Diastereoselection During Allylindium Addition to Norbornyl α-Diketones

Faiz A. Khan*[a] and Jyotirmayee Dash[a]

Keywords: Allylation / Diastereoselectivity / α-Diketones / Indium / Regioselectivity

We report a highly regio- and diastereoselective allylindium addition to norbornyl α-diketones that leads to acyloins. The diastereoselection in the case of monosubstituted derivatives greatly depends on the nature of the 5-*endo* substituents. Non-chelating groups direct the addition from the sterically less congested *exo*-face, diagonal to the substituent, while chelating substituents, such as an alkoxy or acetoxy units, induce a complete reversal in the selectivities. The presence of an oxygen atom directly linked to the norbornyl framework is crucial for eliciting a chelating effect because an acetoxymethyl (–CH_2OAc) group exhibits normal behavior and acts as a non-chelating group. The dramatic influence (reversal) of an apparently innocuous *exo*-Me substituent is noted.

Introduction

The study of indium-mediated Barbier-type reactions that form carbon−carbon bonds has emerged as one of the most exciting areas of research in organic synthesis.[1,2] Since its discovery by Butsugan,[3] the allylindium addition to carbonyl compounds has found wide-ranging current interest; generally it proceeds with high levels of chemo-, regio-, and diastereoselectivity.[1] The regio- and diastereoselectivity in allylindium addition is a topic of continuing discussion.[2,4] There are, however, few reports on allylindium addition to α-diketones.[5,6] As part of a program designed to explore the intriguing chemistry of norbornyl α-diketones,[7] and in continuation of our work on indium-mediated reactions,[7b,8] we have studied the impact of chelating and non-chelating 5-*endo* substituents on the stereochemical outcome during allylindium addition in these systems. We have found that allylindium addition to norbornyl α-diketones is a highly regio- and diastereoselective process that leads to excellent yields of acyloins. Interestingly, we have observed a complete reversal in diastereoselection upon switching to oxygenated 5-*endo*-substituents that are connected to the norbornyl framework directly through an oxygen atom.

Results and Discussion

The reaction is particularly interesting for monosubstituted diketones **1a**−**f** and **2a**,**b**,**d**,**f**; it leads to the corresponding two diastereoisomeric allylation products **3** and **4** for chloro derivatives and **5** and **6** for bromo derivatives (Scheme 1, Table 1). Unlike indium-mediated reductions of norbornyl α-diketones,[7b] where the reduction occurs such as to furnish both possible regioisomers, **7** (major) and **8**, but with the exclusive formation of *endo*-acyloins (*endo*-hydroxy groups), the coupling of the allylindium reagent is highly regioselective. The reagent adds predominantly to the less-congested carbonyl group, diagonal to the *endo* substituent.

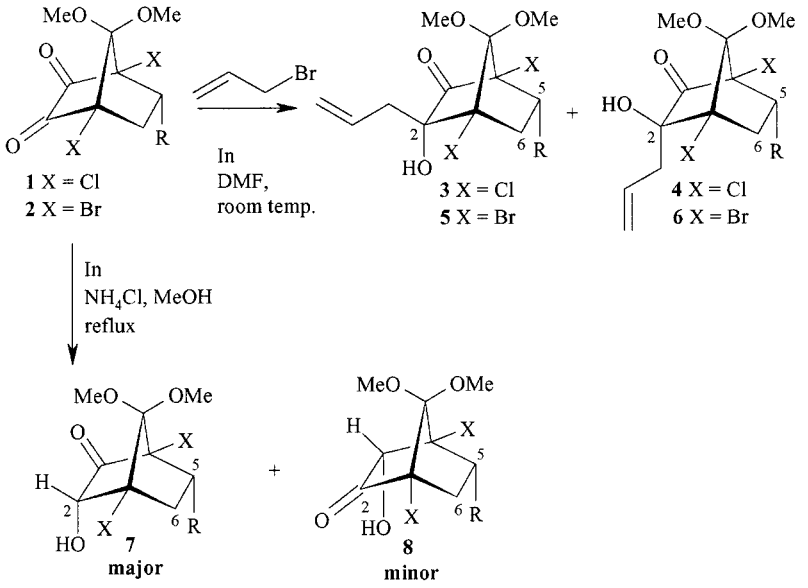
The diastereoselectivities of the reactions are greatly dependent on the *endo* substituents (Table 1). While allylindium addition takes place exclusively from the *endo* face in the case of camphorquinone,[6b] *exo* addition is favored, interestingly, in the cases of **1a**, **2a**, **1c**, and **1e** and leads to the corresponding *endo* alcohols **3** and **5** as the major products (Table 1).

A complete reversal of product stereoselectivity was observed when allylindium addition was performed with 5-*endo* ethoxy (**1b** and **2b**) and 5-*endo* acetoxy (**1d** and **2d**) derivatives. The product distributions in these cases favor of *exo* isomers **4** and **6**, which suggests a chelation-controlled mechanism (Entries 4, 5, 7−9, and 11−14; Table 1). Furthermore, the reversal in selectivity was induced only by a substituent directly attached through an oxygen atom, e.g., for OAc but not for CH_2OAc (Entries 10 and 11; Table 1). The allylations involving 5-*endo* methyl ester derivatives **1f** and **2f** were not selective giving **3f/4f** and **5f/6f** in nearly 1:1 ratios. The presence of water and other additives, such as 10% HCl or LiF, do not seem to alter the diastereoselection (Entries 2, 3, 5, 8, 9, 12, and 14).

The stereochemical assignments are based on extensive analysis of NMR spectroscopic data. The diagnostic effect of an *endo*-OH unit at C-2 on the *endo*-6-H proton was quite revealing. The *endo*-6-H proton was significantly de-

[a] Department of Chemistry, Indian Institute of Technology, Kanpur-208 016, India
Fax: (internat.) +91-512-2597436
E-mail: faiz@iitk.ac.in
Supporting information for this article is available on the WWW under http://www.eurjoc.org or from the author.

  DOI: 10.1002/ejoc.200400044



Scheme 1. Indium-mediated allylation and reduction of diketones **1** and **2**

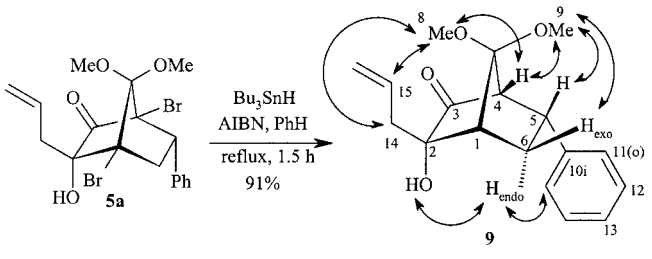
Table 1. Indium-mediated allylation of monosubstituted α-diketones

Entry[a]	Substrate	R	Time (h)	Yield (%)[b]	Product ratio (*endo*:*exo*)[c] (for X = Cl, **3:4,** for X = Br, **5:6**)
1	**1a**, X = Cl	Ph	4	94	82:18
2			3	91	84:16[f]
3			5	92	84:16[e]
4	**1b**, X = Cl	OEt	3.5	93	14:86
5			9	94	14:86[f]
6	**2a**, X = Br	Ph	6	93	89:11
7	**2b**, X = Br	OEt	5	94	18:82
8			8	91	25:75[d]
9			8	93	17:83[g]
10	**1c**, X = Cl	CH_2OAc	1.5	71	77:23
11	**1d**, X = Cl	OAc	5	92	23:77
12			5	93	25:75[g]
13	**2d**, X = Br	OAc	5	91	25:75
14			5	90	25:75[g]
15	**1e**, X = Cl	$SiMe_3$	5	91	91:9
16	**1f**, X = Cl	CO_2Me	6	92	43:57
17	**2f**, X = Br	CO_2Me	5	94	45:55

[a] All reactions were performed using 2 equiv. of indium metal and vigorously stirring it with allyl bromide in DMF. [b] Isolated yields of analytically pure alcohols. [c] The product distributions in all cases were determined by integrating 400-MHz ^1H NMR spectra of the unpurified product mixtures. [d] DMF/10% HCl (2:1). [e] DMF, LiF. [f] THF/H_2O (1:1). [g] DMF/H_2O (1:1).

shielded (0.5−0.7 ppm) while the *exo*-6-H proton consistently experienced shielding (0.2−0.3 ppm).[9] Further structural proof came from 2D NMR spectra (COSY, NOESY, HMBC, and HMQC) of the bridgehead-reduced carbinol **9** obtained from **5a** (Scheme 2). The reduction of **5a** using Bu_3SnH in benzene was performed purposely to observe further couplings of the bridgehead hydrogen atom.

The shielding effect of a vicinal $SiMe_3$ group overrides the deshielding effect of an *endo*-OH group on protons attached to C-6. As a result of these conflicting effects, unambiguous identification of the major *endo* alcohol was not possible from NMR spectroscopic data alone. Therefore, we performed an X-ray crystallographic analysis of **3e** (Fig-



Scheme 2. Bu_3SnH-mediated reduction of bridgehead bromine atoms; NOESY correlations in **9**: *exo*-6-H/5-H (*cis*), 4-H/5-H, *endo*-6-H/1-H, *endo*-6-H/OH, *endo*-6-H/11-H(o), 9-H/5-H, 9-H/*exo*-6-H, 9-H/4-H, 8-H/14-Ha,b, 8-H/15-H, 8-H/4-H; W-coupling of 1.9 Hz between 4-H and *exo*-6-H.

