Indium-Mediated Regio- and Diastereoselective Reduction of Norbornyl α-Diketones

Faiz Ahmed Khan,* Jyotirmayee Dash, and Ch. Sudheer[a]

Abstract: A novel, efficient, and regio- as well as diastereoselective conversion of non-enolizable bicyclic α-diketones into synthetically useful acyloins mediated by indium metal is described. The reduction is highly diastereoselective, leading exclusively to *endo*-acyloins (*endo*-hydroxyl groups) in excellent yields, and tolerates a variety of sensitive substituents, such as acetate, ester, and bridgehead halogens. The regioselectivity in the reductions of monosubstituted α-diketones varied from 70:30 to 100:0 for the two possible isomeric alcohols. The methodology is extended to the synthesis of highly functionalized cyclopentane carboxaldehydes, potential building blocks in organic syntheses, by cleavage of the acyloins by treating them with $Pb(OAc)_4$ in MeOH/PhH. Allylindium additions to carboxaldehydes **22** have been found to be highly diastereoselective.

Keywords: diketones · diastereoselectivity · indium · reduction · regioselectivity

Introduction

Indium-mediated reactions have gained considerable importance in the recent past due to their mild nature and the versatility of the reagent for a number of useful transformations.[1] Since the discovery of the indium-mediated, Barbier-type C–C bond-forming reaction by Butsugan and co-workers,[2] allylindium addition to carbonyl compounds has found wide-ranging current interest, and generally proceeds with high levels of chemo-, regio-, and diastereoselectivity.[1] In comparison with other metals, the unique properties associated with indium metal, in particular functional group tolerance, high stereoselectivity, ease of handling, and reactions in aqueous media, make its use a practical alternative for C–C bond-forming reactions. However, although indium has been widely used in synthetically useful carbonyl addition reactions,[2] there are only a limited number of reports in the literature on indium-mediated reductions.[3] The use of indium metal as a reducing agent was first reported for the reductive coupling of imines to give 1,2-diamines.[4] The reducing power of indium (E^0 (In^{3+}/In^0) = −0.34 V) is lower than that of other popular reducing agents used in organometallic reactions, such as tin, chromium(II), aluminum, and magnesium. However, its first ionization potential (5.8 eV) is close to those of alkali metals such as sodium or lithium and much lower than those of zinc, magnesium, or tin. In addition, unlike alkali metals, indium is not sensitive to boiling water or alkali and does not readily form oxides in air. Since the ionization potential is directly associated with the capability of the metal to release electrons, indium-mediated reactions apparently proceed by a single-electron transfer (SET) mechanism and the metal has been used as a mild potential reducing agent for a number of useful transformations. Some of the important reactions include stereoselective reductive elimination of 1,2-dibromides to give *trans*-alkenes,[5] reduction of terminal alkynes to alkenes,[6] reduction of C=C bonds in activated conjugated alkenes,[6] and selective reductions of the heterocyclic rings in quinolines and quinoxalines[7] and of aromatic nitro groups.[7]

In continuation of our ongoing research program, we became interested in norbornyl-based acyloins possessing bridgehead halogens. It occurred to us that the corresponding α-diketones could be suitable precursors, provided that an efficient and selective method could be developed. We focused our attention on indium metal as a potential reducing agent.[3] As an extension of our interest in indium-mediated reactions,[8] we report herein a mild, efficient, and stereoselective route to acyloins by indium-mediated reduction of non-enolizable α-diketones.[9] The acyloin (α-hydroxy ketone) functional group often plays an important role in organic synthesis and occurs widely in natural products as well as in advanced intermediates en route to several target molecules.[10] Conventionally, α-hydroxy ketones are prepared by acyloin condensation reactions,[11] oxidation of eno-

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lates,[12] and reduction of α-diketones.[13] However, the problems associated with reduction of α-diketones, such as over-reduction to a diol or to an α-methylene ketone,[14] make this procedure less attractive.[15] Thallium(III)-promoted α-oxidation of ketones to α-acetoxy ketones is the most recent addition to the growing list of methodologies.[16]

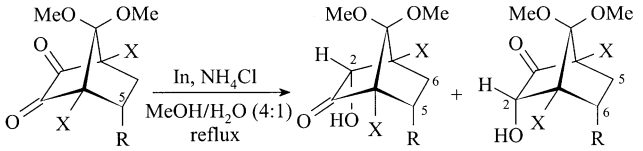
Results and Discussion

Norbornyl α-diketones were prepared according to a remarkably efficient methodology that employs catalytic $RuCl_3 \cdot 3H_2O$ and stoichiometric $NaIO_4$ for oxidation of the corresponding tetrahalonorbornyl derivatives, recently developed in our laboratory.[17] The tetrahalonorbornyl derivatives are easily accessible, and have been used as inextricable templates in organic synthesis.[18] The α-diketones were reduced by using indium metal (cut into small pieces) in MeOH/H_2O (4:1) at reflux temperature in the presence of either NH_4Cl, LiCl or NaCl (Table 1, Table 2, Table 5). Both chloro and bromo derivatives underwent smooth transformation to the corresponding acyloins in a regio- and stereoselective manner.

Reduction of monosubstituted α-diketones: The results obtained with indium in aqueous MeOH and NH_4Cl for monosubstituted α-diketones are summarized in Table 1. The α-diones **1a–g** and **2a–e** were efficiently reduced to furnish **3a–g** and **5a–e** as the major, and **4b–g, 6b–e** as the minor *endo* alcohols. Although mechanistically both the carbonyl groups are simultaneously involved in the electron-transfer process, formally it appears as though the carbonyl group reduction takes place exclusively at the *exo* face of the diketones **1** and **2**, at either the carbonyl diagonally opposite to or that on the same side as the *endo* substituent. The major alcohols **3a–g** and **5a–e**, with the *endo*-OH group diagonally opposite (δ-carbon) to the *endo* substituent, are regioisomeric with the minor alcohols **4b–g, 6b–e**, in which the *endo*-OH group is present on the same side as the substituent (γ-carbon; 1,3-relationship). The reaction proceeded in high yield and was highly stereoselective, leading predominantly to *endo* alcohols; the regioselectivity varied from 70:30 to 100:0 for the two regioisomeric alcohols (Table 1).

The product distributions of alcohols **3, 5** and **4, 6** were determined by integration of relevant signals in the 400 MHz ^1H NMR spectra of the crude reaction mixtures, usually before column purification; in a few cases, the mixture was first filtered through a short column of silica gel. The diketones **1a** and **2a**, bearing an *endo*-phenyl substituent, furnished essentially a single regioisomer, **3a** and **5a**, respectively (entries 1 and 8, Table 1). The yields were generally high in aqueous MeOH, except in the case of substrates **1, 2d** (*endo*-OAc derivatives, entries 4 and 11, Table 1) and **2c** (*endo*-CH_2OAc derivative, entry 10, Table 1). We studied the reactions in different solvent systems and in the presence of various additives (Table 2), and the comparison between aqueous MeOH and aqueous THF is particularly interesting.

Table 1. Indium-mediated reduction of monosubstituted α-diketones to acyloins.[a]



X=Cl **1a-g**, X=Br **2a-e** | X=Cl, **3a-g**, X=Br **5a-e** | X=Cl, **4b-g**, X=Br, **6b-e**

Entry	Substrate	R	Time [h]	Yield [%][b]	Product ratio **3**:**4** for **1**, **5**:**6** for **2**
1	**1a**	Ph	12	97	100:0
2	**1b**	OEt	12	100	71:29
3	**1c**	CH_2OAc	4	84	93:7
4	**1d**	OAc	12	68	100:0
5	**1e**	CO_2Me	6	76[c]	65:35
6	**1f**	$SiMe_3$	7	96	81:19
7	**1g**	CH_2OMe	9	99	80:20
8	**2a**	Ph	4	52	100:0
9	**2b**	OEt	9	83	81:19
10	**2c**	CH_2OAc	12	34	85:15
11	**2d**	OAc	6	40	100:0
12	**2e**	CO_2Me	10	68[c]	68:32

[a] All reactions were run using two equivalents of indium metal. [b] Isolated yields of analytically pure **3**+**4** (or **5**+**6**). [c] THF/H_2O (4:1) was used.

Table 2. Comparison of yield and regioselectivity in different solvent systems.[a]

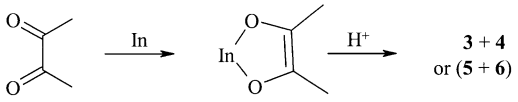
Entry	Substrate	Solvent/ H_2O (4:1)	Additive	Time [h]	Yield [%][b]	Product ratio[c] **3**:**4** for **1** **5**:**6** for **2**
1	**1a**	MeOH/ H_2O	–	14	96	100:0
2			NH_4Cl	12	97	100:0
3			NaCl	12	95	100:0
4		MeOH/ 10% HCl	–	13	95	100:0
5		MeOH	–	40	no reaction	
6	**1b**	THF	NH_4Cl	23	no reaction	
7	**1c**	MeOH/ H_2O	NH_4Cl	4	84	93:7
8		THF/H_2O		15	96	64:36
9	**1d**	MeOH/ H_2O	NH_4Cl	12	68	100:0
10		THF/H_2O	LiCl	16	90	70:30
11	**1e**	MeOH/ H_2O	MCl[d]	6	~30% crude	
12		THF/H_2O	NH_4Cl	11	96[e]	51:49
13		THF/H_2O	NH_4Cl	6	76	65:35
14	**2a**	MeOH/ H_2O	NH_4Cl	4	52	100:0
15		THF/H_2O	NH_4Cl	16	91	100:0
16	**2c**	MeOH/ H_2O	NH_4Cl	12	34	85:15
17		THF/H_2O	NH_4Cl	5	68	85:15
18	**2d**	MeOH/ H_2O	NH_4Cl	6	40	100:0
19		THF/H_2O	LiCl	6	85	80:20

[a] All reactions were run using two equivalents of indium metal. [b] Isolated yields of analytically pure **3**+**4** (or **5**+**6**). [c] For **1** X = Cl, **3**:**4**; for **2** X = Br, **5**:**6.** [d] MCl (NH_4Cl or LiCl). [e] Slow addition of the substrate to the reagent.

The reactions performed in MeOH/H_2O (4:1) proceeded faster than those conducted in THF/H_2O (4:1). The reaction was sluggish in anhydrous THF or MeOH (entries 5 and 6, Table 2). The presence of an additive MCl (NH_4Cl, LiCl, or NaCl) was found not to be essential for the reaction to occur (entries 1 and 11, Table 2), but it was found to enhance the rate. The reaction with substrate **1a** was also performed in MeOH containing 10% HCl (entry 4, Table 2), which gave the desired product **3a** in high yield.

By changing the solvent system to THF/H_2O (4:1), the yields were considerably improved in those cases where aqueous MeOH gave poor results (entries 7–19, Table 2). However, for the substrates **1c, 1d**, and **2d**, while the use of aqueous THF enhanced the yield of the reaction, its regioselectivity was diminished (compare entries 7/8, 9/10, 18/19 in Table 2). In the case of the *endo*-OAc derivative **1d**, only one regioisomer (based on ^{1}H NMR analysis of the crude product) was formed in 68% yield by using MeOH as solvent (entry 9, Table 2), while performing the reaction in aqueous THF afforded a 70:30 mixture of acyloins **3d** and **4d** in 90% yield (entry 10, Table 2).

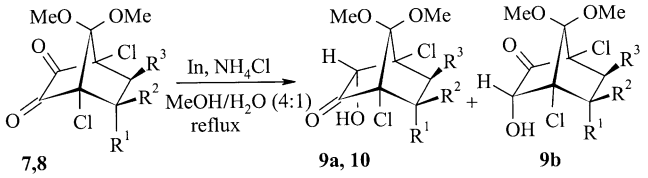
When the reduction of **1e** was conducted in aqueous methanolic medium, the products could not be isolated from the substrate (a long streak on the TLC plate and a very poor yield of the crude product ~30%, entry 11, Table 2). Conversely, the reaction proceeded smoothly in THF/H_2O showing moderate regioselectivity (entry 13, Table 2), and a near quantitative yield was obtained by slow addition of the substrate, although the regioselectivity dropped to 51:49 (entry 12, Table 2). Therefore, aqueous THF was the preferred medium with other ester substrates **2e, 7, 12a,b**, and **17** (vide infra). The solvent system THF/H_2O (4:1) gave satisfactory results in the case of ester derivatives **1e**, **2e**, and **17**, which reacted sluggishly in aqueous methanolic medium. The two solvent systems appear to play an important role with respect to the regioselectivity of the reaction and the product yields. In MeOH/H_2O, the regioselectivity is high compared with that achieved in aqueous THF, but for sensitive substrates the latter gives better results in terms of yield. The α-diketone moiety in the norbornyl system is constrained into a cisoid conformation and electron transfer is presumed to lead to an acyloinate intermediate as shown in Scheme 1. For norbornyl derivatives with a C_5-*endo* substituent, the acyloinate intermediate collapses to the acyloin upon protonation in such a way as to place the hydroxy group furthest away, as in the major regioisomer, on steric grounds.



Scheme 1.

