (e) Nicolaou, K. C.; Edmonds, D. J.; Bulger, P. G. *Angew. Chem., Int. Ed. Engl.* **2006**, *45*, 7134; (f) Pellissier, H. *Tetrahedron* **2006**, *62*, 1619; (g) Pellissier, H. *Tetrahedron* **2006**, *62*, 2143.
3. For reviews, please see: (a) Danishefsky, S. *Acc. Chem. Res.* **1979**, *12*, 66; (b) Wong, H. N. C.; Hon, M.-Y.; Tse, C.-W.; Yip, Y.-C. *Chem. Rev.* **1989**, *89*, 165; (c) Reissig, H.-U.; Zimmer, R. *Chem. Rev.* **2003**, *103*, 1151; (d) Yu, M.; Pagenkopf, B. L. *Tetrahedron* **2005**, *61*, 321; (e) Wenkert, E. *Acc. Chem. Res.* **1980**, *13*, 27; (f) Kulinkovich, O. G. *Chem. Rev.* **2003**, *103*, 2597; (g) Paquette, L. A. *Chem. Rev.* **1986**, *86*, 733; (h) Reissig, H. U. *Top. Curr. Chem.* **1988**, *144*, 73; (i) Rubin, M.; Rubina, M.; Gevorgyan, V. *Chem. Rev.* **2007**, *107*, 3117.
4. Some recent examples: (a) Venkatesh, C.; Singh, P. P.; Ila, H.; Junjappa, H. *Eur. J. Org. Chem.* **2006**, 5378; (b) Bajtos, B.; Yu, M.; Zhao, H.; Pagenkopf, B. L. *J. Am. Chem. Soc.* **2007**, *129*, 9631; (c) Takasu, K.; Nagao, S.; Ihara, M. *Adv. Synth. Catal.* **2006**, *348*, 2376; (d) Shi, M.; Yang, Y.-H.; Xu, B. *Tetrahedron* **2005**, *61*, 1893; (e) Pohlhaus, P. D.; Johnson, J. S. *J. Org. Chem.* **2005**, *70*, 1057; (f) Gupta, A.; Yadav, V. K. *Tetrahedron Lett.* **2006**, *47*, 8043; (g) Sliwinska, A.; Czardybon, W.; Warkentin, J. *Org. Lett.* **2007**, *9*, 695; (h) Carson, C. A.; Kerr, M. A. *J. Org. Chem.* **2005**, *70*, 8242; (i) Kang, Y.-B.; Tang, Y.; Sun, X.-L. *Org. Bioorg. Chem.* **2006**, 299; (j) Christie, S. D. R.; Davoile, R. J.; Jones, R. C. F. *Org. Bioorg. Chem.* **2006**, 2683; (k) Morra, N. A.; Morales, C. L.; Bajtos, B.; Wang, X.; Jang, H.; Wang, J.; Yu, M.; Pagenkopf, B. L. *Adv. Synth. Catal.* **2006**, *348*, 2385; (l) Korotkov, V. S.; Larionov, O. V.; Hofmeister, A.; Magull, J.; de Meijere, A. *J. Org. Chem.* **2007**, *72*, 7504; (m) Korotkov, V. S.; Larionov, O. V.; de Meijere, A. *Synthesis* **2006**, *21*, 3542.
5. (a) Young, I. S.; Kerr, M. A. *Angew. Chem., Int. Ed.* **2003**, *42*, 3023; (b) Young, I. S.; Kerr, M. A. *Org. Lett.* **2004**, *6*, 139; (c) Sibi, M. P.; Ma, Z.; Jasperse, C. P. *J. Am. Chem. Soc.* **2005**, *127*, 5764; (d) Sapeta, K.; Kerr, M. A. *J. Org. Chem.* **2007**, *72*, 8597; (e) Kang, Y.-B.; Sun, X.-L.; Tang, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 3918.