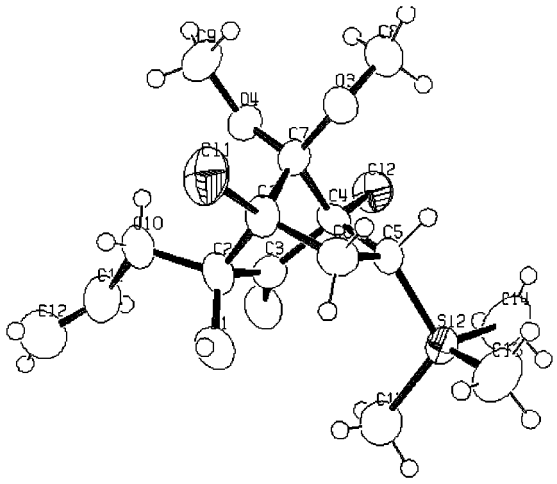


Figure 1. Crystal structure of compound **3e**.

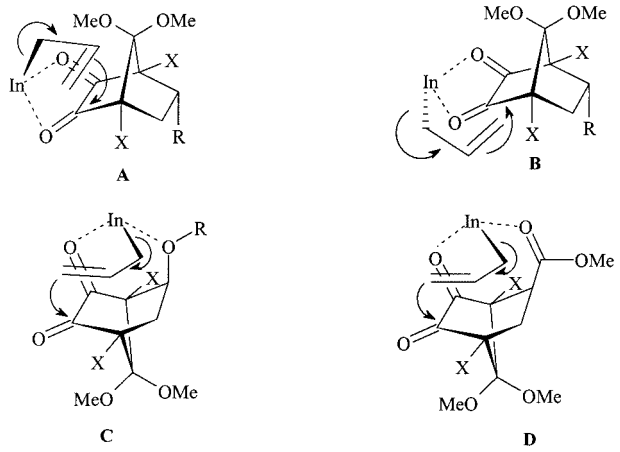
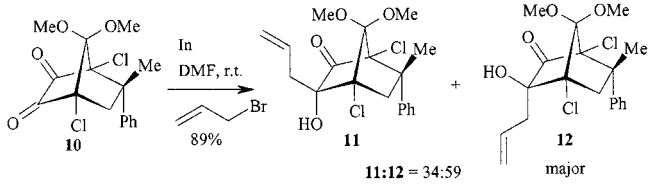


Figure 3. Transition state models for the observed diastereoselectivity.

ure 1). A similar situation in the case of the major *exo* alcohol **4d** prompted its single-crystal X-ray analysis also. Figure 2 represents the ORTEP diagram of **4d**.

The predominant formation of *endo* alcohols **3** and **5** can be explained by considering transition states **A** and **B** (Figure 3) in which the coordination of the allylindium reagent to α-diketone moiety is followed by allyl group transfer to the sterically less-congested C-2 carbonyl group preferentially from the *exo*-face (**A**) to furnish the products. The less-favored *endo* addition in **B** is responsible for the minor alcohols **4** and **6**. A complete reversal of the diastereofacial selectivity in acetoxy and ethoxy derivatives **1b/2b** and **1d/2d** leads to the *exo* alcohols **4b/d** and **6b/d** as predominant products, possibly because of chelation of the indium reagent to the heteroatom directly attached to the norbornyl derivatives, which involves a six-membered ring (shown in **C**, Figure 3). The result obtained for derivative **1c**, where the CH_2OAc unit acts as a non-chelating group, further supports our assumption. On the other hand, the formation of the 1:1 mixture of alcohols from the *endo* methyl ester derivatives **1f** and **2f** could be due presumably to less-effective chelation of the indium reagent to the ester carbonyl group in **D** as compared to **C** (seven- vs. six-membered ring), which, thus, allows transition state **A** to compete effectively.

We were intrigued by the surprising result obtained when an *exo*-Me group is placed at C-5 in **1a**. A significant alteration in diastereoselection was observed for **10** relative to



Scheme 3. Allylindium addition to diketone **10**

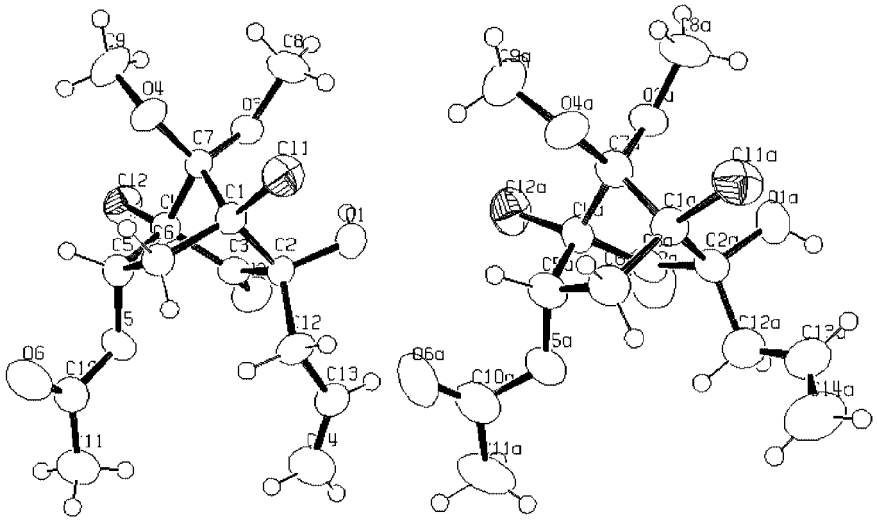


Figure 2. Crystal structure of compound **4d**, showing two crystallographically independent molecules: left, **4d** (1); right **4d** (2)

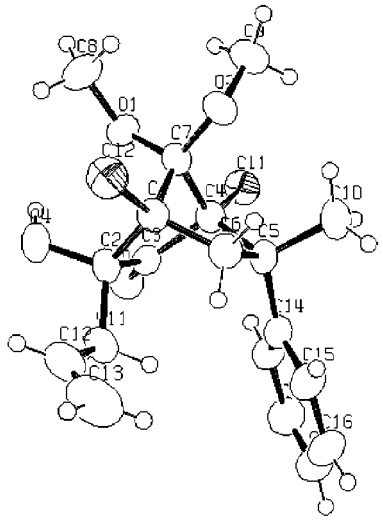
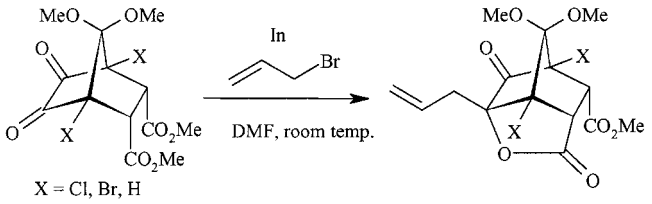


Figure 4. Crystal structure of compound **12**

1a. Three products were observed (34:59:7) from the ^{1}H NMR spectrum of the unpurified mixture (Scheme 3). We assign the structures for the two major compounds to be those of **11** and **12**, with the diastereoselection in favor of *exo* alcohol **12**. The structure of **12** was confirmed by X-ray crystallographic data (Figure 4). The dramatic influence (reversal) exerted by the remote, apparently innocuous, *exo*-Me group is far from understood.

For the purpose of comparison, we performed a Zn-mediated allylation on **1a**. Treatment of **1a** with allylzinc in a mixture of sat. NH_4Cl and DMF (1:1) at room temperature afforded **3a** and **4a** in a ratio of 57:43 in combined 83% of yield (Scheme 4); this result clearly indicates a downgrade in yield as well as selectivity.

The allylindium additions to disubstituted α-diketones **13a**−**f** and **14a**−**c**,**e**,**f** proceed with complete diastereoselection. The *endo* alcohols **15a**−**f** and **16a**−**c**,**e**,**f** were formed exclusively in excellent yields (Table 2). The diester derivatives **17**−**19** underwent subsequent cyclization after the initial allylindium addition, leading to the corresponding lactones **20**−**22** (Scheme 5).



17	X = Cl	9 h	**20** 97%
18	X = Br	11 h	**21** 95%
19	X = H	7 h	**22** 95%

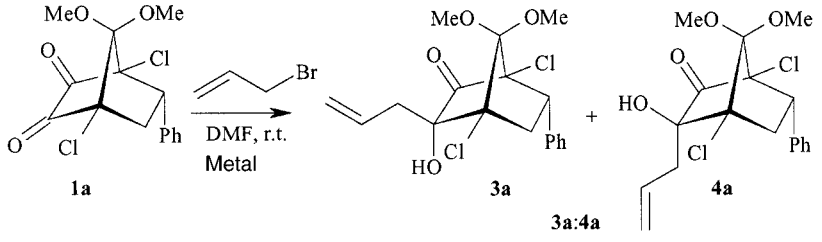
Scheme 5. Allylation of the diester derivatives

The structural variations in dihalonorbornyl α-diketones lead to interesting stereochemical outcomes during allylindium additions. The product distributions that arise from a reversal in selectivities have been carefully assigned and will be exploited in selective organic synthesis.

Experimental Section

General Information: Melting points are uncorrected. IR spectra were recorded as KBr pellets (solids) or thin films (liquids). ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$ and are reported in the δ scale. Tetramethylsilane was used as the internal standard. Column chromatography was performed using silica gel (100−200 mesh); ethyl acetate/hexane was used as eluent.