The derivatives **7** and **8** follow the same trend as their monosubstituted counterparts (Table 3), demonstrating that an additional *exo* substituent placed either on the vicinal carbon or on the carbon that bears the *endo* substituent has no influence on the regio- and diastereoselectivity (compare with entries 1 and 5, Table 1).

Table 3. Indium-mediated reduction of diketones having *exo* substituents.



Substrate	R^1	R^2	R^3	Products	Time [h]	Yield [%]	Ratio
7	CO_2Me	H	Me	**9a,b**	7	75	67:33
					10	87[a]	54:46
8	Ph	Me	H	**10**	9	95	100:0

[a] THF/H_2O (4:1) is used as a solvent with LiCl.

Structural assignments of the products derived from the monosubstituted derivatives were made on the basis of their ^{1}H and ^{13}C NMR spectra. It is known that in bicyclo [2.2.1] systems the presence of an *endo* oxygen substituent at C_2 has a remarkable deshielding effect on the *endo*-H_6, while the *exo*-H_6 experiences a shielding effect. Thus, comparison of the ^{1}H NMR (400 MHz) shifts for *exo*- and *endo*-H_6 of acyloins with those of the parent α-diketone allows unambiguous confirmation of the stereochemical assignments (Table 4). In compounds **3** and **5**, the *endo*-H_6 consistently shows a deshielding effect ranging from 0.2 to 0.5 ppm, while the *exo*-H_6 is shielded by 0.2 to 0.4 ppm (Figure 1). No such effect is observed in the minor alcohols **4** and **6** (Table 4). In some cases, spin-decoupling experiments were carried out to unambiguously assign the *endo*-H_6 and *exo*-H_6 protons and to measure the W-couplings (see Experimental Section). The 400 MHz ^{1}H NMR spectra of the parent diketone and the major and minor α-hydroxy carbonyl compounds clearly show the deshielding of H_a and the shielding of H_b in the case of **3b** (see Supporting Information for spectra of **1b**, **3b**, and **4b**). The shielding and deshielding effects on the protons attached to carbons C(5) and C(6) of the major and minor acyloins are summarized in Figure 1. Further proof of the structures of both isomers **3, 5** and **4, 6** was provided by the W-coupling between the carbinol *exo*-H_2 and the *exo*-H_6 (0.7–2.4 Hz). In the ^{13}C NMR spectra, C_6

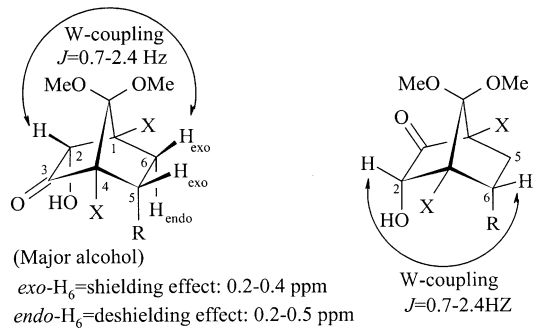
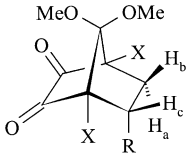
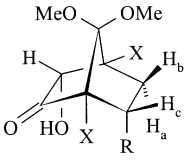


Figure 1. The basis for the ^{1}H NMR assignments of the regioisomeric acyloins.

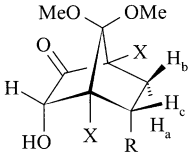
Table 4. Comparison of 400 MHz ^{1}H NMR chemical shift values [ppm] for H_a, H_b, and H_c in monosubstituted diketones and the corresponding acyloins.



1a-g (X=Cl)
2a-e (X=Br)



3a-g
5a-e

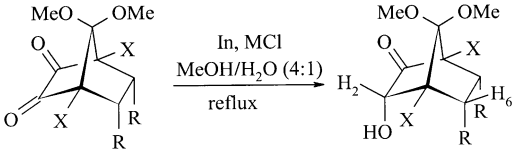


4b-g
6b-e

Diketone	H_a	H_b	H_c	acyloin	H_a	H_b	H_c
1a	2.48	3.07	3.91	**3a**	2.92	2.67	3.74
1b	2.13	2.98	4.28	**3b**	2.48	2.63	4.13
				4b	1.96	2.77	4.39
1c	2.18	2.75	3.02	**3c**	2.46	2.40	2.88–2.81
				4c	1.84	2.61	3.04–2.96
1d	2.06	3.14	5.48	**3d**	2.48	2.76	5.35
				4d	1.89	2.97	5.54
1e	2.37	2.83	3.61–3.58	**3e**	2.55	2.64	3.41
				4e	2.56	2.48	3.49
1f	1.90	2.19	2.67	**3f**	1.96	2.25	2.38
				4f	1.75	2.03	2.47
1g	2.32	2.62	2.83	**3g**	2.43-3.36	2.69	
				4g	2.06	2.46	2.88
2a	2.53	3.13	3.96	**5a**	2.98	2.76	3.78
2b	2.18	2.99	4.31	**5b**	2.54	2.70	4.17
				6b	2.01	2.80	4.44–4.41
2c	2.16	2.73	2.98	**5c**	2.54	2.48	2.88
				6c	1.90	2.66	3.07–2.99
2d	2.12	3.18	5.51	**5d**	2.54	2.86–2.80	5.38
				6d	1.95	3.01	5.56
2e	2.40	2.89	3.64	**5e**	2.70	2.62	3.47
				6e	2.59–2.56	3.56	
7	2.41	1.47[a]	3.27	**9b**	2.90	1.39[a]	3.08
				9c	2.52	1.32[a]	3.20
8	2.80	3.08	1.80[a]	**10b**	3.48	2.53	1.69[a]

[a] Shift for *exo* Me.

Table 5. Indium-mediated reduction of disubstituted α-diketones to acyloins.[a]



X=Cl **11a-f**
X=Br **12a,b**

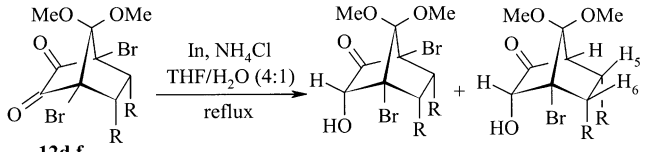
In, MCl
$MeOH/H_2O$ (4:1)
reflux

X=Cl **13a-f**
X=Br **14a,b**

Entry	Substrate	R	Product	Time [h]	Yield [%][b]
1	**11a**	CH_2OAc	**13a**	14	88[c]
2	**11b**	$-CH_2OCH_2OCH_2-$	**13b**	6	94
3	**11c**	$-(CH_2)_3-$	**13c**	8	100
4	**11d**	$-(CH_2)_4-$	**13d**	7	100
5				5	100[d]
6	**11e**	$-(CH_2)_6-$	**13e**	7	100
7	**11f**	$-CH_2OCH_2-$	**13f**	11	95
8	**12a**	CH_2OAc	**14a**	6	67[c,e]
9	**12b**	$-CH_2OCH_2OCH_2-$	**14b**	7	72[c,e]

[a] All reactions were run using two equivalents of indium metal and, unless otherwise specified, in the presence of NH_4Cl. [b] Isolated yields of analytically pure sample. [c] LiCl was used. [d] NaCl was used. [e] THF/H_2O (4:1).

Table 6. Indium-mediated reduction of disubstituted α-diketones.



12d,f

In, NH_4Cl
THF/H_2O (4:1)
reflux

14d,f + **15,16**

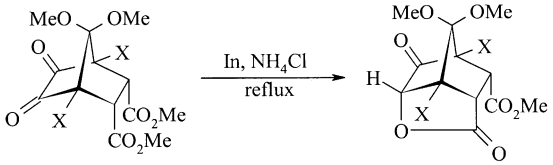
	R	Products	Time [h]	Yield [%]
12d	$-(CH_2)_4-$	**14d**, **15**	6	72, 13
12f	$-CH_2OCH_2-$	**14f**, **16**	8	22, 44

is consistently shielded by 3–4 ppm due to the presence of the *endo*-OH at C_2. The structures of the major and minor acyloins **3b** and **4b** were unequivocally confirmed by their X-ray crystal structures (see Supporting Information for ORTEP diagrams of compounds **3b** and **4b**).

Reduction of disubstituted α-diketones: In the case of disubstituted derivatives **11a–f** and **12a,b**, indium-mediated reduction proceeds stereoselectively to furnish the *endo* alcohols **13a–f** and **14a,b** in excellent yields (Table 5). The characteristic W-coupling between the carbinol *exo*-H_2 and *exo*-H_6 could be observed for each product.

When indium-mediated reduction of the diketone **12d** was carried out, the corresponding α-hydroxy carbonyl compound **14d** was formed in 72% yield along with the minor product **15** in 13% yield (Table 6). The product **15** was formed by over-reduction of **12d** (or **14d**); the bromine α to the carbonyl group was reduced. The alcohol **15** was characterized on the basis of the coupling shown by the bridgehead proton with the *exo*-H_5 ($J = 5.7$ Hz) and W-coupling between the carbinol *exo*-H_2 and the *exo*-H_6 (as indicated in the structure of **15**). Similarly, the reduction of diketone **12f** furnished a mixture of acyloins **14f** and **16**. Characteristic ^{13}C NMR signals for bromine-bearing bridgehead and carbinol carbons at $\delta = 67.2$, 83.2 ppm and $\delta = 63.0$, 83.0 ppm for **15** and **16**, respectively, confirmed the structural assignments.

Following indium-mediated reduction of diester derivatives **17** and **18**, the initially produced *endo* alcohols cyclized to furnish the corresponding lactones **19** and **20** (Scheme 2).



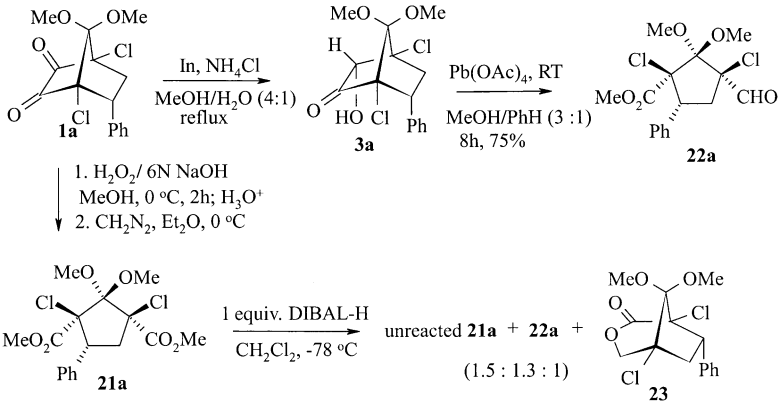
17 X=Cl 23 h THF/H_2O (4:1) **19** 83%
18 X=H 15 h $MeOH/H_2O$ (4:1) **20** 71%

Scheme 2. Indium-mediated reduction of diester derivatives.

The formation of these lactones provides additional proof of exclusive *endo* diastereoselection. The ^{1}H NMR spectra of lactones **19** and **20** feature three singlets due to OMe groups; in their ^{13}C NMR spectra the carbonyl groups give

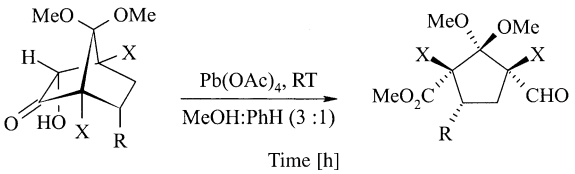
rise to signals at $\delta = 198.7$ and 188.8 ppm, the lactone carbonyls at $\delta = 175.0$ and 171.5 ppm, and the ester carbonyls at $\delta = 169.5$ and 166.9 ppm for **19** and **20**, respectively.

Cleavage of acyloins: After successfully developing the methodology for the regioselective reduction of diketones, it occurred to us that the cleavage of acyloins, particularly in the case of monosubstituted norbornyl derivatives, could be highly fruitful in achieving stereoselective transformation and may lead to derivatives that are not easily accessible by other means. For example, attempted selective reduction of the diester derivative **21a**, obtained by alkaline H_2O_2 cleavage of diketone **1a**,[17] using one equivalent of DIBAL-H at −78 °C, furnished a mixture (Scheme 3). The five-membered



Scheme 3. Cleavage of acyloin **3a** by lead tetraacetate.

ring aldehyde **22a**, the bicyclic lactone **23**, and the unreacted bis(α-chloro ester) cyclopentane derivative **21a** were formed in a ratio of 1.3:1:1.5, thus disqualifying this as a useful route to aldehyde **22a**. On the other hand, treatment of acyloin **3a**, obtained by indium-mediated reduction of **1a**, with $Pb(OAc)_4$ in MeOH/PhH (3:1) furnished the aldehyde **22a** in good yield, thus constituting an efficient and stereoselective route to highly functionalized cyclopentane carboxaldehydes. The procedure was efficiently extended to other derivatives **3b**, **3d**, **3f**, and **5b**, allowing access to the corresponding cyclopentane carboxaldehydes in good yields (Scheme 4).