6. Perreault, C.; Goudreau, S. R.; Zimmer, L. E.; Charette, A. B. *Org. Lett.* **2008**, *10*, 689.
7. Ivanova, O. A.; Budynina, E. M.; Grishin, Y. K.; Trushkov, I. V.; Verteletskii, P. V. *Angew. Chem., Int. Ed.* **2008**, *47*, 1107.
8. (a) Du, D.; Wang, Z. *Tetrahedron Lett.* **2008**, *49*, 956. and references cited therein; (b) Yang, Y.-H.; Shi, M. *Org. Lett.* **2006**, *8*, 1709; (c) Shi, M.; Tang, X.-Y.; Yang, Y.-H. *J. Org. Chem.* **2008**, *73*, 5311; (d) Shi, M.; Tang, X.-Y.; Yang, Y.-H. *Org. Lett.* **2007**, *9*, 4017.
9. *Physical data for compound* **4a**: Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56 (d, J = 7.2 Hz, 2H), 7.42 (t, J = 7.2 Hz, 1H), 7.28–7.33 (m, 2H), 7.17–7.25 (m, 8H), 7.08–7.14 (m, 2H), 6.97 (d, J = 8.7 Hz, 2H), 6.68 (d, J = 8.7 Hz, 2H), 5.07 (dd, J = 12.3 Hz, J = 12.3 Hz, 2H), 4.89 (dd, J = 12.3 Hz, J = 12.3 Hz, 2H), 3.63 (S, 3H), 3.13–3.28 (m, 4H), 2.31–2.40 (m, 1H), 2.09–2.19 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.2, 169.2, 169.1, 158.6, 137.2, 135.6, 135.5, 134.6, 133.2, 128.9, 128.7, 128.5, 128.2, 114.2, 67.3, 67.2, 55.4, 50.4, 46.1, 38.5, 35.5; HRMS (ESI) calcd for $C_{34}H_{32}O_6$ $(M+Na)^+$: 559.2091, found 559.2100; IR (film): ν 3061, 3034, 2958, 2931, 2911, 2836, 1739, 1678, 1613, 1514, 1448, 1378, 1338, 1251, 1233, 1146, 1030, 984, 912, 822, 740, 731.
10. *Typical procedure for the tandem [3+2] cycloaddition/ring opening process of functionalized cyclopropanes and enol silyl ethers*: A 25 mL three-necked flask was charged with $Sc(OTf)_3$ (20 mol %) and heated to 120 °C for 1 h under N_2. After the flask was cooled to 0 °C, a solution of cyclopropane (0.3 mmol) in 1 mL of dry CH_2Cl_2 was added. The mixture was stirred for 15 min at 0 °C. A solution of enol silyl ether (0.45 mmol) in 1 mL of dry CH_2Cl_2 was added dropwise to the flask over 2 min. After being stirred at 0 °C for 10 min, the mixture was gently warmed to room temperature and stirred overnight. Solvent was evaporated in vacuo and the residue was purified by flash chromatography on silica gel to afford the product.
11. (a) Cazeau, P.; Duboudin, F.; Moulines, F.; Babot, O.; Dunogues, J. *Tetrahedron* **1987**, *43*, 2075; (b) Walshe, N. D. A.; Goodwin, G. B. T.; Smith, G. C.; Woodward, F. E. *Org. Synth.* **1993**, *8*, 1; (c) Duhamel, P.; Hennequin, L.; Poirier, J. M.; Tavel, G.; Vottero, C. *Tetrahedron* **1986**, *42*, 4777.
12. (a) Mapelli, C.; Turocy, G.; Switzer, F. L.; Stammer, C. H. *J. Org. Chem.* **1989**, *54*, 145; (b) Wolfe, S.; Ro, S.; Kim, C.-K.; Shi, Z. *Can. J. Chem.* **2001**, *79*, 1238.
13. The crystallographic data (excluding structure factors) of **8o** have been deposited with the Cambridge Crystallographic Data Center as Supplementary Publication No. CCDC 686008. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).