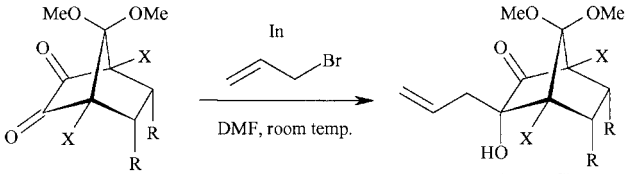
General Procedure for the Indium-Mediated Allylation of α-Diketones: A mixture of α-diketone (1 mmol), indium metal (2 mmol, cut into small pieces), and allyl bromide (4 mmol) in DMF (1 mL) was stirred at room temperature for the specified time (Table 1 and 2). After completion of the reaction, as monitored by TLC, the reaction mixture was quenched with a few drops of 5% HCl and extracted with diethyl ether. The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4 and then the solvents were evaporated. The resulting residue was purified by silica gel column chromatography to provide the pure homoallylic alcohols. In each case, the ^{1}H NMR spectrum of the crude product,



In	4 h	94%	82:18
Zn, sat. NH_4Cl	3 h	81%	57:43

Scheme 4. Comparison of the allylations of the diketone **1a** using Zn and In.

Table 2. Indium-mediated allylation of disubstituted α-diketones to form acyloins



13 X = Cl
14 X = Br
15 X = Cl
16 X = Br

Entry[a]	Substrate	R	Time (h)	Product	Yield[b] (%)
1	**13a**, X = Cl	$-(CH_2)_3-$	6	**15a**	97
2	**14a**, X = Br	$-(CH_2)_3-$	7	**16a**	98
3	**13b**, X = Cl	$-(CH_2)_4-$	8	**15b**	96
4	**14b**, X = Br	$-(CH_2)_4-$	7	**16b**	97
5	**13c**, X = Cl	$-(CH_2)_5-$	5	**15c**	96
6	**14c**, X = Br	$-(CH_2)_5-$	5	**16c**	97
7	**13d**, X = Cl	$-(CH_2)_6-$	6	**15d**	98
8	**13e**, X = Cl	$-CH_2OCH_2-$	5	**15e**	95
9	**14e**, X = Br	$-CH_2OCH_2-$	6	**16e**	95
10	**13f**, X = Cl	CH_2OAc	10	**15f**	98
11	**14f**, X = Br	CH_2OAc	9	**16f**	99

[a] All reactions were performed using 2 equiv. of indium metal and vigorously stirring it with allyl bromide in DMF. [b] Isolated yields of analytically pure alcohols.

before column purification, was obtained to record the product distribution.

Spectral Data For Monosubstituted Acyloins 3−6

Acyloin 3a/4a: Yield: 349 mg, 94% (82:18) from **1a** (329 mg, 1 mmol). The diastereoisomers were separated by column chromatography (SiO_2; 5% ethyl acetate/hexane).

Major Isomer 3a: Colorless solid, m.p. 118−120 °C. ^{1}H NMR: δ = 7.39−7.24 (m, 5 H), 6.22−6.13 (m, 1 H), 5.42 (d, *J* = 10.0 Hz, 1 H), 5.37 (d, *J* = 17.1 Hz, 1 H), 3.77 (s, 3 H), 3.71 (dd, *J* = 12.4, 5.4 Hz, 1 H), 3.65 (s, 3 H), 3.17 (s, 1 H, D_2O exchangeable), 3.13 (dd, *J* = 12.8, 5.5 Hz, 1 H), 2.97 (dd, *J* = 13.8, 5.4 Hz, 1 H), 2.76 (dd, $J_1 = J_2$ = 12.7 Hz, 1 H), 2.74 (dd, *J* = 13.9, 10.0 Hz, 1 H) ppm. ^{13}C NMR: δ = 202.0, 135.4, 131.7, 129.4, 128.1, 127.7, 123.1, 103.5, 81.6, 78.5, 73.5, 51.6 (2 C), 48.1, 39.8, 37.4 ppm. IR (KBr): $\tilde{\nu}$ = 3500, 2950, 1760, 1620 cm^{-1}. $C_{18}H_{20}Cl_2O_4$ (371.3): calcd. C 58.23, H 5.43; found C 58.29, H 5.47.

Irradiation of the olefinic proton at δ = 6.22−6.13 ppm (m, 1 H, olefinic) was performed to assign the allylic CH_2 and C(6)H_{exo} protons. Two protons, one proton of the allylic CH_2 unit and the C(6)H_{exo} proton, appeared together as a multiplet.

Minor Isomer 4a: ^{1}H NMR: δ = 7.32−7.21 (m, 5 H), 5.98−5.88 (m, 1 H), 5.07 (d, *J* = 10.0 Hz, 1 H), 4.83 (d, *J* = 17.1 Hz, 1 H), 4.05 (dd, *J* = 13.0, 4.2 Hz, 1 H), 3.77 (s, 3 H), 3.68 (s, 3 H), 3.20 (dd, $J_1 = J_2$ = 13.0 Hz, 1 H), 2.46 (dd, *J* = 13.0, 4.2 Hz, 1 H), 2.16−2.06 (m, 2 H) ppm. ^{13}C NMR: δ = 203.1, 137.8, 130.7, 128.7, 127.2, 126.9, 119.2, 105.4, 80.4, 80.0, 72.7, 52.4, 52.1, 44.8, 39.7, 36.6 ppm.

Acyloin 5a/6a: Yield: 214 mg, 93% (89:11) from **2a** (209 mg, 0.5 mmol). The diastereoisomers were separated by column chromatography (SiO_2; 5% ethyl acetate/hexane).

Major Isomer 5a: Colorless solid, m.p. 78−80 °C. ^{1}H NMR: δ = 7.37−7.22 (m, 5 H), 6.23−6.13 (m, 1 H), 5.43 (d, *J* = 10.4 Hz, 1 H), 5.39 (d, *J* = 17.2 Hz, 1 H), 3.81 (s, 3 H), 3.73 (dd, *J* = 12.6, 5.5 Hz, 1 H), 3.69 (s, 3 H), 3.22 (dd, *J* = 12.6, 5.4 Hz, 1 H), 3.21 (s, 1 H, D_2O exchangeable), 2.99 (dd, *J* = 13.6, 5.2 Hz, 1 H), 2.89 (dd, $J_1 = J_2$ = 12.7 Hz, 1 H), 2.71 (dd, *J* = 13.6, 10.0 Hz, 1 H) ppm. ^{13}C NMR: δ = 201.3, 135.7, 131.8, 129.5, 128.0, 127.7, 123.1, 103.6, 78.8, 76.1, 67.2, 51.7, 51.6, 49.4, 41.8, 39.6 ppm. IR (KBr): $\tilde{\nu}$ = 3500, 2952, 1763, 1632, 1496, 1447 cm^{-1}. $C_{18}H_{20}Br_2O_4$ (460.2): calcd. C 46.98, H 4.38; found C 47.03, H 4.35.

Minor Isomer 6a: ^{1}H NMR: δ = 7.32−7.21 (m, 5 H), 6.02−5.92 (m, 1 H), 5.09 (d, *J* = 10.0 Hz, 1 H), 4.85 (d, *J* = 17.0 Hz, 1 H), 4.08 (dd, *J* = 13.1, 4.2 Hz, 1 H), 3.82 (s, 3 H), 3.73 (s, 3 H), 3.30 (dd, $J_1 = J_2$ = 13.1 Hz, 1 H), 2.50 (dd, *J* = 13.1, 4.2 Hz, 1 H), 2.19−2.10 (m, 2 H) ppm. ^{13}C NMR: δ = 202.5, 138.1, 130.7, 129.8, 128.7, 127.1, 119.3, 105.7, 80.4, 73.3, 66.7, 52.7, 52.3, 46.6, 39.7, 36.9 ppm.

Acyloin 3b/4b: Yield: 315 mg, 93% (14:86) from **1b** (297 mg, 1 mmol). The diastereoisomers were separated by column chromatography (SiO_2; 2% ethyl acetate/hexane).

Minor Isomer 3b: ^{1}H NMR: δ = 6.28−6.18 (m, 1 H), 5.29 (d, *J* = 10.0 Hz, 1 H), 5.25 (d, *J* = 17.3 Hz, 1 H), 4.13 (dd, *J* = 9.3, 2.2 Hz, 1 H), 3.68 (m, 1 H), 3.67 (s, 3 H), 3.58 (s, 3 H), 3.53 (dq, *J* = 9.5, 7.1 Hz, 1 H), 3.15 (s, 1 H, D_2O exchangeable), 2.84 (dd, *J* = 14.4, 6.3 Hz, 1 H), 2.74 (dd, *J* = 12.9, 9.3 Hz, 1 H), 2.73−2.67 (m, 1 H), 2.66 (dd, *J* = 12.9, 2.2 Hz, 1 H), 1.13 (t, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR: δ = 199.3, 132.4, 120.6, 103.3, 80.9, 79.9, 79.3, 73.7, 66.7, 51.8, 51.6, 39.71, 39.67, 15.1 ppm.

Major Isomer 4b: Colorless solid, m.p. 66−68 °C. ^{1}H NMR: δ = 6.15−6.05 (m, 1 H), 5.18 (d, *J* = 8.8 Hz, 1 H), 5.15 (d, *J* = 16.3 Hz, 1 H), 4.12 (dd, *J* = 9.8, 1.4 Hz, 1 H), 3.69−3.64 (m, 1 H), 3.67 (s, 3 H), 3.61 (s, 3 H), 3.50 (dq, *J* = 9.5, 7.1 Hz, 1 H), 2.98 (dd, *J* = 13.7, 9.8 Hz, 1 H), 2.68 (dd, *J* = 14.6, 6.1 Hz, 1 H), 2.57 (dd, *J* = 14.6, 7.8 Hz, 1 H), 2.26 (dd, *J* = 13.7, 1.2 Hz, 1 H), 1.13 (t, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR: δ = 200.1, 131.5, 118.7, 105.6, 81.3, 80.3, 79.7, 72.4, 66.6, 52.3, 51.8, 39.4, 36.5, 15.1 ppm. IR

(KBr): $\tilde{\nu}$ = 3500, 2950, 1780, 1640 cm^{-1}. $C_{14}H_{20}Cl_2O_5$ (339.2): calcd. C 49.57, H 5.94; found C 49.54, H 5.97.