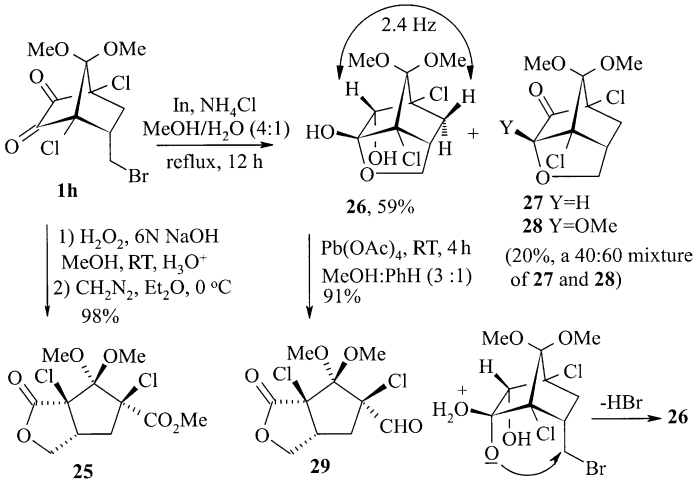


	Time [h]	
3a X=Cl, R=Ph	8	**22a** 75%
3b X=Cl, R=OEt	7	**22b** 77%
3d X=Cl, R=OAc	4.5	**22d** 79%
3f X=Cl, R=TMS	5	**22f** 71%
5b X=Br, R=OEt	6	**24** 78%

Scheme 4. Cleavage of acyloins by lead tetraacetate.

A direct alkaline cleavage of diketone **1h**, derived from an allyl bromide adduct, gave the γ-lactone derivative **25** bearing an α-haloester substituent (Scheme 5).[19] While discrimination between the two reducible moieties, that is to say the ester and lactone groups of lactone derivative **25**, would be difficult, by carrying out a cleavage reaction after indium-mediated reduction of **1h**, such a distinction is possible. Indeed, cleavage of the diol **26** with lead tetraacetate in MeOH/PhH (3:1) furnished the fused γ-lactone cyclopentanoid derivative **29**,[19] having groups distinctively different in reactivity towards hydride-based reducing agents, thereby providing a handle for selective transformation.

When the diketone **1h**, bearing an *endo*-bromomethyl substituent, was subjected to indium-mediated reduction, three products **26, 27**, and **28** were isolated (Scheme 5). The reduction occurred first, and was followed by intramolecular displacement leading to the diol **26** as the major product in 59% yield, along with the minor isomer **27**. However, a competing reaction of intramolecular nucleophilic displacement of bromine by the alkoxide generated by the addition of MeOH to the carbonyl group was observed under the reaction conditions, leading to the formation of trimethoxy oxa-tricyclo

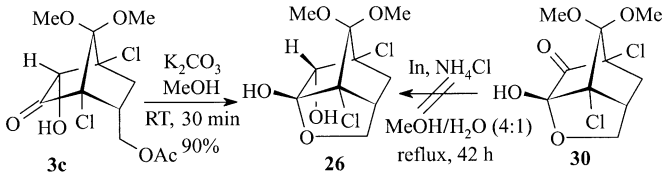


Scheme 5. Preparation of a functionalized γ-lactone derivative.

ketone **28**. The products **27** and **28** were recovered in the form of a colorless solid as an inseparable mixture, in a ratio of 40:60 as determined by ^1H NMR spectroscopy (Scheme 5). However, the two compounds were isolated in pure form by way of two different independent reactions; the formation of **27** is discussed below (Scheme 7).

The diol **26** was characterized from its 400 MHz ^1H NMR spectral data on the basis of W-coupling ($J = 2.4$ Hz) between the carbinol hydrogen at C_2 and the *exo* proton.[19]

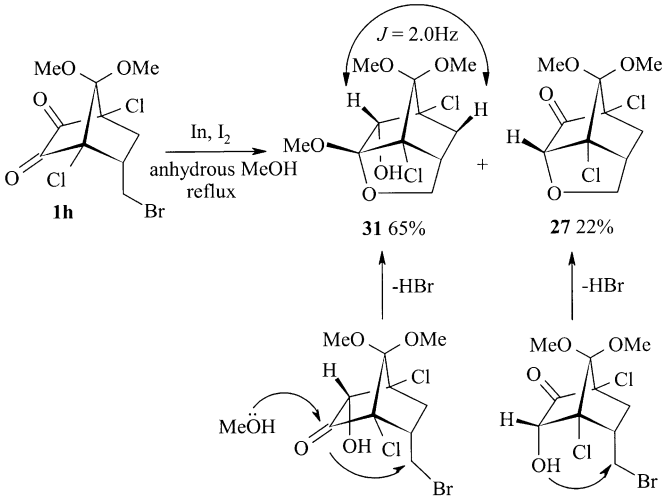
Further chemical proof for the structure **26** came from the deprotection of the acetate group of the mixture of acyloins **3c** and **4c** (93:7) obtained from the indium-mediated reduction of **1c**. Treatment of the mixture of acyloins **3c** and **4c** with K_2CO_3 in MeOH furnished the diol **26** in 90% yield (Scheme 6).



(from **3c:4c**, 93:7 reaction mixture)

Scheme 6.

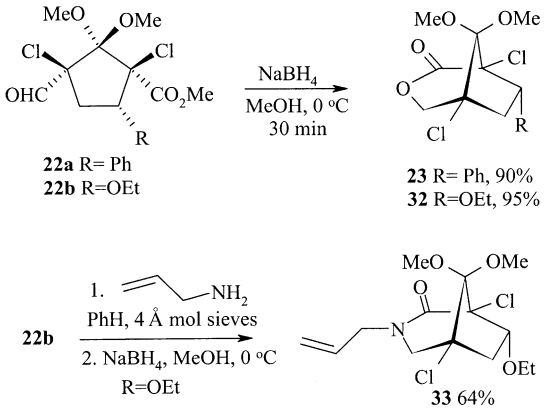
In an attempted indium-mediated reduction of **1h** in the presence of iodine in anhydrous MeOH under reflux conditions, two products **31** and **27** were obtained in high yield (Scheme 7). Compound **31** shows characteristic W-coupling



Scheme 7. Indium-mediated reduction of diketone **1h**.

of 2.0 Hz in its ^{1}H NMR spectrum. Following the initial indium-mediated reduction, intramolecular displacement occurred to furnish the alcohol **31** as the major product and oxa tricycle **27** as the minor one**.** The fact that reaction proceeds via the reduction of the α-diketone **1h** was further proved by separately treating the α-keto hemiacetal **30**[19] with indium in aqueous MeOH under reflux conditions for 42 h. The attempted reaction failed to give **26** and the starting material was recovered (Scheme 6).

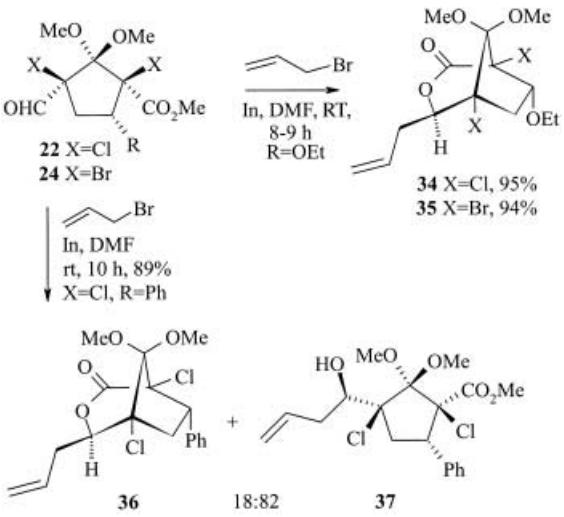
Having obtained the functionalized cyclopentane carboxaldehydes **22** and **24**, we performed various reactions with them, which are presented in Scheme 8 and Scheme 9. The bicyclo[3.2.1]lactones **23**, **32** and lactam **33** were conveniently prepared. Sodium borohydride reduction of the aldehydes **22a** and **22b** furnished the bicyclo[3.2.1]lactones **23** and **32** in excellent yields by lactonization of the alcohol function produced (Scheme 8). A one-pot synthesis of bicyclic amide



Scheme 8. Synthesis of bicyclo[3.2.1]lactones and a lactam.

33 was also easily achieved. The aldehyde **22b** was condensed with allylamine and the resulting imine was reduced with $NaBH_4$ in the same pot to provide bicyclo[3.2.1]lactam **33** in 64% yield (Scheme 8).

The aldehydes **22a,b** and **24** were also subjected to indium-promoted allylation[1] (Scheme 9). While sodium borohydride reduction of these aldehydes led exclusively to



Scheme 9. Allylindium addition to cyclopentane carboxaldehydes.

the lactones **23** and **32**, interestingly, allylindation was found to proceed with high diastereoselection. When the ethoxy-substituted aldehydes **22b** and **24** were subjected to Barbier-type allylation with indium metal and allyl bromide in DMF at room temperature, the initially formed major diastereomers underwent lactonization to give the single diastereomers **34** and **35**, respectively, in near quantitative yields. On the other hand, subjecting the phenyl-substituted derivative **22a** to the same reaction for 10 h led to a mixture of the cyclized diastereomer **36** and its uncyclized form **37** in an 18:82 ratio. The product distribution in each case was determined by 400 MHz ^{1}H NMR analysis of the crude reaction mixture prior to column purification. In the ^{13}C NMR spectra, the signal of the carbinol carbon of alcohol **37** appeared at δ =

85.8 ppm, while that of the corresponding carbon of the lactone **36** appeared at $\delta = 89.2$ ppm. Three singlets due to OMe groups were seen in the ^{1}H NMR spectrum of the cyclopentane derivative **37**. Clear cross-peaks between the OMe and allylic CH_2 protons in the 500 MHz ^{1}H/^{1}H NOESY spectrum confirm the relative stereochemistry in lactones **34** and **36**. The origins of the NOE correlations seen in the ^{1}H/^{1}H NOESY spectra of **34** and **36** are shown in Figure 2. The ^{1}H/^{1}H NOESY spectra of **34** and **36** are presented in Figure 3 and Figure 4, respectively. The connectivity is indicated in the spectra. The connectivity was unambiguously established by means of HMBC, HSQC, COSY, and DEPT experiments (see Supporting Information). The structure of **37** was unequivocally confirmed through a single-crystal X-ray analysis (Figure 5).

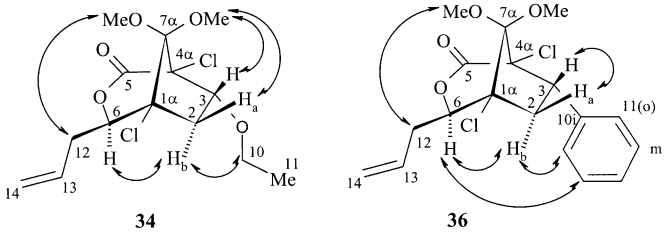


Figure 2. NOESY correlations in **34** and **36**.

The high selectivity observed in the reactions of ethoxy derivatives **22b** and **24** may be explained by invoking a chelation-controlled allyl transfer involving transition state **38** as shown in Figure 6. Similarly, in the case of the phenyl derivative **22a**, a chelation model involving OMe and ester groups present on vicinal carbons in the transition state **39** would account for the product formed.

Conclusion

In summary, we have described a novel, efficient, and regio- as well as diastereoselective conversion of non-enolizable bicyclic α-diketones into synthetically useful acyloins mediated by indium metal. The reaction tolerates a variety of sensitive substituents, such as acetate, ester, and bridgehead halogens. Furthermore, this methodology has been applied to the synthesis of highly functionalized cyclopentane carboxaldehydes, potential building blocks in organic synthesis, by cleavage of the acyloins under $Pb(OAc)_4$/MeOH/PhH conditions. Allylindium additions to carboxaldehydes have been found to be highly diastereoselective.

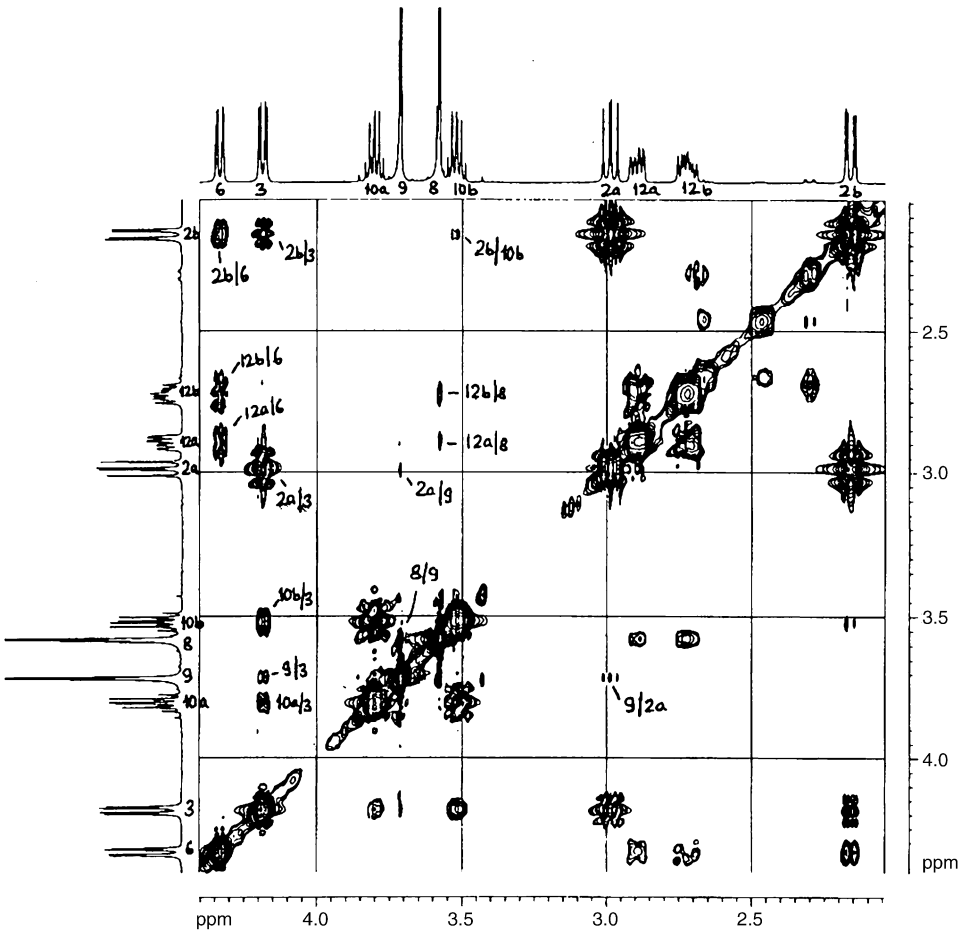


Figure 3. 500 MHz ^{1}H/^{1}H NOESY spectrum of **34** in $CDCl_3$ solution.