Acyloin 5b/6b: Yield: 201 mg, 94% (18:82) from **2b** (193 mg, 0.5 mmol). The diastereoisomers were separated by column chromatography (SiO_2; 3% ethyl acetate/hexane).

Minor Isomer 5b: Spectra recorded with an enriched sample of the minor isomer (**5b/6b**, 78:22), ^1H NMR: δ = 6.28−6.18 (m, 1 H), 5.29 (d, *J* = 10.7 Hz, 1 H), 5.24 (d, *J* = 17.6 Hz, 1 H), 4.17 (dd, *J* = 9.0, 2.4 Hz, 1 H), 3.71 (s, 3 H), 3.69−3.65 (m, 1 H), 3.62 (s, 3 H), 3.58−3.53 (m, 1 H), 3.14 (s, 1 H, D_2O exchangeable), 2.87−2.79 (m, 2 H), 2.84 (dd, *J* = 14.4, 6.3 Hz, 1 H), 2.78 (dd, *J* = 13.1, 2.7 Hz, 1 H), 1.13 (t, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR: δ = 198.6, 132.4, 120.8, 103.3, 81.0, 79.4, 73.9, 67.1, 66.7, 51.9, 51.6, 41.9, 41.6, 15.1 ppm.

Major Isomer 6b: Colorless solid, m.p. 78−80 °C. ^1H NMR: δ = 6.18−6.08 (m, 1 H), 5.17 (d, *J* = 9.8 Hz, 1 H), 5.15 (d, *J* = 17.1 Hz, 1 H), 4.19 (dd, *J* = 9.5, 1.7 Hz, 1 H), 3.71 (s, 3 H), 3.70−3.63 (m, 1 H), 3.66 (s, 3 H), 3.54 (dq, *J* = 9.3, 7.1 Hz, 1 H), 2.90 (dd, *J* = 13.6, 9.8 Hz, 1 H), 2.69 (dd, *J* = 14.4, 5.9 Hz, 1 H), 2.55 (dd, *J* = 14.4, 7.8 Hz, 1 H), 2.38 (dd, *J* = 13.6, 1.7 Hz, 1 H), 1.13 (t, *J* = 7.0 Hz, 3 H) ppm. ^{13}C NMR: δ = 199.1, 131.5, 118.7, 105.7, 81.3, 80.2, 74.3, 66.6, 66.4, 52.5, 52.1, 40.9, 36.8, 15.1 ppm. IR (KBr): $\tilde{\nu}$ = 3523, 2980, 1781, 1624 cm^{-1}. $C_{14}H_{20}Br_2O_5$ (428.1): calcd. C 39.28, H 4.71; found C 39.31, H 4.74.

Acyloin 3c,4c: Yield: 78 mg, 71% (77:23) from **1c** (98 mg, 0.3 mmol). The diastereoisomers were separated by column chromatography (SiO_2; 3% ethyl acetate/hexane).

Major Isomer 3c: Colorless solid, m.p. 106−108 °C. ^1H NMR: δ = 6.25−6.08 (m, 1 H), 5.39 (d, *J* = 10.2 Hz, 1 H), 5.30 (d, *J* = 17.3 Hz, 1 H), 4.10 (dd, *J* = 11.4, 5.5 Hz, 1 H), 3.94 (dd, *J* = 11.2, 8.5 Hz, 1 H), 3.69 (s, 3 H), 3.61 (s, 3 H), 3.02 (s, 1 H, D_2O exchangeable), 2.87−2.80 (m, 2 H), 2.70−2.64 (dd, *J* = 13.9, 6.6 Hz, 1 H), 2.60 (dd, *J* = 12.4, 4.4 Hz, 1 H), 2.51 (dd, $J_1 = J_2$ = 12.2 Hz, 1 H), 2.03 (s, 3 H) ppm. ^{13}C NMR: δ = 202.0, 170.6, 131.8, 122.7, 103.3, 78.4, 78.1, 73.6, 62.8, 51.8, 51.6, 41.2, 39.7, 34.6, 20.7 ppm. IR (KBr): $\tilde{\nu}$ = 3300, 2900, 1760, 1690, 1600 cm^{-1}. $C_{15}H_{20}Cl_2O_6$ (367.2): calcd. C 49.06, H 5.49; found C 49.01, H 5.52.

Minor Isomer 4c: Spectra recorded using an enriched sample of the minor isomer. ^1H NMR: δ = 6.17−6.09 (m, 1 H), 5.23−5.18 (m, 2 H), 4.15 (dd, *J* = 12.2, 6.6 Hz, 1 H), 4.00 (dd, *J* = 12.0, 4.2 Hz, 1 H), 3.71 (s, 3 H), 3.66 (s, 3 H), 2.91−2.85 (m, 1 H), 2.74 (dd, *J* = 14.9, 6.1 Hz, 1 H), 2.67 (dd, $J_1 = J_2$ = 13.0 Hz, 1 H), 2.61 (dd, *J* = 14.9, 8.2 Hz, 1 H), 2.25 (dd, *J* = 13.1, 4.7 Hz, 1 H), 2.02 (s, 3 H) ppm. ^{13}C NMR: δ = 202.7, 170.3, 131.2, 119.3, 105.3, 80.2, 78.5, 72.5, 61.2, 52.5, 52.0, 41.1, 36.5, 34.2, 20.6 ppm.

Acyloin 3d/4d: Yield: 104 mg, 92% (23:77) from **1d** (100 mg, 0.32 mmol). The diastereoisomers were separated by column chromatography (SiO_2; 5% ethyl acetate/hexane).

Minor Isomer 3d: Colorless crystals (dichloromethane/hexane), m.p. 125−126 °C. ^1H NMR: δ = 6.26−6.18 (m, 1 H), 5.42−5.37 (m, 2 H), 5.32 (dd, *J* = 10.0, 2.7 Hz, 1 H), 3.69 (s, 3 H), 3.61 (s, 3 H), 2.95 (s, 1 H, D_2O exchangeable), 2.89 (dd, *J* = 13.9, 5.7 Hz, 1 H), 2.84 (dd, *J* = 13.4, 10.0 Hz, 1 H), 2.74 (dd, *J* = 13.6, 2.7 Hz, 1 H), 2.69 (dd, *J* = 14.1, 9.5 Hz, 1 H), 2.04 (s, 3 H) ppm. ^{13}C NMR: δ = 199.5, 170.1, 131.6, 122.9, 103.0, 78.7, 78.5, 73.3, 73.1, 52.0, 51.6, 39.7, 38.9, 20.8 ppm. IR (KBr): $\tilde{\nu}$ = 3500, 2950, 1780, 1730, 1620 cm^{-1}. $C_{14}H_{18}Cl_2O_6$ (353.2): calcd. C 47.61, H 5.14; found C 47.67, H 5.20. Irradiation of the olefinic proton at δ = 6.26−6.18 ppm (m, 1 H, olefinic) was undertaken to assign the allylic CH_2 and C(6)H_{exo} and C(6)H_{endo} protons; it resulted in the disappearance of the corresponding couplings in the allylic CH_2 proton.

Major Isomer 4d: Colorless crystals (dichloromethane/hexane), m.p. 75−76 °C. ^1H NMR: δ = 6.11−6.00 (m, 1 H), 5.36 (dd, *J* = 10.3, 2.0 Hz, 1 H), 5.18 (d, *J* = 10.0 Hz, 1 H), 5.12 (d, *J* = 17.1 Hz, 1 H), 3.67 (s, 3 H), 3.61 (s, 3 H), 2.98 (dd, *J* = 14.4, 10.3 Hz, 1 H), 2.58 (dd, *J* = 14.6, 6.4 Hz, 1 H), 2.44 (dd, *J* = 14.6, 7.8 Hz, 1 H), 2.20 (dd, *J* = 14.4, 2.0 Hz, 1 H), 2.07 (s, 3 H) ppm. ^{13}C NMR: δ = 199.7, 169.5, 130.8, 119.3, 105.3, 80.1, 79.2, 73.3, 72.1, 52.4, 52.2, 39.0, 36.8, 20.7 ppm. IR (KBr): $\tilde{\nu}$ = 3500, 2954, 1786, 1739, 1640 cm^{-1}. $C_{14}H_{18}Cl_2O_6$ (353.2): calcd. C 47.61, H 5.14; found C 47.65, H 5.11.

Acyloin 5d/6d: Yield: 101 mg, 91% (25:77) from **2d** (100 mg, 0.25 mmol). The diastereoisomers were separated by column chromatography (SiO_2; 5% ethyl acetate/hexane).

Minor Isomer 5d: Spectrum recorded using an enriched sample of the minor isomer (**5d/6d**, 78:22). ^1H NMR: δ = 6.27−6.14 (m, 1 H), 5.43−4.33 (m, 2 H), 5.35 (dd, *J* = 9.8, 2.7 Hz, 1 H), 3.73 (s, 3 H), 3.64 (s, 3 H), 2.96 (s, 1 H, D_2O exchangeable), 2.95 (dd, *J* = 13.6, 9.9 Hz, 1 H), 2.90 (dd, *J* = 13.6, 5.6 Hz, 1 H), 2.83 (dd, *J* = 13.4, 2.7 Hz, 1 H), 2.65 (dd, *J* = 13.9, 9.8 Hz, 1 H), 2.04 (s, 3 H) ppm. ^{13}C NMR: δ = 198.8, 170.0, 131.7, 122.6, 102.9, 78.6, 74.4, 71.7, 66.3, 52.0, 51.6, 41.8, 40.7, 20.5 ppm.