Experimental Section

General: All reactions were performed in oven-dried apparatus. The solvents used were purified by distillation from the drying agents indicated: MeOH (Mg), THF and Et_2O (sodium benzophenone ketyl), CH_2Cl_2 (P_4O_{10}), DMF (benzene/water azeotrope, distilled under vacuum), benzene (Na). The solvents MeOH, CH_2Cl_2, and DMF were stored over 4 Å molecular sieves. Column chromatography was performed on Acme's silica gel (100–200 mesh) with ethyl acetate/hexane mixtures as eluents. Melting points are uncorrected. IR spectra were recorded from samples in KBr pellets (solids) or as thin films (liquids). ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded from solutions in $CDCl_3$ unless otherwise mentioned, and are reported on the δ scale in ppm. Tetramethylsilane was used as an internal standard. Data are reported as follows: (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; integration; coupling constant(s) in Hz).

General procedure for the indium-mediated reduction of α-diketones: A mixture of the α-diketone (0.3 mmol), indium metal (0.6 mmol, cut into small pieces), NH_4Cl (0.9 mmol) in MeOH (4 mL), and water (1 mL) was refluxed for the specified time (refer to Table 1, Table 3, Table 4, Table 6, and Scheme 2). After completion of the reaction, as monitored by TLC, the reac-

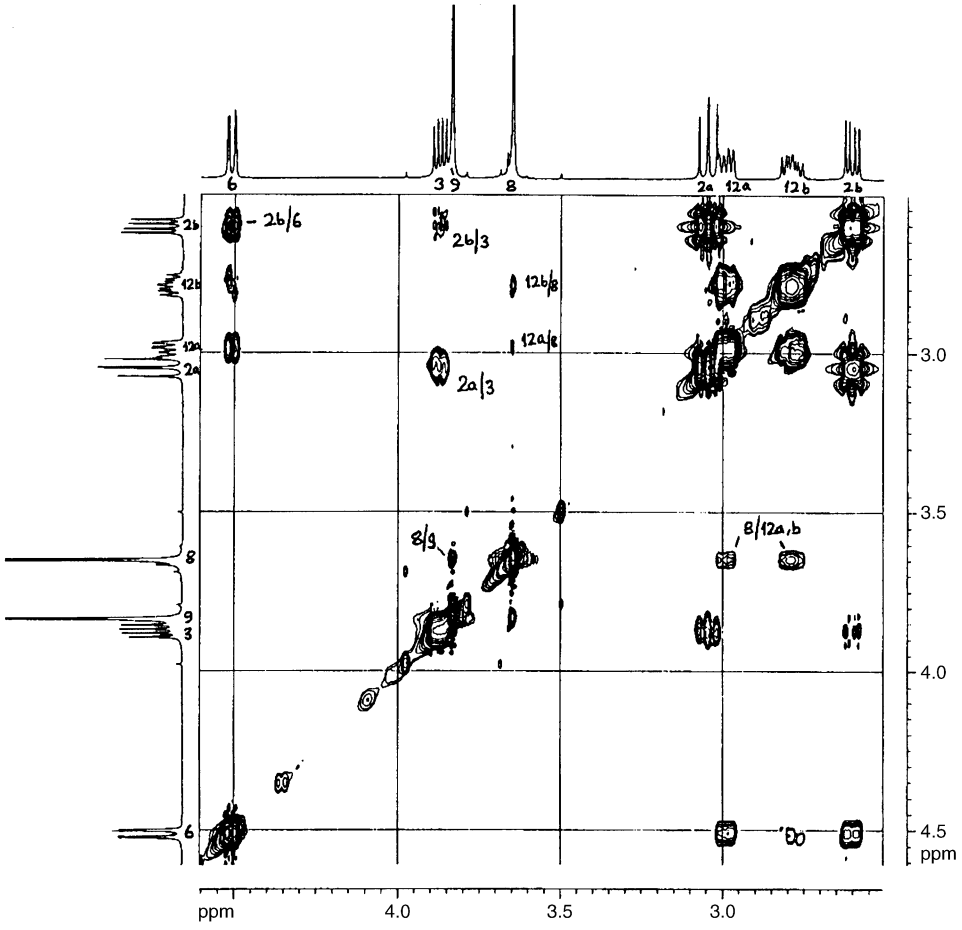


Figure 4. 500 MHz ^{1}H/^{1}H NOESY spectrum of **36** in $CDCl_3$ solution.

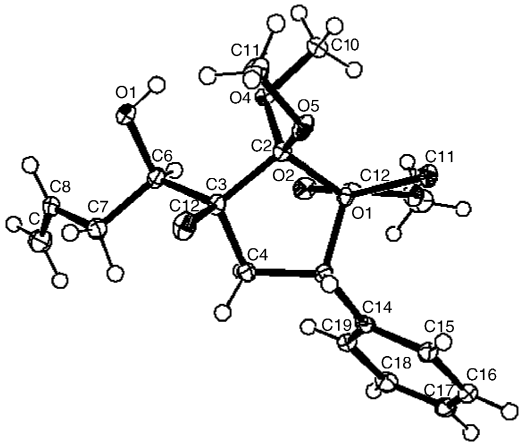


Figure 5. X-ray crystal structure of compound **37**.

tion mixture was quenched with 5% aq HCl (1 mL) and extracted with ethyl acetate. The combined organic layers were washed once with brine and dried over anhydrous Na_2SO_4. Concentration followed by column chromatography on silica gel gave the acyloins in the specified yields.

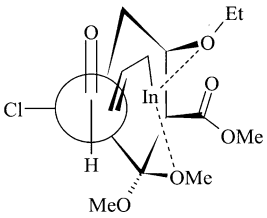
Spectral data for monosubstituted acyloins

Acyloin 3a: Yield 100%; colorless solid, m.p. 106–108°C; ^{1}H NMR: δ = 7.29–7.26 (m, 5H; aromatic), 4.56 (brs, 1H), 3.79 (s, 3H; OMe), 3.74 (dd, 1H, J = 12.2, 5.6 Hz; 5-H_{exo}), 3.73 (brs, 1H, D_2O exchangeable; OH), 3.65 (s, 3H; OMe), 2.92 (dd, 1H, J = 13.1, 5.6 Hz; 6-H_{endo}), 2.67 ppm (dt, 1H, J = 13.1, 1.9 Hz; 6-H_{exo}); ^{13}C NMR: δ = 200.3 (C=O), 134.9, 129.4, 128.2, 127.9, 103.3, 82.0, 78.3 (carbinol C), 69.7, 51.8 (OMe), 51.7 (OMe), 48.7, 34.4 ppm; IR (KBr): $\tilde{\nu}$ = 3500, 2950, 1770, 1100 cm^{-1}; elemental analysis calcd (%) for $C_{15}H_{16}Cl_2O_4$: C 54.40, H 4.87; found: C 54.41, H 4.90.

Acyloins 3b, 4b: Yield 100%; mixture of regioisomers (71:29). The regioisomers were separated by column chromatography on silica gel with 5% ethyl acetate/hexane as eluent.

Major isomer 3b: Colorless solid, m.p. 102–104°C; ^{1}H NMR: δ = 4.46 (dd, 1H, J = 6.2, 1.6 Hz; carbinol H), 4.13 (dd, 1H, J = 9.5, 2.2 Hz; 5-H_{exo}), 3.68 (s, 3H; OMe), 3.67 (dq, 1H, merged with OMe; OCH_2), 3.59 (s, 3H; OMe), 3.52 (dq, 1H, J = 9.0, 7.1 Hz; OCH_2), 2.98 (d, 1H, J = 6.2 Hz, D_2O exchangeable; OH), 2.63 (ddd, J = 13.1, 9.5, 1.6 Hz; 6-H_{exo}), 2.48 (dd, J = 13.1, 2.2 Hz; 6-H_{endo}), 1.13 ppm (t, 3H, J = 7.1 Hz; Me); ^{13}C NMR: δ = 197.5 (C=O), 103.1 (C_7), 80.9, 80.1, 79.0, 69.4, 66.7, 51.9, 51.8, 36.9, 15.1 ppm; IR (KBr): $\tilde{\nu}$ = 3400, 2900, 1780, 1440 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_{16}Cl_2O_5$: C 44.17, H 5.39; found: C 43.87, H 5.10.

Minor isomer 4b: Colorless solid, m.p. 113–115°C; ^{1}H NMR: δ = 4.70 (d, 1H, J = 11.0 Hz; carbinol H), 4.45 (dd, 1H, J = 11.0, 2.2 Hz; OCH_2), 4.39 (td, 1H, J = 9.8, 2.2 Hz; 6-H_{exo}), 3.66 (s, 3H; OMe), 3.64 (m, 1H; OCH_2), 3.62 (s, 3H; OMe), 2.77 (dd, 1H, J = 13.3, 9.6 Hz; 5-H_{exo}), 1.96 (dd, 1H, J = 13.3, 2.7 Hz; 5-H_{endo}), 1.23 ppm (t, 3H, J = 7.0 Hz; Me); ^{13}C NMR: δ = 201.1 (C=O), 102.5 (C_7), 83.4, 81.1, 74.3, 70.2, 67.7, 51.8, 51.7, 40.4, 15.1 ppm; IR (KBr): $\tilde{\nu}$ = 3500, 2950, 1720, 1380 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_{16}Cl_2O_5$: C 44.17, H 5.39; found: C 44.23, H 5.42.



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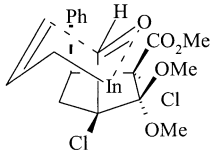

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Figure 6. Proposed origin of the selectivity observed in allylindium additions.

Acyloins 3c, 4c: Yield 84%; inseparable mixture of regioisomers (93:7); colorless solid, m.p. 86–87°C; IR (KBr): $\tilde{\nu}$ = 3300, 2900, 1760, 1690, 1200 cm^{-1}; elemental analysis calcd (%) for $C_{12}H_{16}Cl_2O_6$: C 44.06, H 4.92; found: C 44.20, H 5.18.

Major isomer 3c: ^{1}H NMR: δ = 4.43 (dd, 1H, J = 5.1, 1.7 Hz; carbinol H), 4.10 (dd, 1H, J = 11.8, 4.6 Hz), 3.96 (dd, 1H, J = 11.8, 6.6 Hz), 3.70 (s, 3H; OMe), 3.62 (s, 3H; OMe), 3.43 (d, 1H, J = 5.1 Hz, D_2O exchangeable; OH), 2.88–2.81 (m, 1H; 5-H_{exo}), 2.46 (dd, 1H, J = 12.8, 5.6 Hz; 6-H_{endo}), 2.40 (dt, 1H, J = 12.8, 1.7 Hz; 6-H_{exo}), 2.03 ppm (s, 3H; OCOMe); ^{13}C NMR: δ = 200.1 (C=O), 170.6 (O–C=O), 102.9, 78.4, 78.3, 69.6, 61.6, 51.8, 51.6, 41.9, 31.2, 20.6 ppm.

Minor isomer 4c: ^{1}H NMR: δ = 4.62 (brs, 1H; carbinol H), 4.47 (dd, 1H, J = 11.6, 3.4 Hz), 4.37 (dd, 1H, J = 11.6, 9.7 Hz), 3.70 (s, 3H; OMe), 3.62 (s, 3H; OMe), 3.04–2.96 (m, 1H, J = 1.7 Hz + others; 6-H_{exo}), 2.61 (t, 1H, J = 13.1 Hz; 5-H_{exo}), 2.06 (s, 3H; OAc), 1.84 ppm (dd, 1H, J = 13.1, 5.6 Hz; 5-H_{endo}); ^{13}C NMR: δ = 201.6 (C=O), 171.4 (O−C=O), 102.7, 79.9, 74.7, 72.3, 64.7, 51.8 (OMe), 51.7 (OMe), 42.9, 37.6, 20.9 ppm.