Major Isomer 6d: Colorless solid, m.p. 82−83 °C. ^1H NMR: δ = 6.18−6.07 (m, 1 H), 5.44 (dd, *J* = 10.0, 5.4 Hz, 1 H), 5.22 (d, *J* = 10.0 Hz, 1 H), 5.15 (d, *J* = 17.1 Hz, 1 H), 3.74 (s, 3 H), 3.69 (s, 3 H), 3.09 (dd, *J* = 14.4, 10.0 Hz, 1 H), 2.61 (dd, *J* = 14.6, 6.4 Hz, 1 H), 2.46 (dd, *J* = 14.6, 7.8 Hz, 1 H), 2.30 (dd, *J* = 14.6, 2.0 Hz, 1 H), 2.05 (s, 3 H) ppm. ^{13}C NMR: δ = 198.9, 169.5, 130.9, 119.4, 105.5, 80.0, 74.9, 72.1, 65.7, 52.6, 52.3, 40.5, 37.0, 20.6 ppm. IR (KBr): $\tilde{\nu}$ = 3500, 2950, 1740 (br), 1630 cm^{-1}. $C_{14}H_{18}Br_2O_6$ (442.1): calcd. C 38.04, H 4.10; found C 38.10, H 4.13.

Acyloin 3e/4e: Yield: 231 mg, 91% (91:9) from **1e** (225 mg, 0.69 mmol). The diastereoisomers were separated by column chromatography (SiO_2; hexane).

Major Isomer 3e: Colorless crystals (hexane), m.p. 107−108 °C. ^1H NMR: δ = 6.21−6.11 (m, 1 H), 5.36 (d, *J* = 10.0 Hz, 1 H), 5.30 (d, *J* = 16.8 Hz, 1 H), 3.66 (s, 3 H), 3.57 (s, 3 H), 2.84 (dd, *J* = 13.5, 5.6 Hz, 1 H), 2.83 (s, 1 H, D_2O exchangeable), 2.62 (dd, *J* = 12.5, 6.1 Hz, 1 H), 2.61 (dd, *J* = 13.6, 9.3 Hz, 1 H), 2.35 (dd, *J* = 13.1, 12.5 Hz, 1 H), 1.91 (dd, *J* = 13.1, 6.0 Hz, 1 H), 0.00 (s, 9 H) ppm. ^{13}C NMR: δ = 203.7, 131.9, 122.7, 103.3, 79.0, 78.2, 74.0, 51.6, 51.4, 39.7, 33.1, 30.9, −1.7 ppm. IR (KBr): $\tilde{\nu}$ = 3500, 2955, 1774, 1641 cm^{-1}. $C_{15}H_{24}Cl_2O_4Si$ (367.3): calcd. C 49.05, H 6.59; found C 49.10, H 6.62. Irradiation of the signal of the olefinic proton at δ = 6.22−6.13 ppm (m, 1 H, olefinic) was undertaken to assign the allylic CH_2 and C(6)H_{exo} protons. Two protons — one proton of the allylic CH_2 unit and the C(6)H_{exo} proton — appeared as a multiplet. After irradiation, one coupling constant (*J* = 5.6 Hz) disappeared from one of the allylic CH_2 protons [δ = 2.84 ppm (dd, *J* = 13.5, 5.6 Hz, 1 H, allylic CH_2)].

Minor Isomer 4e: Colorless solid, m.p. 108−110 °C. ^1H NMR: δ = 6.11−6.01 (m, 1 H), 5.14 (d, *J* = 9.5 Hz, 1 H), 5.11 (d, *J* = 15.6 Hz, 1 H), 3.64 (s, 3 H), 3.57 (s, 3 H), 2.52 (dd, *J* = 15.3, 6.1 Hz, 1 H), 2.48 (dd, *J* = 14.6, 9.5 Hz, 1 H), 2.39 (dd, *J* = 14.6, 7.8 Hz, 1 H), 2.06−2.00 (m, 2 H), 0.00 (s, 9 H) ppm. ^{13}C NMR: δ = 203.8, 131.2, 119.1, 103.3, 79.9, 72.4, 52.4, 51.9, 36.2, 33.4, 29.8, −0.995 ppm. IR (KBr): $\tilde{\nu}$ = 3500, 2950, 1770, 1610 cm^{-1}.

Acyloin 3f/4f: Yield: 98 mg, 92%, inseparable mixture of regioisomers (43:57) from **1f** (93 mg, 0.3 mmol); obtained as a viscous liquid. ^{1}H NMR (from the mixture): δ = 6.30−6.20 (m, 1 H, olefinic, minor isomer), 6.15−6.05 (m, 1 H, olefinic, major isomer), 5.24−5.17 (m, 4 H, olefinic), 3.73 (s, 3 H, OMe), 3.72 (s, 3 H, OMe), 3.71 (s, 6 H, OMe), 3.65 (s, 3 H, OMe), 3.61 (s, 3 H, OMe), 3.46 (dd, *J* = 12.7, 4.4 Hz, 1 H, major isomer), 3.42 (dd, *J* = 12.2, 3.9 Hz, 1 H, minor isomer), 2.83−2.71 (m, 5 H), 2.65 (dd, J_1 = J_2 = 12.7 Hz, 1 H), 2.60 (dd, *J* = 13.9, 7.9 Hz, 1 H), 2.50 (dd, *J* = 13.6, 4.3 Hz, 1 H, major isomer) ppm. A decoupling experiment was undertaken to assign the vinylic proton and the C(5)H_{exo} proton of both the *endo* and *exo* isomers.

^{13}C NMR (Major isomer, from the mixture): δ = 201.0 (−C=O), 170.8 (−O−C=O), 131.1, 119.2, 105.1, 80.2, 77.8, 72.0, 52.8, 52.3, 51.9, 46.7, 36.4, 34.3 ppm. ^{13}C NMR (Minor isomer, from the mixture): δ = 199.9, 172.9, 132.6, 119.3, 103.2, 79.4, 77.9, 73.6, 53.2, 51.8, 51.6, 47.7, 39.9, 34.4 ppm. IR (KBr): ṽ = 3500, 2950, 1780−1740, 1620 cm^{-1}. $C_{14}H_{18}Cl_2O_6$ (353.2): calcd. C 47.61, H 5.14; found C 47.66, H 5.17.

Acyloin 5f/6f: Yield: 125 mg, 94%, inseparable mixture of regioisomers (45:55) from **2f** (120 mg, 0.3 mmol); obtained as a viscous liquid. ^{1}H NMR (from the mixture): δ = 6.22−6.13 (m, 1 H, minor isomer), 6.11−6.01 (m, 1 H, major isomer), 5.17−5.06 (m, 4 H), 3.674 (s, 6 H), 3.667 (s, 3 H), 3.66 (s, 3 H), 3.62 (s, 3 H), 3.59 (s, 3 H), 3.44 (dd, *J* = 12.7, 4.4 Hz, 1 H, major isomer), 3.39 (dd, *J* = 12.0, 4.1 Hz, 1 H, minor isomer), 2.86−2.79 (m, 2 H), 2.76−2.65 (m, 4 H), 2.53−2.46 (m, 1 H), 2.47 (dd, *J* = 13.4, 4.3 Hz, 1 H, major isomer) ppm. ^{13}C NMR (Major isomer, from the mixture): δ = 200.3, 171.0, 131.2, 119.5, 105.3, 80.1, 70.7, 65.5, 52.8, 52.6, 52.0, 48.4, 36.8, 36.2 ppm. ^{13}C NMR (Minor isomer, from the mixture): δ = 199.3, 172.9, 132.8, 119.3, 103.4, 79.6, 70.9, 66.9, 53.2, 51.9, 51.8, 49.2, 42.1, 36.5 ppm. IR (KBr): ṽ = 3500, 2950, 1770 (br), 1620 cm^{-1}. $C_{14}H_{18}Br_2O_6$ (442.1): calcd. C 38.04, H 4.10; found C 38.10, H 4.07.

Acyloin 11: Colorless solid (contaminated with the undetected isomer), m.p. 86−90 °C. ^{1}H NMR: δ = 7.46−7.44 (m, 2 H), 7.28−7.21 (m, 2 H), 7.16−7.12 (m, 1 H), 6.18−6.13 (m, 1 H), 5.24 (d, *J* = 10.0 Hz, 1 H), 5.19 (d, *J* = 17.1 Hz, 1 H), 3.75 (s, 3 H), 3.62 (s, 3 H), 3.58 (d, *J* = 12.0 Hz, 1 H), 2.77 (dd, *J* = 13.7, 6.1 Hz, 1 H), 2.68 (d, *J* = 12.0 Hz, 1 H), 2.60 (dd, *J* = 13.7, 9.3 Hz, 1 H), 2.42 (s, 1 H, D_2O exchangeable), 1.64 (s, 3 H) ppm. ^{13}C NMR: δ = 200.7, 145.1, 132.2, 128.0, 126.4, 126.3, 122.3, 103.6, 84.2, 77.7, 73.7, 51.7, 51.5, 46.7, 45.4, 40.0, 31.6 ppm.

Acyloin 12: Colorless crystals (dichloromethane/hexane, 1:2), m.p. 103−105 °C. ^{1}H NMR: δ = 7.31−7.28 (m, 2 H), 7.22−7.19 (m, 2 H), 7.13−7.10 (m, 1 H), 5.72−5.62 (m, 1 H), 4.88 (d, *J* = 10.2 Hz, 1 H), 4.45 (d, *J* = 17.1 Hz, 1 H), 3.67 (s, 3 H), 3.59 (s, 3 H), 3.31 (s, 1 H, D_2O exchangeable), 2.95 (d, *J* = 13.0 Hz, 1 H), 2.83 (d, *J* = 13.0 Hz, 1 H), 1.89 (dd, *J* = 14.4, 7.3 Hz, 1 H), 1.71 (dd, *J* = 14.4, 6.8 Hz, 1 H), 1.58 (s, 3 H) ppm. ^{13}C NMR: δ = 202.3, 145.6, 130.7 128.7, 126.9, 126.2, 119.1, 105.6, 84.5, 80.0, 73.0, 52.2, 51.7, 47.1, 46.3, 36.8, 32.1 ppm. IR (KBr): ṽ = 3500, 2950, 1770, 1620 cm^{-1}. $C_{19}H_{22}Cl_2O_4$ (385.3): calcd. C 59.23, H 5.76; found C 59.27, H 5.79.

Disubstituted Acyloins

Acyloin 15a: Yield: 163 mg (97%) from **13a** (147 mg, 0.5 mmol); colorless solid, m.p. 70−72 °C. ^{1}H NMR: δ = 6.11−6.00 (m, 1 H), 5.37 (d, *J* = 9.8 Hz, 1 H), 5.29 (d, *J* = 17.1 Hz, 1 H), 3.64 (s, 3 H), 3.55 (s, 3 H), 3.46−3.40 (m, 1 H), 2.99 (dd, *J* = 13.6, 5.4 Hz, 1 H), 2.90 (ddd, J_1 = J_2 = 12.0, J_3 = 7.4 Hz, 1 H), 2.83 (s, 1 H, D_2O exchangeable), 2.68 (dd, *J* = 13.6, 9.8 Hz, 1 H), 2.56−2.47 (m, 1 H), 1.91−1.80 (m, 1 H), 1.73−1.65 (m, 1 H), 1.61−1.46 (m, 2 H), 1.39−1.30 (m, 1 H) ppm. ^{13}C NMR: δ = 204.0, 131.5, 123.2, 106.0, 81.0, 78.9, 74.9, 52.9, 51.7, 51.1, 49.8, 41.6, 26.7, 25.8, 25.1 ppm. IR (KBr): ṽ = 3500, 2950, 1770, 1610 cm^{-1}. $C_{15}H_{20}Cl_2O_4$ (335.2): calcd. C 53.74, H 6.01; found C 53.80, H 6.04.

Acyloin 16a: Yield: 125 mg (98%) from **14a** (115 mg, 0.3 mmol); colorless solid, m.p. 72−74 °C. ^{1}H NMR: δ = 6.12−6.02 (m, 1 H), 5.41 (d, *J* = 10.0 Hz, 1 H), 5.32 (d, *J* = 17.0 Hz, 1 H), 3.72 (s, 3 H), 3.63 (s, 3 H), 3.61−3.54 (m, 1 H), 3.08−3.02 (m, 1 H), 3.01−2.96 (m, 1 H), 2.90 (s, 1 H, D_2O exchangeable), 2.66 (dd, *J* = 13.6, 10.3 Hz, 1 H), 2.53 (ddd, J_1 = J_2 = 12.4, J_3 = 5.9 Hz, 1 H), 1.88−1.71 (m, 2 H), 1.66−1.49 (m, 2 H), 1.43−1.33 (m, 1 H), ppm. ^{13}C NMR: δ = 203.4, 131.5, 123.2, 106.1, 81.3, 72.6, 69.3, 54.8, 51.8, 51.3, 50.9, 43.6, 26.2, 26.1, 25.5 ppm. IR (KBr): ṽ = 3500, 2900, 1777, 1620 cm^{-1}. $C_{15}H_{20}Br_2O_4$ (424.1): calcd. C 42.48, H 4.75; found C 42.52, H 4.69.

Acyloin 15b: Yield: 101 mg (96%) from **13b** (92 mg, 0.3 mmol); colorless solid, m.p. 108−110 °C. ^{1}H NMR: δ = 6.19−6.09 (m, 1 H), 5.39 (d, *J* = 10.0 Hz, 1 H), 5.31 (d, *J* = 17.1 Hz, 1 H), 3.67 (s, 3 H), 3.58 (s, 3 H), 3.10−3.03 (m, one coupling: *J* = 11.2 Hz; 1 H), 2.94 (dd, *J* = 13.8, 5.4 Hz, 1 H), 2.90 (s, 1 H, D_2O exchangeable), 2.70 (dd, *J* = 13.7, 9.8 Hz, 1 H), 2.50 (ddd, *J* = 13.3, 12.8, 4.4 Hz, 1 H), 2.30 (ddd, J_1 = J_2 = 11.2, J_3 = 5.7 Hz, 1 H), 1.68−1.54 (m, 4 H), 1.35−1.22 (m, 2 H), 1.14−1.03 (m, 1 H) ppm. ^{13}C NMR: δ = 203.2, 131.7, 122.9, 103.5, 81.0, 80.2, 76.6, 51.8, 51.4, 45.1, 42.3, 41.5, 20.6, 20.3, 19.6, 18.8 ppm. IR (KBr): ṽ = 3500, 2900, 1760, 1620 cm^{-1}. $C_{16}H_{22}Cl_2O_4$ (349.3): calcd. C 55.02, H 6.35; found C 55.08, H 6.38.

Acyloin 16b: Yield: 128 mg (97%) from **14b** (119 mg, 0.3 mmol); colorless solid, m.p. 112−114 °C. ^{1}H NMR: δ = 6.18−6.08 (m, 1 H), 5.40 (d, *J* = 10.0 Hz, 1 H), 5.32 (d, *J* = 17.1 Hz, 1 H), 3.75 (s, 3 H), 3.63 (s, 3 H), 3.13 (ddd, J_1 = J_2 = 11.2, J_3 = 7.2 Hz, 1 H), 2.97 (dd, *J* = 13.7, 5.6 Hz, 1 H), 2.93 (s, 1 H, D_2O exchangeable), 2.66 (dd, *J* = 13.7, 10.0 Hz, 1 H), 2.53 (ddd, J_1 = J_2 = 13.7, J_3 = 4.6 Hz, 1 H), 2.30 (ddd, J_1 = J_2 = 11.2, J_3 = 5.1 Hz, 1 H), 1.72−1.55 (m, 4 H), 1.45−1.33 (m, 1 H), 1.24−1.17 (m, 1 H), 1.14−1.13 (m, 1 H) ppm. ^{13}C NMR: δ = 202.6, 131.8, 123.0, 103.4, 81.3, 74.4, 71.6, 52.0, 51.6, 47.4, 43.8, 43.7, 20.7, 20.3, 19.9, 19.4 ppm. IR (KBr): ṽ = 3500, 2950, 1770, 1628 cm^{-1}. $C_{16}H_{22}Br_2O_4$ (438.2): calcd. C 43.86, H 5.06; found C 43.90, H 5.01.

Acyloin 15c: Yield: 105 mg (96%) from **13c** (96 mg, 0.3 mmol); obtained as a viscous liquid. ^{1}H NMR: δ 6.16−6.06 (m, 1 H), 5.38 (d, *J* = 10.0 Hz, 1 H), 5.31 (d, *J* = 17.1 Hz, 1 H), 3.70 (s, 3 H), 3.58 (s, 3 H), 3.12 (dt, *J* = 12.5, 3.6 Hz, 1 H,), 2.94 (dd, *J* = 13.8, 5.7 Hz, 1 H), 2.87 (s, 1 H, D_2O exchangeable), 2.68 (dd, *J* = 13.9, 9.6 Hz, 1 H), 2.50 (dd, J_1 = J_2 = 12.4 Hz, 1 H), 2.26−2.17 (m, 1 H), 2.01−1.89 (m, 3 H), 1.80−1.78 (m, 1 H), 1.68−1.63 (m, 1 H), 1.22−1.08 (m, 3 H), 1.00−0.95 (m, 1 H) ppm. ^{13}C NMR: δ = 202.9, 131.7, 123.0, 103.1, 81.4, 80.2, 77.0, 51.8, 51.4, 50.7, 48.7, 41.6, 31.0, 30.7, 28.8, 25.5, 24.5 ppm. IR (KBr): ṽ = 3400, 2900, 1760, 1620 cm^{-1}. $C_{17}H_{24}Cl_2O_4$ (363.3): calcd. C 56.21, H 6.66; found C 56.24, H 6.69.

Acyloin 16c: Yield: 132 mg (97%) from **14c** (123 mg, 0.3 mmol); colorless solid, m.p. 93−195 °C. ^{1}H NMR: δ = 6.15−6.05 (m, 1 H), 5.38 (d, *J* = 9.8 Hz, 1 H), 5.31 (d, *J* = 17.1 Hz, 1 H), 3.75 (s, 3 H), 3.63 (s, 3 H), 3.12 (dt, *J* = 12.5, 3.5 Hz, 1 H,), 2.96 (dd, *J* = 13.9, 5.6 Hz, 1 H), 2.90 (s, 1 H, D_2O exchangeable), 2.53 (dd, *J* = 13.9, 9.8 Hz, 1 H), 2.54 (dd, J_1 = J_2 = 12.1 Hz, 1 H), 2.24−2.15 (m, 1 H), 2.04−1.97 (m, 3 H), 1.77−1.67 (m, 2 H), 1.21−1.08 (m, 3 H), 0.99−0.90 (m, 1 H) ppm. ^{13}C NMR: δ = 202.3, 131.7, 122.9,

102.1, 81.5, 75.2, 72.5, 52.2, 52.1, 51.4, 49.5, 43.6, 30.8, 30.6, 29.1, 26.2, 25.0 ppm. IR (KBr): $\tilde{\nu}$ = 3500, 2950, 1770, 1628 cm^{-1}. $C_{17}H_{24}Br_2O_4$ (452.2): calcd. C 45.16, H 5.35; found C 45.21, H 5.31.