For both the isomers **3c** and **4c**, J = 1.7 Hz for 2-H_{exo} and 6-H_{exo} was confirmed by decoupling experiments.

Acyloins 3d, 4d: Yield 90%; mixture of regioisomers (70:30) in THF/H_2O.

Major isomer 3d (from MeOH/H_2O reaction, 68%): Colorless solid, m.p. 97–99°C; ^{1}H NMR: δ = 5.35 (dd, 1H, J = 10.2, 3.2 Hz; 5-H_{exo}), 4.52 (dd, 1H, J = 4.6, 2.2 Hz; carbinol H), 3.71 (s, 3H; OMe), 3.62 (s, 3H; OMe), 3.48 (d, 1H, J = 4.9 Hz, D_2O exchangeable; OH), 2.76 (ddd, 1H, J = 13.6, 10.2, 2.2 Hz; 6-H_{exo}), 2.48 (dd, 1H, J = 13.6, 3.2 Hz; 6-H_{endo}), 2.06 ppm (s, 3H; OCOMe); ^{13}C NMR: δ = 197.5 (C=O), 170.1 (O−C=O), 102.7, 78.7, 78.3, 73.3, 69.1, 51.9, 51.8, 35.9, 20.6 ppm; IR (KBr): $\tilde{\nu}$ = 3300, 2900, 1760, 1700, 1360, 1200 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_{14}Cl_2O_6$: C 42.19, H 4.51; found: C 41.93, H 4.89.

Minor isomer 4d (from the mixture): ^{1}H NMR: δ = 5.54 (ddd, 1H, J = 10.1, 3.2, 1.8 Hz; 6-H_{exo}), 4.61 (dd, 1H, J = 1.8 Hz; carbinol H), 3.69 (s, 3H; OMe), 3.65 (s, 3H; OMe), 2.97 (dd, 1H, J = 14.0, 10.1 Hz; 5-H_{exo}), 2.16 (s, 3H; OCOMe), 1.89 ppm (dd, 1H, J = 14.0, 3.2 Hz; 5-H_{endo}); ^{13}C NMR: δ = 200.5 (C=O), 169.3 (O−C=O), 102.6, 80.9, 76.9, 73.9, 70.2, 52.0, 51.8, 40.3, 20.8 ppm.

Acyloins 3e, 4e: Yield 76%; mixture of regioisomers (65:35). The regioisomers were separated by flash column chromatography on silica gel with 10% ethyl acetate/hexane as eluent.

Major isomer 3e: Colorless solid, m.p. 103–105°C; ^{1}H NMR: δ = 4.43 (dd, 1H, J = 8.9, 1.7 Hz; carbinol H), 3.77 (brs, 1H, D_2O exchangeable; OH), 3.75 (s, 3H; OMe), 3.72 (s, 3H; OMe), 3.61 (s, 3H; OMe), 3.41 (dd, 1H, J = 11.5, 4.1 Hz; 5-H_{exo}), 2.64 (dd, 1H, J = 12.9, 4.1 Hz; 6-H_{exo}), 2.55 ppm (dt, 1H, J = 12.9, 1.7 Hz; 6-H_{endo}); ^{13}C NMR: δ = 198.6 (C=O), 173.3 (O−C=O), 103.1, 79.0 (2C), 69.4, 53.4 (OMe), 52.0 (OMe), 51.8 (OMe), 48.7, 32.0 ppm; IR (KBr): $\tilde{\nu}$ = 3300, 2900, 1760, 1700, 1370, 1200 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_{14}Cl_2O_6$: C 42.19, H 4.51; found C 42.37, H 4.57.

Minor isomer 4e: Colorless solid, m.p. 122–124°C; ^{1}H NMR: δ = 4.59 (d, 1H, J = 5.6 Hz; carbinol H), 3.75 (s, 3H; OMe), 3.71 (s, 3H; OMe), 3.67 (d, 1H, J = 6.1 Hz, D_2O exchangeable; OH), 3.63 (s, 3H; OMe), 3.49 (dd, 1H, J = 10.4, 6.7 Hz; 6-H_{exo}), 2.56–2.48 ppm (m, 2H); ^{13}C NMR: δ = 200.3 (C=O), 172.0 (O−C=O), 103.1, 79.8, 73.9, 71.9, 52.8 (OMe), 51.9 (2C; OMe), 45.5, 34.2 ppm; IR (KBr): $\tilde{\nu}$ = 3400, 2900, 1760, 1700, 1360, 1340 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_{14}Cl_2O_6$: C 42.19, H 4.51; found C 42.22, H 4.53.

Acyloins 3f, 4f: Yield: 96%; mixture of regioisomers (81:19). The regioisomers were separated by column chromatography on silica gel with 2% ethyl acetate/hexane as eluent.

Major isomer 3f: Colorless solid, m.p. 100–101°C; ^{1}H NMR: δ = 4.37 (dd, 1H, J = 4.2, 2.0 Hz; carbinol H), 3.67 (s, 3H; OMe), 3.58 (s, 3H; OMe), 3.03 (d, 1H, J = 4.2 Hz, D_2O exchangeable; OH), 2.38 (dd, 1H, J = 12.3, 6.8 Hz; 5-H_{exo}), 2.25 (dt, 1H, J = 12.5, 2.0 Hz; 6-H_{exo}), 1.95 (dd, 1H, J = 12.9, 6.8 Hz; 6-H_{endo}), 0.0 ppm (s, 9H; $SiMe_3$); ^{13}C NMR: δ = 201.9 (C=O), 103.0, 79.1, 78.2, 70.1, 51.7, 51.4, 31.2, 30.2, −1.96 ppm; IR (KBr): $\tilde{\nu}$ = 3400, 2900, 1760, 1440, 1200 cm^{-1}; elemental analysis calcd (%) for $C_{12}H_{20}Cl_2O_4Si$: C 44.04, H 6.16; found: C 43.97, H 6.20.

Minor isomer 4f: Colorless solid, m.p. 119–121°C; ^{1}H NMR: δ = 4.57 (s, 1H; carbinol H), 3.72 (s, 3H; OMe), 3.61 (s, 3H; OMe), 2.89 (d, 1H, J = 4.2 Hz, D_2O exchangeable; OH), 2.47 (t, 1H, J = 12.7 Hz; 5-H_{exo}), 2.03 (ddd, 1H, J = 13.1, 6.1, 2.0 Hz; 6-H_{exo}), 1.75 (dd, 1H, J = 12.1, 6.2 Hz; 6-H_{endo}), 0.08 ppm (s, 9H; $SiMe_3$); ^{13}C NMR: δ = 203.1 (C=O), 103.8, 80.3 (carbinol C), 76.0, 75.0, 54.0, 52.3, 34.9, 30.8, 0.00 ppm; IR (KBr): $\tilde{\nu}$ = 3400, 2900, 1750, 1420, 970 cm^{-1}; elemental analysis calcd (%) for $C_{12}H_{20}Cl_2O_4Si$: C 44.04, H 6.16; found: C 44.18, H 6.02.

Acyloins 3g, 4g: Yield 99%; inseparable mixture of regioisomers (80:20); colorless solid, m.p. 98–99°C; IR (KBr): $\tilde{\nu}$ = 3300, 2900, 1760, 1380, 1180, 1040 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_{16}Cl_2O_5$: C 44.17, H 5.39; found C 43.98, H 5.12.

Major isomer 3g: ^{1}H NMR: δ = 4.30 (dd, 1H, J = 10.7, 1.2 Hz; carbinol H), 3.94 (d, 1H, J = 10.7 Hz, D_2O exchangeable; OH), 3.70 (s, 3H; OMe), 3.59 (s, 3H; OMe), 3.54 (dd, 1H, J = 10.3, 3.5 Hz), 3.38 (dd, 1H, J = 10.3, 2.0 Hz), 3.25 (s, 3H; OMe), 2.69 (m, 1H; 5-H_{exo}), 2.43–2.36 ppm (m, 2H, J = 1.4 Hz + others); ^{13}C NMR: δ = 199.7 (C=O), 102.9, 79.1 (carbinol C), 74.6, 70.3, 67.9, 58.8 (OMe), 51.9 (OMe), 51.7 (OMe), 44.6, 29.7 ppm.

Minor isomer 4g: ^{1}H NMR: δ = 5.51 (d, 1H, J = 11.7 Hz, D_2O exchangeable; OH), 4.51 (qt, 1H, J = 11.7, 0.7 Hz; carbinol H), 3.88 (dd, 1H, J = 10.7, 1.7 Hz), 3.70 (s, 3H; OMe), 3.63 (s, 3H; OMe), 3.44 (s, 3H; OMe), 3.40–3.36 (m, 1H, buried under peaks of major isomer), 2.88 (tddd, 1H, J = 12.1, 6.1, 4.6, 1.7 Hz; 6-H_{exo}), 2.46 (dd, 1H, J = 12.7, 1.4 Hz; 5-H_{exo}), 2.06 ppm (dd, 1H, J = 12.7, 6.1 Hz; 5-H_{endo}); ^{13}C NMR: δ = 202.0 (C=O), 103.1, 79.5 (carbinol C), 78.9, 73.3, 67.2, 59.3, 51.7 (OMe), 51.6 (OMe), 43.3, 32.9 ppm.

Acyloin 5a: Yield 91%; colorless solid, m.p. 115–118°C; ^{1}H NMR: δ = 7.31–7.23 (m, 5H; aromatic), 4.58 (brs, 1H; carbinol H), 3.84 (s, 3H; OMe), 3.78 (dd, 1H, J = 12.2, 5.9 Hz; 5-H_{exo}), 3.71 (s, 3H; OMe), 3.34 (brs, 1H, D_2O exchangeable; OH), 2.98 (dd, 1H, J = 13.1, 5.6 Hz; 6-H_{endo}), 2.76 ppm (ddd, 1H, J = 13.1, 12.2, 2.2 Hz; 6-H_{exo}); ^{13}C NMR: δ = 200.4 (C=O), 135.3, 129.5, 128.1, 127.9, 103.5, 79.0 (carbinol C), 75.9, 61.6, 52.0 (OMe), 51.8 (OMe), 50.2, 36.4 ppm; IR (KBr): $\tilde{\nu}$ = 3500, 2950, 1750, 1100 cm^{-1}; elemental analysis calcd (%) for $C_{15}H_{16}Br_2O_4$: C 42.89, H 3.84; found: C 42.78, H 3.92.

Acyloins 5b, 6b: Yield 83%; mixture of regioisomers (81:19). The regioisomers were separated by column chromatography on silica gel with 5% ethyl acetate/hexane as eluent.

Major isomer 5b: Colorless solid, m.p. 100–102°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.49 (dd, 1H, J = 5.8, 1.7 Hz; carbinol H), 4.17 (dd, 1H, J = 9.5, 2.7 Hz; 5-H_{exo}), 3.73 (s, 3H; OMe), 3.67 (qd, 1H, J = 9.7, 7.1 Hz), 3.64 (s, 3H; OMe), 3.54 (qd, 1H, J = 9.7, 7.1 Hz), 2.99 (d, 1H, J = 6.1 Hz, D_2O exchangeable; OH), 2.70 (ddd, 1H, J = 13.2, 9.5, 2.0 Hz; 6-H_{exo}), 2.54 (dd, 1H, J = 13.2, 2.7 Hz; 6-H_{endo}), 1.14 ppm (t, 3H, J = 7.1 Hz; Me); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.5 (C=O), 103.1, 81.3, 79.7, 73.2, 66.8, 61.0, 52.0 (OMe), 51.9 (OMe), 38.5, 15.1 ppm (Me); IR (KBr): $\tilde{\nu}$ = 3300, 2850, 1760, 1200 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_{16}Br_2O_5$: C 34.05, H 4.16; found C 34.01, H 4.14.

Minor isomer: Colorless solid, m.p. 107–109°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.69 (d, 1H, J = 11.0 Hz; carbinol H), 4.44–4.41 (m, 2H, J = 1.5 Hz + others), 3.71 (s, 3H; OMe), 3.67 (s, 3H; OMe), 3.64 (q, 2H, J = 7.1 Hz), 2.80 (dd, 1H, J = 13.4, 9.0 Hz; 5-H_{exo}), 2.01 (dd, 1H, J = 13.4, 2.5 Hz; 5-H_{endo}), 1.23 ppm (t, 3H, J = 7.1 Hz; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.2 (C=O), 102.5 (C_7), 85.1 (C_2), 81.8 (C_6), 67.7, 66.5, 62.2, 51.9 (2C, OMe), 41.9, 15.1 ppm; IR (KBr): $\tilde{\nu}$ = 3250, 2800, 1760, 1200 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_{16}Br_2O_5$: C 34.05, H 4.16; found: C 33.96, H 4.21.

Acyloins 5c, 6c: Yield 68%; colorless viscous liquid, inseparable mixture of regioisomers (85:15); IR (KBr): $\tilde{\nu}$ = 3400, 2950, 1740, 1200 cm^{-1}; elemental analysis calcd (%) for $C_{12}H_{16}Br_2O_6$: C 34.64, H 3.88; found: C 34.57, H 3.76.

Major isomer 5c: ^{1}H NMR: δ = 4.46 (brs; carbinol H), 4.13 (dd, 1H, J = 11.7, 4.4 Hz), 3.95 (dd, 1H, J = 11.7, 6.6 Hz), 3.75 (s, 3H; OMe), 3.67 (s, 3H; OMe), 2.88 (m, 1H; 5-H_{exo}), 2.54 (dd, 1H, J = 12.8, 5.4 Hz; 6-H_{endo}), 2.48 (dt, 1H, J = 12.8, 2.0 Hz; 6-H_{exo}), 2.03 ppm (s, 3H; OCOMe); ^{13}C NMR: δ = 200.2 (C=O), 170.7 (O−C=O), 102.9, 79.0, 71.4, 64.8, 62.1, 52.0 (OMe), 51.7 (OMe), 43.3, 33.0, 20.6 ppm.

Minor isomer 6c: ^{1}H NMR: δ = 4.63 (brs, 1H; carbinol H), 4.50 (dd, 1H, J = 11.7, 3.4 Hz), 4.35 (dd, 1H, J = 11.7, 9.5 Hz), 3.75 (s, 3H; OMe), 3.67 (s, 3H; OMe), 3.07–2.99 (m, 1H, J = 2.0 Hz + others; 6-H_{exo}), 2.66 (dd, 1H, J = 13.2, 11.9 Hz; 5-H_{exo}), 2.05 (s, 3H; OAc), 2.01 (brs, 1H; OH), 1.90 ppm (dd, 1H, J = 13.2, 5.4 Hz; 5-H_{endo}); ^{13}C NMR: δ = 201.5 (C=O), 171.0 (O−C=O), 103.0, 80.8 (carbinol C), 66.6, 64.4, 61.2, 51.98 (OMe), 51.9 (OMe), 44.5, 39.2, 20.9 ppm.

Acyloins 5d, 6d: Yield 85%; mixture of regioisomers (80:20) in THF/H_2O.

Major isomer 5d: Yield 63%; colorless solid, m.p. 95–96°C; ^{1}H NMR: δ = 5.38 (m, 1H; 5-H_{exo}), 4.54 (dd, 1H, J = 4.3, 2.1 Hz; carbinol H), 3.75 (s, 3H; OMe), 3.66 (s, 3H; OMe), 3.44 (brs, 1H; OH), 2.86–2.80 (m, 1H; 6-H_{exo}), 2.54 (dd, 1H, J = 13.6, 3.2 Hz; 6-H_{endo}), 2.06 ppm (s, 3H;

OCOMe); ^{13}C NMR: δ = 197.4 (C=O), 170.0 (O−C=O), 102.9, 79.2 (carbinol C), 74.6, 71.1, 60.4, 52.1 (2C), 37.6, 20.7 ppm; IR (KBr): $\tilde{\nu}$ = 3350, 2900, 1740, 1710, 1420 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_{14}Br_2O_6$: C 32.86, H 3.51; found: C 32.91, H 3.40.

Minor isomer 6d: ^{1}H NMR: δ = 5.56 (dd, 1H, J = 10.0, 2.0 Hz; 6-H$_{exo}$), 4.57 (m, 1H, J = 2.0 Hz + others; carbinol H), 3.74 (s, 3H; OMe), 3.70 (s, 3H; OMe), 3.01 (dd, 1H, J = 14.1, 10.0 Hz; 5-H$_{exo}$), 2.16 (s, 3H; OCOMe), 1.95 ppm (dd, 1H, J = 14.1, 2.7 Hz; 5-H$_{endo}$); ^{13}C NMR: δ = 200.6 (C=O), 169.0 (O−C=O), 103.5, 78.3, 74.9, 67.6, 61.7, 51.98 (OMe), 51.96 (OMe), 41.8, 22.6 ppm.

Acyloins 5e, 6e: Yield 68%; mixture of regioisomers (68:32).

Major isomer 5e (separated from the mixture by crystallization from $CHCl_3$/hexane): Colorless solid, m.p. 125–126°C; ^{1}H NMR: δ = 4.47 (dd, 1H, J = 9.2, 2.0 Hz; carbinol H), 3.758 (s, 3H; OMe), 3.75 (s, 3H; OMe), 3.66 (s, 3H; OMe), 3.47 (dd, 1H, J = 11.2, 4.1 Hz; 5-H$_{exo}$), 2.70 (dd, 1H, J = 13.2, 4.1 Hz; 6-H$_{endo}$), 2.62 ppm (dt, 1H, J = 11.2, 2.0 Hz; 6-H$_{exo}$); ^{13}C NMR: δ = 198.6 (C=O), 173.3 (O−C=O), 103.4, 79.7, 70.7, 60.7, 53.4 (OMe), 52.3 (OMe), 52.0 (OMe), 50.4, 33.9 ppm; IR (KBr): $\tilde{\nu}$ = 3300, 2900, 1760–1700 cm^{-1} (br); elemental analysis calcd (%) for $C_{11}H_{14}Br_2O_6$: C 32.86, H 3.51; found: C 32.78, H 3.48.

Minor isomer 6e (from the mixture): ^{1}H NMR: δ = 4.62 (brs, 1H; carbinol H), 3.76 (s, 3H; OMe), 3.757 (s, 3H; OMe), 3.69 (s, 3H; OMe), 3.56 (ddd, 1H, J = 10.8, 6.5, 2.0 Hz; 6-H$_{exo}$), 2.59–2.56 ppm (m, 2H); ^{13}C NMR: δ = 200.4 (C=O), 172.4 (O−C=O), 103.4, 80.8, 65.9, 63.0, 52.9 (OMe), 52.2 (OMe), 52.1 (OMe), 47.3, 36.2 ppm.

Irradiation of the carbinol proton 2-H$_{exo}$, both in **5e** and **6e**, resulted in the disappearance of the W-coupling to the 6-H$_{exo}$ proton.

Acyloins 9a,b: Yield 75%; inseparable mixture of regioisomers (67:33); colorless solid, m.p. 94–107°C; IR (KBr): $\tilde{\nu}$ = 3300, 2900, 1760, 1200 cm^{-1}; elemental analysis calcd (%) for $C_{12}H_{16}Cl_2O_6$: C 44.06, H 4.93; found: C 44.21, H 4.89.

Major isomer 9a: ^{1}H NMR: δ = 4.50 (d, 1H, J = 7.1 Hz; carbinol H), 3.74 (s, 3H; OMe), 3.68 (s, 3H; OMe), 3.59 (s, 3H; OMe), 3.54 (d, 1H, J = 8.1 Hz, D_2O exchangeable; OH), 3.08 (d, 1H, J = 6.1 Hz; 5-H$_{exo}$), 2.90 (quintet, 1H, J = 7.1 Hz; 6-H$_{endo}$), 1.39 ppm (d, 3H, J = 7.1 Hz; Me); ^{13}C NMR: δ = 198.7 (C=O), 171.8 (O−C=O), 103.4, 79.2 (carbinol C), 77.8, 72.7, 56.4, 53.1, 51.7 (OMe), 51.6 (OMe), 35.6, 17.6 ppm (Me).

Minor isomer 9b: ^{1}H NMR: δ = 4.54 (dd, 1H, J = 6.5, 1.5 Hz; carbinol H), 3.95 (brs, 1H, D_2O exchangeable; OH), 3.78 (s, 3H; OMe), 3.68 (s, 3H; OMe), 3.61 (s, 3H; OMe), 3.20 (d, 1H, J = 7.3 Hz; 6-H$_{exo}$), 2.52 (quintet, 1H, J = 6.8 Hz; 5-H$_{endo}$), 1.32 ppm (d, 3H, J = 6.8 Hz; Me); ^{13}C NMR: δ = 200.1 (C=O), 172.2 (O−C=O), 103.5, 79.6 (carbinol C), 77.6, 71.3, 54.5, 52.8, 51.6, 51.4, 38.2, 17.1 ppm (Me).

Acyloin 10: Yield 95%; colorless solid, m.p. 118–120°C; ^{1}H NMR: δ = 7.50–7.48 (m, 2H), 7.28–7.24 (m, 2H), 7.20–7.16 (m, 1H), 4.29 (d, 1H, J = 2.0 Hz; carbinol H), 3.75 (s, 3H; OMe), 3.60 (s, 3H; OMe), 3.48 (d, 1H, J = 12.9 Hz; 6-H$_{endo}$), 2.53 (dd, 1H, J = 12.9, 2.0 Hz; 6-H$_{exo}$), 1.69 ppm (s, 3H; Me); ^{13}C NMR: δ = 199.4 (C=O), 143.1, 128.0, 126.8, 126.5, 103.2, 84.7, 77.1, 69.1, 51.3, 51.2, 46.3, 41.9, 29.9 ppm; IR (KBr): $\tilde{\nu}$ = 3500, 2950, 1770, 1470, 1290, 1200, 1090, 1040, 960 cm^{-1}; elemental analysis calcd (%) for $C_{16}H_{18}Cl_2O_4$: C 55.67, H 5.26; found: C 55.43, H 5.31.

Disubstituted acyloins

Acyloin 13a: Yield 88%; m.p. 103–105°C; ^{1}H NMR: δ = 4.57 (dd, 1H, J = 16.2, 12.2 Hz), 4.56 (s, 1H), 4.52 (d, 1H, J = 1.5 Hz; carbinol H), 4.25 (dd, 2H, J = 12.3, 6.1 Hz, one H is D_2O exchangeable), 4.13 (dd, 1H, J = 12.3, 4.4 Hz), 3.71 (s, 3H; OMe), 3.60 (s, 3H; OMe), 3.24–3.18 (m, 1H, J = 1.5 Hz + others; 6-H$_{exo}$), 3.02–2.97 (m, 1H), 2.06 (s, 3H; OCOMe), 2.00 ppm (s, 3H; OCOMe); ^{13}C NMR: δ = 199.4 (C=O), 171.0 (O−C=O), 170.3 (O−C=O), 101.9, 79.9 (carbinol C), 78.2, 72.2, 60.9, 58.9, 52.0 (OMe), 51.8 (OMe), 44.7, 43.7, 20.9, 20.5 ppm; IR (KBr): $\tilde{\nu}$ = 3500, 2950, 1760 (br), 1380 cm^{-1}; elemental analysis calcd (%) for $C_{15}H_{20}Cl_2O_8$: C 45.13, H 5.05; found: C 44.26, H 5.07.

Acyloin 13b: Yield 94%; colorless solid, m.p. 147–148°C; ^{1}H NMR: δ = 6.02 (d, 1H, J = 11.7 Hz, D_2O exchangeable; OH), 5.19 (d, 1H, J = 5.9 Hz), 4.56–4.33 (m, 5H), 3.88 (d, 1H, J = 14.9 Hz), 3.68 (s, 3H; OMe), 3.63 (s, 3H; OMe), 3.10 (d, 1H, J = 10.8 Hz), 2.84 ppm (d, 1H, J = 11.2 Hz); ^{13}C NMR: δ = 200.3 (C=O), 102.1, 100.1, 79.0 (carbinol C), 78.7, 72.9, 68.9, 67.1, 51.7 (2C), 49.5, 48.6 ppm; IR (KBr): $\tilde{\nu}$ = 3150, 2800, 1755, 1420 cm^{-1}; elemental analysis calcd (%) for $C_{12}H_{16}Cl_2O_6$: C 44.06, H 4.92; found: C 44.24, H 5.02.

Acyloin 13c: Yield 100%; colorless solid, m.p. 111–113°C; ^{1}H NMR: δ = 4.64 (d, 1H, J = 1.5 Hz; carbinol H), 3.64 (s, 3H; OMe), 3.56 (s, 3H; OMe), 3.19–3.12 (m, 1H, J = 1.7 Hz + others; 6-H$_{exo}$), 3.02–2.97 (m, 1H; 5-H$_{exo}$), 2.30–2.24 (m, 1H), 1.67–1.47 ppm (m, 5H); ^{13}C NMR: δ = 202.0 (C=O), 105.2, 80.1 (carbinol C), 79.1, 71.2, 51.6, 51.3, 50.4, 50.0, 25.8, 25.4, 25.2 ppm; IR (KBr): $\tilde{\nu}$ = 3400, 2900, 1740, 1420, 1400, 900 cm^{-1}; elemental analysis calcd (%) for $C_{12}H_{16}Cl_2O_4$: C 48.83, H 5.46; found: C 48.47, H 5.51.

Acyloin 13d: Yield 100%; colorless solid, m.p. 133–134°C; ^{1}H NMR: δ = 4.62 (d, 1H, J = 2 Hz; carbinol H), 3.65 (s, 3H; OMe), 3.56 (s, 3H; OMe), 3.41 (brs, 1H, D_2O exchangeable; OH), 2.74–2.66 (m, 1H, J = 2.0 Hz + others; 6-H$_{exo}$), 2.48 (ddd, 1H, J = 13.9, 12.3, 4.9 Hz; 5-H$_{exo}$), 2.02 (ddt, 1H, J_1 = J_2 = 13.4, J_3 = 3.6 Hz), 1.68 (m, 2H), 1.55–1.45 (m, 2H), 1.36–1.29 (m, 1H), 1.21–1.13 (m, 1H), 0.97 ppm (ddt, 1H, J = 13.4, 13.3, 5.6 Hz); ^{13}C NMR: δ = 201.8 (C=O), 103.1, 80.8 (carbinol C), 80.0, 72.5, 51.6 (2C), 44.5, 43.0, 19.7, 18.9, 18.4, 17.6 ppm; IR (KBr): $\tilde{\nu}$ = 3400, 2900, 1760, 1440, 1080 cm^{-1}; elemental analysis calcd (%) for $C_{13}H_{18}Cl_2O_4$: C 50.50, H 5.87; found C 49.69, H 5.56.