Acyloin 15d: Yield: 111 mg (98%) from **13d** (101 mg, 0.3 mmol); colorless solid, m.p. 82−84 °C. ^{1}H NMR: δ = 6.17−6.06 (m, 1 H), 5.36 (d, J = 9.8 Hz, 1 H), 5.29 (d, J = 17.1 Hz, 1 H), 3.71 (s, 3 H), 3.58 (s, 3 H), 2.87 (dd, J = 13.9, 5.6 Hz, 1 H), 2.82 (dd, J_1 = J_2 = 11.2 Hz, 1 H), 2.75 (s, 1 H, D_2O exchangeable), 2.65 (dd, J = 13.9, 9.5 Hz, 1 H, allylic CH_2), 2.51 (dd, J_1 = J_2 = 11.2 Hz, 1 H), 2.05−1.94 (m, 1 H), 1.84−1.72 (m, 4 H), 1.62−1.48 (m, 2 H), 1.40−1.07 (5H) ppm. ^{13}C NMR: δ = 202.6, 131.8, 122.7, 102.7, 80.8 (2C), 77.9, 51.9, 51.4, 49.1, 48.7, 41.3, 31.6, 30.8, 25.7, 25.0, 23.8, 21.1 ppm. IR (KBr): $\tilde{\nu}$ = 3510, 2923, 1773, 1638 cm^{-1}. $C_{18}H_{26}Cl_2O_4$ (377.3): calcd. C 57.30, H 6.95; found C 57.35, H 6.91.

Acyloin 15e: Yield: 96 mg (95%) from **13e** (89 mg, 0.3 mmol); colorless solid, m.p. 84−86 °C. ^{1}H NMR: δ = 6.17−6.06 (m, 1 H), 5.13 (d, J = 10.0 Hz, 1 H), 5.09 (d, J = 17.1 Hz, 1 H), 4.97 (s, 1 H, D_2O exchangeable), 4.52 (d, J = 10.7 Hz, 1 H), 3.83 (d, J = 11.0 Hz, 1 H), 3.68 (s, 3 H), 3.62 (s, 3 H), 3.62−3.50 (m, 2 H), 3.38 (dd, J = 10.7, 6.6 Hz, 1 H), 3.21 (ddd, J_1 = J_2 = 8.8, J_3 = 2.0 Hz, 1 H), 2.87−2.76 (m, 2 H) ppm. ^{13}C NMR: δ = 202.9, 132.7, 117.8, 105.2, 82.4, 76.9, 73.6, 67.1, 66.8, 53.0, 51.9, 51.2, 49.2, 41.1 ppm. IR (KBr): $\tilde{\nu}$ = 3520, 2900, 1775, 1630 cm^{-1}. $C_{14}H_{18}Cl_2O_5$ (337.2): calcd. C 49.87, H 5.38; found C 49.82, H 5.41.

Acyloin 16e: Yield: 121 mg (95%) from **14e** (115 mg, 0.3 mmol); colorless solid, m.p. 76 °C. ^{1}H NMR: δ = 6.08−5.98 (m, 1 H), 5.07 (d, J = 10.0 Hz, 1 H), 5.09 (d, J = 17.3 Hz, 1 H), 4.85 (s, 1 H, D_2O exchangeable), 4.46 (d, J = 10.7 Hz, 1 H), 3.75 (d, J = 10.2 Hz, 1 H), 3.66 (s, 3 H), 3.64 (dd, J = 10.5, 6.4 Hz, 1 H), 3.60 (s, 3 H), 3.54 (dd, J = 10.8, 7.3 Hz, 1 H), 3.32 (dd, J = 10.7, 6.7 Hz, 1 H), 3.27 (ddd, J_1 = J_2 = 9.7, J_3 = 2.0 Hz, 1 H), 2.78−2.66 (m, 2 H) ppm. ^{13}C NMR: δ = 202.3, 132.7, 117.9, 105.4, 82.6, 70.0, 67.4, 67.3, 67.1, 54.8, 52.0, 51.3, 50.5, 43.2 ppm. IR (KBr): $\tilde{\nu}$ = 3500, 2900, 1760, 1620 cm^{-1}. $C_{14}H_{18}Br_2O_5$ (426.1): calcd. C 39.46, H 4.26; found C 39.41, H 4.29.

Acyloin 15f: Yield: 129 mg (98%) from **13f** (119 mg, 0.3 mmol); colorless solid (dichloromethane/hexane), m.p. 139−140 °C. ^{1}H NMR: δ = 6.17−6.06 (m, 1 H), 5.40 (d, J = 9.3 Hz, 1 H), 5.31 (d, J = 17.1 Hz, 1 H), 4.50−4.40 (m, 2 H), 4.21−4.11 (m, 2 H), 3.73 (s, 3 H), 3.61 (s, 3 H), 3.33 (ddd, J_1 = J_2 = 10.1, J_3 = 2.2 Hz, 1 H), 3.07−3.01 (m, 1 H), 3.06 (s, 1 H, D_2O exchangeable), 2.84 (dd, J = 13.6, 5.6 Hz, 1 H), 2.64 (dd, J = 13.9, 9.3 Hz, 1 H), 2.06 (s, 3 H), 1.99 (s, 3 H) ppm. ^{13}C NMR: δ = 201.1, 170.6, 170.2, 131.3, 123.4, 102.3, 80.0, 77.6, 76.7, 61.1, 59.9, 52.1, 51.8, 46.9, 43.1, 40.4, 21.0, 20.6 ppm. IR (KBr): $\tilde{\nu}$ = 3500, 2950, 1760 (br), 1600 cm^{-1}. $C_{18}H_{24}Cl_2O_8$ (439.3): calcd. C 49.22, H 5.51; found C 49.26, H 5.49.

Acyloin 16f: Yield: 157 mg (99%) from **14f** (146 mg, 0.3 mmol); colorless solid (dichloromethane/hexane), m.p. 143−144 °C. ^{1}H NMR: δ = 6.20−6.09 (m, 1 H), 5.41 (d, J = 10.0 Hz, 1 H), 5.32 (d, J = 17.1 Hz, 1 H), 4.48 (d, J = 5.4 Hz, 2 H), 4.17 (d, J = 6.6 Hz, 2 H), 3.78 (s, 3 H), 3.65 (s, 3 H), 3.39 (ddd, J_1 = J_2 = 11.6, J_3 = 5.6 Hz, 1 H), 3.08 (s, 1 H, D_2O exchangeable), 3.05 (ddd, J_1 = J_2 = 11.7, J_3 = 6.5 Hz, 1 H), 2.84 (dd, J = 13.7, 5.6 Hz, 1 H), 2.60 (dd, J = 13.9, 9.8 Hz, 1 H), 2.06 (s, 3 H), 1.99 (s, 3 H) ppm. ^{13}C NMR: δ = 200.7, 170.6, 170.2, 131.4, 123.4, 102.2, 80.1, 71.3, 71.2, 61.9, 60.3, 52.3, 51.9, 48.3, 44.0, 42.6, 21.0, 20.6 ppm. IR (KBr): $\tilde{\nu}$ = 3350, 2900, 1770, 1730, 1610 cm^{-1}. $C_{18}H_{24}Br_2O_8$ (528.2): calcd. C 40.93, H 4.58; found C 40.97, H 4.55.

Keto Lactone 20: Yield: 110 mg (97%) from **17** (111 mg, 0.3 mmol); colorless solid (dichloromethane/hexane), m.p. 142−143 °C. ^{1}H NMR: δ = 6.20−6.10 (m, 1 H), 5.26−5.21 (m, 2 H), 3.87 (d, J = 11.0 Hz, 1 H), 3.79 (s, 3 H), 3.71 (s, 3 H), 3.63 (s, 3 H), 3.49 (d, J = 11.0 Hz, 1 H), 2.81 (AB q, J = 7.1, 1.3 Hz, 2 H) ppm. ^{13}C NMR: δ = 191.9, 170.6, 166.9, 129.8, 119.7, 101.5, 87.5, 76.3, 75.7, 53.4, 52.4, 52.1, 52.0, 50.6, 34.8 ppm. IR: $\tilde{\nu}$ = 2960, 1795 (br), 1738, 1643 cm^{-1}. $C_{15}H_{16}Cl_2O_7$ (379.2): calcd. C 47.51, H 4.25; found C 47.54, H 4.23.

Keto Lactone 21: Yield: 133 mg (95%) from **18** (137 mg, 0.3 mmol); colorless solid (dichloromethane/hexane), m.p. 140−142 °C. ^{1}H NMR: δ = 6.22−6.11 (m, 1 H), 5.26−5.20 (m, 2 H), 3.88 (d, J = 10.9 Hz, 1 H), 3.75 (s, 3 H), 3.72 (s, 3 H), 3.67 (s, 3 H), 3.56 (d, J = 10.9 Hz, 1 H), 2.84 (dt, 1/2 AB q, J = 7.1, 1.3 Hz, 1 H), 2.75 (dt, 1/2 AB q, J = 7.1, 1.3 Hz, 1 H) ppm. ^{13}C NMR: δ = 190.5, 170.8, 167.0, 130.1, 119.5, 101.7, 87.5, 68.7, 67.2, 54.1, 53.3, 52.5, 52.2, 51.8, 37.0 ppm. IR: $\tilde{\nu}$ = 2950, 1780 (br), 1730, 1630 cm^{-1}. $C_{15}H_{16}Br_2O_7$ (468.1): calcd. C 38.49, H 3.45; found C 38.51, H 3.47.