Irradiation of the carbinol proton 2-H$_{exo}$ in **13d** resulted in the disappearance of W-coupling with the 6-H$_{exo}$ proton.

Acyloin 13e: Yield 100%; m.p. 168–170°C; ^{1}H NMR: δ = 4.55 (d, 1H, J = 1.7 Hz; carbinol H), 3.71 (s, 3H; OMe), 3.59 (s, 3H; OMe), 3.12 (brs, 1H, D_2O exchangeable; OH), 2.64 (t, 1H, J = 10.9 Hz), 2.52 (t, 1H, J = 11.0 Hz), 1.98–1.94 (m, 1H), 1.86–1.80 (m, 2H), 1.64–1.59 (m, 4H), 1.28–1.09 ppm (m, 5H); ^{13}C NMR: δ = 200.8 (C=O), 102.2, 80.6 (2C), 73.9, 51.74 (OMe), 51.70 (OMe), 48.1, 46.9, 31.0, 30.7, 25.8, 25.2, 23.4, 21.1 ppm; IR (KBr): $\tilde{\nu}$ = 3300, 2800, 1740, 1420 cm^{-1}; elemental analysis calcd (%) for $C_{15}H_{22}Cl_2O_4$: C 53.42, H 6.58; found: C 52.97, H 6.38.

Acyloin 13f: Yield 95%; m.p. 153–154°C; ^{1}H NMR: δ = 4.54 (d, 1H, J = 10.5 Hz; carbinol H), 4.46 (d, 1H, J = 9.8 Hz), 3.80 (d, 1H, J = 10.7 Hz), 3.70 (s, 3H; OMe), 3.68 (d, 1H, J = 7.3 Hz, D_2O exchangeable; OH), 3.61 (s, 3H; OMe), 3.49 (dd, 1H, J = 10.7, 6.3 Hz), 3.38 (dd, 1H, J = 6.3, 1.4 Hz; 6-H$_{exo}$), 3.37–3.33 (m, 1H), 3.19 ppm (dd, 1H, J = 9.8, 6.1 Hz); ^{13}C NMR: δ = 200.6 (C=O), 104.5, 80.4 (carbinol C), 77.4, 69.1, 67.2, 66.6, 51.8 (OMe), 51.5 (OMe), 50.2, 49.8 ppm; IR (KBr): $\tilde{\nu}$ = 3150, 2800, 1740, 1400 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_{14}Cl_2O_5$: C 44.46, H 4.75; found: C 44.15, H 4.69.

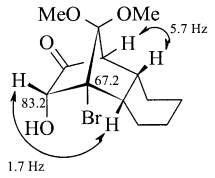
Acyloin 14a: Yield 67%; colorless solid, m.p. 138–140°C; ^{1}H NMR: δ = 4.63–4.54 (m, 3H), 4.28 (dd, 1H, J = 12.3, 6.0 Hz), 4.17 (dd, 1H, J = 12.3, 4.0 Hz), 3.76 (s, 3H; OMe), 3.66 (s, 3H; OMe), 3.26–3.19 (m, 1H, J = 1.7 Hz + others; 6-H$_{exo}$), 3.05–2.98 (m, 1H), 2.06 (s, 3H; OCOMe), 2.00 ppm (s, 3H; OCOMe); ^{13}C NMR: δ = 199.3 (C=O), 170.8, 170.2, 101.9, 80.7, 71.6, 64.9, 61.5, 59.3, 52.3, 52.0, 45.9, 44.9, 21.0, 20.5 ppm; IR (KBr): $\tilde{\nu}$ = 3350, 2900, 1710, 1220 cm^{-1}; elemental analysis calcd (%) for $C_{15}H_{20}Br_2O_8$: C 36.91, H 4.13; found: C 37.04, H 4.21.

Acyloin 14b: Yield 72%; colorless solid, m.p. 171–172°C; ^{1}H NMR: δ = 6.02 (d, 1H, J = 11.9 Hz, D_2O exchangeable; OH), 5.18 (d, 1H, J = 6.8 Hz), 4.63–4.31 (m, 5H), 3.86 (d, 1H, J = 13.6 Hz), 3.73 (s, 3H), 3.68 (s, 3H), 3.13 (d, 1H, J = 11.5 Hz), 2.85 ppm (d, 1H, J = 11.2 Hz); ^{13}C NMR: δ = 200.0 (C=O), 102.2, 100.1, 79.7, 73.4, 69.6, 67.6, 66.7, 51.9, 51.8, 50.4, 49.9 ppm; IR (KBr): $\tilde{\nu}$ = 3200, 2800, 1750, 1430, 960 cm^{-1}; elemental analysis calcd (%) for $C_{12}H_{16}Br_2O_6$: C 34.64, H 3.88; found: C 34.37, H 3.79.

Acyloin 14d: Yield 72%; colorless solid, m.p. 138–139°C; ^{1}H NMR: δ = 4.66 (brs, 1H; carbinol H), 3.75 (s, 3H; OMe), 3.66 (s, 3H; OMe), 3.15 (brs, 1H; OH), 2.81–2.74 (m, 1H, J = 1.7 Hz + others; 6-H$_{exo}$), 2.60–2.52 (m, 1H), 2.10–1.99 (m, 1H), 1.79–1.67 (m, 2H), 1.64–1.52 (m, 2H), 1.43–1.33 (m, 1H), 1.26–1.14 (m, 1H), 1.07–0.96 ppm (m, 1H); ^{13}C NMR: δ = 201.3 (C=O), 103.0, 81.7 (carbinol C), 73.4, 65.6, 51.9 (OMe), 51.8 (OMe), 46.3, 44.6, 19.9, 19.1, 18.9, 18.2 ppm; IR (KBr): $\tilde{\nu}$ = 3400, 2900, 1750, 1100 cm^{-1}; elemental analysis calcd for $C_{13}H_{18}Br_2O_4$: C 39.22, H 4.56; found: C 39.31, H 4.61.

Irradiation of the carbinol proton 2-H$_{exo}$ resulted in the disappearance of W-coupling with the 6-H$_{exo}$ proton.

Acyloin 15: Yield 13%; obtained as a colorless solid, m.p. 54–55°C; ^{1}H NMR: δ = 4.63 (brs, 1H; carbinol H), 3.51 (s, 3H; OMe), 3.48 (s, 3H;



OMe), 2.76 (dd, 1H, J = 5.7, 1.7 Hz; bridgehead H), 2.70 (brs, 1H; OH), 2.69–2.61 (m, 1H, J = 1.7 Hz + others; 6-H_{exo}), 2.44–2.35 (m, 1H), 2.05 (dq, 1H, J = 13.4, 3.7 Hz), 1.74–1.66 (m, 2H), 1.62–1.58 (m, 1H), 1.39–1.33 (m, 2H), 1.21–1.10 ppm (m, 2H); ^{13}C NMR: δ = 207.0 (C=O), 105.2, 83.2 (carbinol C), 67.2, 57.5, 51.3 (OMe), 50.9 (OMe), 45.1, 35.2, 21.2, 19.9, 19.6, 17.9 ppm; IR (KBr): $\tilde{\nu}$ = 3400, 2900, 1740, 1100 cm^{-1}; elemental analysis calcd (%) for $C_{13}H_{19}BrO_4$: C 48.92, H 6.00; found: C 49.01, H 5.96.

Acyloin 14f: Yield 22%; m.p. 119–120°C; ^{1}H NMR: δ = 4.56 (d, 1H, J = 10.2 Hz; carbinol H), 4.48 (d, 1H, J = 10.2 Hz), 3.80 (d, 1H, J = 10.5 Hz), 3.74 (s, 3H; OMe), 3.66 (s, 3H; OMe), 3.63 (brs, 1H, D_2O exchangeable; OH), 3.51 (dd, 1H, J = 10.7, 6.6 Hz), 3.46 (dd, 1H, J = 9.3, 7.1 Hz), 3.35 (dd, 1H, J = 10.5, 6.1 Hz), 3.26 ppm (dd, 1H, J = 9.5, 6.4 Hz); ^{13}C NMR: δ = 200.5 (C=O), 104.7, 81.1 (carbinol C), 70.0, 67.5, 66.9, 61.3, 51.9, 51.8, 51.7, 51.3 ppm; IR (KBr): $\tilde{\nu}$ = 3300, 2800, 1740, 1240 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_{14}Br_2O_5$: C 34.22, H 3.65; found: C 34.15, H 3.79.

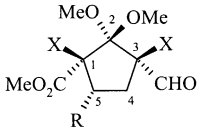
Acyloin 16: Yield 44%; m.p. 112–114°C; ^{1}H NMR: δ = 4.54 (d, 1H, J = 11.2 Hz, carbinol H), 4.42 (d, 1H, J = 9.5 Hz), 3.77 (d, 1H, J = 10.2 Hz), 3.68 (d, 1H, J = 11.2 Hz, D_2O exchangeable; OH), 3.50 (s, 3H; OMe), 3.50 (m, 1H), 3.49 (s, 3H; OMe), 3.38–3.31 (m, 2H), 3.03 (dd, 1H, J = 14.4, 7.3 Hz), 2.80 ppm (dd, 1H, J = 6.6, 1.4 Hz); ^{13}C NMR: δ = 207.0 (C=O), 107.1, 83.0 (carbinol C), 68.7, 66.6, 63.0, 55.6, 51.4, 51.3, 50.9, 41.1 ppm; IR (KBr): $\tilde{\nu}$ = 3400, 2800, 1740, 1250 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_{15}BrO_5$: C 43.02, H 4.92; found C 43.33, H 5.11.

Keto lactone 19: Crude reaction mixture crystallized to give 83% yield; m.p. 165–167°C; ^{1}H NMR: δ = 4.77 (d, 1H, J = 1.5 Hz; 2-H_{exo}), 3.90 (d, 1H, J = 10.8 Hz; 5-H_{exo}), 3.74 (s, 3H; OMe), 3.73 (s, 3H; OMe), 3.65 (s, 3H; OMe), 3.44 ppm (dd, 1H, J = 10.8, 1.9 Hz; 6-H_{exo}); ^{13}C NMR: δ = 188.8 (C=O), 171.5 (O–C=O), 166.9 (O–C=O), 101.4 (C_7), 83.53, 83.45, 72.1, 53.4 (OMe), 52.6 (OMe), 52.3 (OMe), 51.1, 49.7 ppm; IR (KBr): $\tilde{\nu}$ = 2900, 1780–1700 (br), 1420 cm^{-1}; elemental analysis calcd (%) for $C_{12}H_{12}Cl_2O_7$: C 42.50, H 3.57; found: C 42.04, H 3.65.

Keto lactone 20: Yield 71%; colorless solid, m.p. 110°C; ^{1}H NMR: δ = 4.63 (d, 1H, 5.4 Hz; 2-H), 3.71 (s, 3H; OMe), 3.66–3.61 (m, 2H), 3.34 (s, 3H; OMe), 3.31 (s, 3H; OMe), 3.23 (dd, 1H, J = 10.0, 5.1 Hz), 3.04 ppm (m, 1H); ^{13}C NMR: δ = 198.7 (C=O), 175.0 (O–C=O), 169.5 (O–C=O), 106.5, 79.8, 54.3, 52.8, 51.6, 50.5, 48.9, 45.5, 41.0 ppm; IR (KBr): $\tilde{\nu}$ = 2900, 1760, 1700, 1300 cm^{-1}; elemental analysis calcd (%) for $C_{12}H_{14}O_7$: C 53.35, H 5.22; found: C 53.21, H 5.16.

General procedure for the cleavage of acyloins: $Pb(OAc)_4$ (0.5 mmol) was added portionwise over 15 min to a stirred solution of the acyloin (0.2 mmol) in MeOH (3 mL) and benzene (1 mL) at room temperature. After the mixture had been stirred for the required time (monitored by TLC, refer to Scheme 8), water (3 mL) was added and the reaction mixture was extracted with ethyl acetate. The combined organic layers were washed with water, once with dilute $NaHCO_3$ solution, and once with brine, and then dried over anhydrous Na_2SO_4. Concentration followed by chromatography of the crude concentrated reaction mixture on silica gel yielded the pure cyclopentane carboxaldehydes.