Keto Lactone 22: Yield: 88 mg (95%) from **19** (90 mg, 0.3 mmol); colorless solid, m.p. 98 °C. 5.90−5.80 (m, 1 H), 5.26−5.21 (m, 2 H), 3.70 (s, 3 H), 3.62 (dd, J = 10.2, 3.7 Hz, 1 H), 3.40 (dd, J = 5.5, 1.1 Hz, 1 H), 3.32 (s, 3 H), 3.30 (s, 3 H), 3.27 (dd, J = 10.2, 5.1 Hz, 1 H), 3.08 (dd, J = 1.1, 3.5 Hz, 1 H), 3.03 (dd, J = 15.4, 5.1 Hz, 1 H), 2.32 (dd, J = 15.4, 9.2 Hz, 1 H) ppm. ^{13}C NMR: δ = 200.7, 173.9, 169.6, 130.8, 120.2, 106.6, 88.7, 54.9, 52.7, 51.5, 50.2, 49.4, 45.3, 43.1, 33.4 ppm. IR (KBr): $\tilde{\nu}$ = 2950, 1760, 1700, 1630 cm^{-1}. $C_{15}H_{18}O_7$ (310.3): calcd. C 58.06, H 5.85; found C 58.10, H 5.88.

Acyloin 9: A solution of **5a** (92 mg, 0.2 mmol), Bu_3SnH (146 mg, 0.5 mmol), and AIBN (1.6 mg, 0.01 mmol, 5 mol %) in benzene (2 mL) was heated under reflux under an inert atmosphere for 1.5 h. After the disappearance of the starting material (TLC monitoring), the benzene was distilled off using a rotary evaporator. The crude reaction mixture was purified directly by silica gel column chromatography (EtOAc/hexane) to yield the pure product as a colorless solid (55 mg, 91%). M.p. 104−106 °C. ^{1}H NMR: δ = 7.34 (m, 2 H, aromatic), 7.28−7.24 (m, 2 H, aromatic), 7.18−7.14 (m, 1 H, aromatic), 6.02−5.92 (m, 1 H, olefinic), 5.24 (d, J = 10.5 Hz, 1 H, olefinic), 5.20 (d, J = 17.3 Hz, 1 H, olefinic), 3.78 [dt, J = 11.2, 5.2 Hz, 1 H, C(5)H_{exo}], 3.39 [s, 3 H, $C(9)_{OMe}$], 3.29 [s, 3 H, $C(8)_{OMe}$], 3.03 [dd, J = 5.1, 1.9 Hz, 1 H, C(4)H], 2.71−2.66 [m, 1 H, allylic CH_2, C(1)H], 2.63−2.57 [m, 1 H, allylic CH_2, merged with $C(6)H_{endo}$], 2.57 [dd, J = 12.7, 4.8 Hz, 1 H, $C(6)H_{endo}$], 2.29 [ddd, J = 12.7, 11.2, 4.6 Hz, 1 H, $C(2)H_b$], 2.24 (s, 1 H, D_2O exchangeable, OH) ppm. ^{13}C NMR: δ = 212.4 (C-3), 140.5 (C-10), 132.9 (C-11), 128.2 (CH), 128.0 (CH), 126.4 (CH), 120.3 (CH_2, C-16), 109.1 (C-7a), 78.5 (carbinol C), 59.6 (CH), 51.0 (Me), 49.7 (Me), 46.7 (CH), 42.1 (CH_2), 41.2 (CH, C-1), 25.5 (CH_2) ppm. IR (KBr): $\tilde{\nu}$ = 3500, 2950, 1770, 1620 cm^{-1}. $C_{18}H_{22}O_4$ (302.4): calcd. C 71.50, H 7.33; found C 71.56, H 7.37.

X-Ray Crystallographic Analysis: The structures of **3e**, **4d**, and **12** were determined from single-crystal X-ray diffraction data. Data were collected at room temperature on an Enraf−Nonius CAD-4 Mach diffractometer using graphite monochromated Mo-K_α radiation (α = 0.71073 Å). The structures were solved using WinGX (Version 1.64.04), an integrated system of Windows programs for the solution, refinement, and analysis of single-crystal X-ray diffraction data [Louis J. Farrugia, Dept. of Chemistry, University of Glasgow (1997−2002)].[10] The structure was solved initially using SIR97 and then refined with SHELX-97, both of which are incor-

porated in WinGX. The structure was refined by full-matrix least-squares methods on F^2. The hydrogen atom positions were determined initially by geometry and refined by a riding model. Non-hydrogen atoms were refined using anisotropic displacement parameters. CCDC-229437 (for **3e**), -229436 (for **4d**), and -229438 (for **12**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223-336-033; or E-mail: deposit@ccdc.cam.ac.uk].

Supporting Information Available (see also the footnote on the first page of this article): A table providing a comparison of the chemical shift data of diagnostic protons for all of the monosubstituted acyloins with respect to their parent diketones, and NOESY spectrum of compound **9**.

Acknowledgments

We thank the Department of Science and Technology (DST), Council of Scientific and Industrial Research (CSIR), New Delhi, for financial assistance. FAK acknowledges the DST for a Swarnajayanti Fellowship. We are grateful to Dr. M. Grüner, TU Dresden, Germany, for providing the 2D NMR spectrum of compound **9**. X-ray data were collected at the National X-Ray Facility (funded by DST), Dept. of Chemistry, IIT, Kanpur.

[1] For reviews, see: [1a] P. Cintas, *Synlett* **1995**, 1087−1096. [1b] J. A. Marshall, *Chemtracts* **1997**, *10*, 481−496. [1c] A. S. K. Hashmi, *J. Pract. Chem.* **1998**, *340*, 84−89. [1d] C.-J. Li, T.-H. Chan, *Tetrahedron* **1999**, *55*, 11149−11176. [1e] J. Podlech, T. C. Maier, *Synthesis* **2003**, 633−655.

[2] For a recent example, see: K. T. Tan, S. S. Chng, H. S. Cheng, T. P. Loh, *J. Am. Chem. Soc.* **2003**, *125*, 2958−2963, (***(←Author: correct spelling for S. S. Chng?)***) and references cited therein.

[3] S. Araki, H. Ito, Y. Butsugan, *J. Org. Chem.* **1988**, *53*, 1831−1833.

[4] [4a] M. B. Isaac, C. Tak-Hang, *Tetrahedron Lett.* **1995**, *36*, 8957−8960. [4b] L. A. Paquette, T. M. Mitzel, *J. Am. Chem. Soc.* **1996**, *118*, 1931−1937. [4c] L. A. Paquette, T. M. Mitzel, M. B. Isaac, C. F. Crasto, W. W. Schomer, *J. Org. Chem.* **1997**, *62*, 4293−4301. [4d] P. C. Lobben, L. A. Paquette, *J. Org. Chem.* **1998**, *63*, 6990−6998. [4e] L. A. Paquette, R. R. Rothhaar, *J. Org. Chem.* **1999**, *64*, 217−224, and references cited therein.

[5] For allylindium additions to azetidine-2,3-diones, see: [5a] L. A. Paquette, R. R. Rothhaar, M. Isaac, L. M. Rogers, R. D. Rogers, *J. Org. Chem.* **1998**, *63*, 5463−5472. [5b] M. Jayaraman, M. S. Manhas, A. K. Bose, *Tetrahedron Lett.* **1997**, *38*, 709−712.

[6] For a few reports on allyl indium additions to 1,2-diketones, see: [6a] J. Mendez-Andino, L. A. Paquette, *Org. Lett.* **2000**, *2*, 1263−1265. [6b] E. P. Balskus, J. Mendez-Andino, R. M. Arbit, L. A. Paquette, *J. Org. Chem.* **2001**, *66*, 6695−6704. [6c] V. Nair, C. N. Jayan, *Tetrahedron Lett.* **2000**, *41*, 1091−1094. [6d] For a report on gallium-mediated allyl additions to 1,2-diketones, see: V. Nair, S. Ros, C. N. Jayan, *J. Chem. Res., Synop.* **2001**, 551−553.

[7] [7a] For their preparation, see: F. A. Khan, B. Prabhudas, J. Dash, N. Sahu, *J. Am. Chem. Soc.* **2000**, *122*, 9558−9559. For some recent applications, see: [7b] F. A. Khan, J. Dash, N. Sahu, S. Gupta, *Org. Lett.* **2002**, *4*, 1015−1018. [7c] F. A. Khan, N. Sahu, J. Dash, B. Prabhudas, *J. Indian Inst. Sci.* **2001**, *81*, 325−331. [7d] F. A. Khan, J. Dash, *J. Am. Chem. Soc.* **2002**, *124*, 2424−2425. [7e] F. A. Khan, J. Dash, N. Sahu, Ch. Sudheer, *J. Org. Chem.* **2002**, *67*, 3783−3787. [7f] F. A. Khan, J. Dash, *J. Org. Chem.* **2003**, *68*, 4556−4559.

[8] F. A. Khan, B. Prabhudas, *Tetrahedron* **2000**, *56*, 7595−7599.

[9] See supporting information for a comparison of ^{1}H NMR spectroscopic (400 MHz) data for the *exo*- and *endo*-6-H protons of acyloins **3−6** with those of the parent α-diketones **1** and **2** (for Supporting Information see also the footnote on the first page of this article).

[10] L. J. Farrugia, *J. Appl. Crystallogr.* **1999**, *32*, 837−838.

Received January 22, 2003