Cyclopentane carboxaldehydes



Cyclopentane derivative 22a: Yield 75%; colorless viscous liquid; ^{1}H NMR: δ = 9.56 (s, 1H; CHO), 7.34–7.26 (m, 5H; aromatic), 4.05 (dd, 1H, J = 13.6, 7.6 Hz; 5-H_β), 3.80 (dd, 1H, J = 14.7, 13.6 Hz; 4-H_β), 3.72 (s, 3H; OMe), 3.49 (s, 3H; OMe), 3.33 (s, 3H; OMe), 2.25 ppm (dd, 1H, J = 14.7, 7.6 Hz; 4-H_α); ^{13}C NMR: δ = 189.1 (CHO), 167.0 (O–C=O), 134.7, 128.3, 128.2, 110.7, 81.8, 79.6, 53.3, 53.1, 53.0, 52.9, 37.3 ppm; IR (neat): $\tilde{\nu}$ = 2900, 1720, 1330, 800 cm^{-1}; elemental analysis calcd (%) for $C_{16}H_{18}Cl_2O_5$: C 53.20, H 5.02; found: C 53.12, H 5.09.

Cyclopentane derivative 22b: Yield 77%; colorless viscous liquid; ^{1}H NMR: δ = 9.44 (s, 1H; CHO), 4.43 (dd, 1H, J = 10.2, 8.2 Hz; 5-H_β), 3.80 (s, 3H; OMe), 3.79 (m, 1H), 3.64 (m, 3H; OMe), 3.63 (m, 1H), 3.33 (s, 3H; OMe), 3.27 (dd, 1H, J = 15.0, 10.2 Hz; 4-H_β), 2.31 (dd, 1H, J = 15.0, 8.2 Hz; 4-H_α), 1.16 ppm (t, 3H, J = 7.1 Hz; Me); ^{13}C NMR: δ = 188.4 (CHO), 166.4 (O–C=O), 108.7, 85.2, 80.4, 78.6, 67.1, 53.4, 53.1, 53.0, 38.7, 15.3 ppm; IR (neat): $\tilde{\nu}$ = 2900, 1760, 1700, 1330 cm^{-1}; elemental analysis calcd (%) for $C_{12}H_{18}Cl_2O_6$: C 43.79, H 5.51; found: C 43.85, H 5.62.

Cyclopentane derivative 22d: Yield 83%; colorless viscous liquid; ^{1}H NMR: δ = 9.39 (s, 1H; CHO), 5.63 (dd, 1H, J_1 = J_2 = 8.4 Hz; 5-H_β), 3.82 (s, 3H; OMe), 3.70 (s, 3H; OMe), 3.41 (s, 3H; OMe), 3.25 (dd, 1H, J = 15.1, 8.4 Hz; 4-H_β), 2.56 (dd, 1H, J = 15.1, 8.6 Hz; 4-H_α), 2.07 ppm (s, 3H; OMe); ^{13}C NMR: δ = 187.3 (CHO), 169.4 (O–C=O), 165.8 (O–C=O), 108.4, 77.9, 77.71, 77.68, 53.5 (OMe), 53.3 (OMe), 53.1 (OMe), 37.5, 20.6 ppm; IR (neat): $\tilde{\nu}$ = 2900, 1740 (br), 1710, 1380 cm^{-1}; elemental analysis calcd (%) for $C_{12}H_{16}Cl_2O_7$: C 42.00, H 4.70; found: C 41.96, H 4.64.

Cyclopentane derivative 22f: Yield 71%; colorless solid, m.p. 69°C; ^{1}H NMR: δ = 9.53 (s, 1H; CHO), 3.75 (s, 3H; OMe), 3.57 (s, 3H; OMe), 3.33 (s, 3H; OMe), 3.01 (t, 1H, J = 14.5 Hz; 4-H_β), 2.30 (dd, 1H, J = 14.5, 7.3 Hz; 5-H_β), 1.95 (dd, 1H, J = 14.5, 7.3 Hz; 4-H_α), 0.08 ppm (s, 9H; $SiMe_3$); ^{13}C NMR: δ = 190.3 (CHO), 169.0 (O–C=O), 112.3, 80.7, 79.7, 53.6, 53.0 (2C), 38.8, 35.7, −1.6 ppm; IR (KBr): $\tilde{\nu}$ = 2900, 1720 (br), 1430 cm^{-1}; elemental analysis calcd (%) for $C_{13}H_{22}Cl_2O_5Si$: C 43.70, H 6.21; found: C 43.85, H 5.62.

Cyclopentane derivative 24: Yield 78%; colorless viscous liquid; ^{1}H NMR: δ = 9.43 (s, 1H; CHO), 4.55 (dd, 1H, J_1 = J_2 = 8.4 Hz; 5-H_β), 3.81–3.74 (m, 1H), 3.77 (s, 3H; OMe), 3.68–3.62 (m, 1H), 3.67 (s, 3H; OMe), 3.42 (s, 3H; OMe), 3.30 (dd, 1H, J = 14.5, 8.5 Hz; 4-H_β), 2.52 (dd, 1H, J = 15.5, 8.5 Hz; 4-H_α), 1.16 ppm (t, 3H, J = 7.0 Hz; Me); ^{13}C NMR: δ = 187.1 (CHO), 166.4 (O–C=O), 108.0, 85.7, 73.1, 72.8, 67.0, 53.8, 53.5, 53.0, 39.3, 15.3 ppm; IR (KBr): $\tilde{\nu}$ = 2900, 1720 (br), 1460 cm^{-1}; elemental analysis calcd (%) for $C_{12}H_{18}Br_2O_6$: C 34.47, H 4.34; found: C 34.53, H 4.21.

Bicyclic lactone 23: Yield 90%; colorless solid, m.p. 140–142°C; ^{1}H NMR: δ = 7.32 (s, 5H; aromatic), 4.56 (d, 1H, J = 10.0 Hz), 4.30 (d, 1H, J = 10.3 Hz), 3.89 (dd, 1H, J = 12.7, 6.8 Hz), 3.85 (s, 3H; OMe), 3.67 (s, 3H; OMe), 2.97 (t, 1H, J = 14.1 Hz), 2.63 ppm (dd, 1H, J = 14.1, 6.8 Hz); ^{13}C NMR: δ = 165.1 (O–C=O), 134.7, 128.8, 128.5, 128.4, 102.4, 81.2, 74.6, 67.2, 53.2, 52.5, 51.7, 41.0 ppm; IR (KBr): $\tilde{\nu}$ = 2950, 1740, 1440, 1380, 1300 cm^{-1}; elemental analysis calcd (%) for $C_{15}H_{16}Cl_2O_4$: C 54.40, H 4.87; found C 54.71, H 4.67.

Oxa tricyclic ketone 27: Yield 22%; colorless solid, m.p. 68–70°C; ^{1}H NMR: δ = 4.39 (dd, 1H, J = 8.8, 4.2 Hz), 4.29 (brs, 1H), 3.95 (d, 1H, J = 8.8 Hz), 3.71 (s, 3H; OMe), 3.62 (s, 3H; OMe), 2.93 (m, 1H), 2.70 (dd, 1H, J = 12.7, 11.1 Hz), 1.74 ppm (dd, 1H, J = 12.7, 2.0 Hz); ^{13}C NMR: δ = 198.0 (C=O), 102.3, 86.7, 75.4, 75.2, 74.2, 52.2 (OMe), 51.9 (OMe), 45.5, 37.0 ppm; IR (KBr): $\tilde{\nu}$ = 2850, 1760, 1240 cm^{-1}; elemental analysis calcd (%) for $C_{10}H_{12}Cl_2O_4$: C 44.97, H 4.53; found: C 44.53, H 4.57.

Oxa tricyclic ketone 28: Colorless solid; m.p. 76–78°C; ^{1}H NMR: δ = 4.44 (dd, 1H, J = 8.8, 3.6 Hz), 3.84 (s, 3H; OMe), 3.83 (d, 1H, J = 8.5 Hz), 3.66 (s, 3H; OMe), 3.61 (s, 3H; OMe), 2.94 (ddd, 1H, J = 11.0, 2.2, 3.6 Hz), 2.66 (dd, 1H, J = 12.7, 11.0 Hz), 1.85 ppm (dd, 1H, J = 12.7, 2.2, 3.6 Hz); ^{13}C NMR: δ = 196.7 (C=O), 105.1, 102.1, 76.0, 74.2, 72.3, 54.9, 52.4, 51.4, 46.8, 36.1 ppm; IR (KBr): $\tilde{\nu}$ = 2950, 1770, 1430, 1190, 1070 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_{14}Cl_2O_5$: C 44.47, H 4.75; found C 44.52, H 4.71.

Oxatricyclic compound 31: Yield 65%, m.p. 73–75°C; ^{1}H NMR: δ = 4.30–4.25 (m, 2H), 3.77 (d, 1H, J = 8.6 Hz), 3.65 (s, 3H; OMe), 3.63 (s, 3H; OMe), 3.50 (s, 3H; OMe), 3.13 (d, 1H, J = 8.1 Hz, D_2O exchangeable; OH), 2.68 (ddd, 1H, J = 11.0, 2.7, 2.2 Hz; 5-H_{exo}), 2.42 (ddd, 1H, J

= 12.4, 11.0, 2.0 Hz; 6-H_{exo}), 1.98 ppm (dd, 1H, J = 12.4, 2.1 Hz; 6-H_{endo}); ^{13}C NMR: δ = 107.1, 102.0, 77.5, 71.7, 71.5, 70.9, 52.3 (OMe), 51.6 (OMe), 51.1 (OMe), 46.5, 35.4 ppm; IR (KBr): $\tilde{\nu}$ = 3300, 2850, 1440, 1200 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_{16}Cl_2O_5$: C 44.16, H 5.39; found: C 44.23, H 5.89.

Bicyclic lactone 32: Yield 95%; colorless solid, m.p. 82–84°C; ^{1}H NMR: δ = 4.45 (dd, 1H, J = 10.2, 2.1 Hz), 4.23 (dd, 1H, J = 10.7, 3.2 Hz), 4.14 (d, 1H, J = 10.2 Hz), 3.81 (dq, 1H, J = 9.3, 6.8 Hz; OCH_2), 3.73 (s, 3H; OMe), 3.61 (s, 3H; OMe), 3.53 (dq, 1H, J = 9.3, 6.8 Hz; OCH_2), 2.93 (ddd, 1H, J_1 = J_2 = 12.4 Hz, J_3 = 2.2 Hz), 2.19 (dd, 1H, J = 14.1, 3.4 Hz), 1.15 ppm (t, 3H, J = 6.8 Hz; Me); ^{13}C NMR: δ = 164.4 (O–C=O), 101.6, 83.3, 79.9, 73.9, 67.3, 67.1, 52.9, 52.6, 43.4, 15.2 ppm; IR (KBr): $\tilde{\nu}$ = 2900, 1760, 1430, 1320 cm^{-1}; elemental analysis calcd (%) for $C_{11}H_{16}Cl_2O_5$: C 44.17, H 5.39; found: C 44.21, H 5.37.

Bicyclic lactam 33: The aldehyde **22b** (73 mg, 0.23 mmol) was dissolved in benzene (3 mL) and allylamine (0.46 mmol, 26 mg) was added along with a few 4 Å molecular sieves. The reaction mixture was stirred at room temperature for 2 h (until complete consumption of the starting material as monitored by TLC). The benzene was then evaporated in vacuo at room temperature. The residue was dissolved in MeOH and this solution was cooled to 0°C, whereupon $NaBH_4$ (15 mg, 0.40 mmol) was added and the resulting mixture was stirred for 1 h. The MeOH was then evaporated at room temperature, water (5 mL) was added, and the resulting mixture was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated. Purification by column chromatography on silica gel (20–25% ethyl acetate/hexane as eluent) afforded 50 mg (64%) of the pure amide **33**.

Yield 64%; colorless solid, m.p. 140–142°C; ^{1}H NMR: δ = 5.81–5.71 (m, 1H; olefinic H), 5.28 (d, 1H, J = 17.3 Hz; olefinic H), 5.17 (d, 1H, J = 10.2 Hz; olefinic H), 5.02 (d, 1H, J = 5.8 Hz; 7-H_{exo}), 4.37–4.32 (m, 1H), 4.19 (dd, 1H, J = 8.8, 5.3 Hz), 3.96 (dd, 1H, J = 15.3, 7.1 Hz), 3.78 (dq, 1H, J = 9.3, 7.1 Hz; OCH_2), 3.70 (s, 3H; OMe), 3.51 (s, 3H; OMe), 3.49–3.45 (m, 1H; OCH_2), 3.08 (d, 1H, J = 6.1 Hz), 2.55–2.53 (m, 2H), 1.09 ppm (t, 3H, J = 7.1 Hz; Me); ^{13}C NMR: δ = 162.8 (N–C=O), 131.9, 117.9, 102.3, 83.2, 83.1, 80.1, 74.8, 66.9, 52.8 (OMe), 52.6 (OMe), 46.0, 37.1, 15.2 ppm (Me); IR (KBr): $\tilde{\nu}$ = 2900, 1650, 1420, 1300, 1240, 1200 cm^{-1}; elemental analysis calcd (%) for $C_{14}H_{21}Cl_2NO_4$: C 49.72, H 6.26, N 4.14; found: C 42.78, H 6.30, N 4.17.

General procedure for allylindium addition to aldehydes: Indium metal (0.75 mmol, cut into small pieces) and allyl bromide (1 mmol) were added to a solution of aldehyde **22** (0.5 mmol) in DMF (1 mL), and the mixture was stirred at room temperature for the specified time (refer to Scheme 9). 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 layers were washed once with brine, dried over anhydrous Na_2SO_4, and concentrated. The resulting residue was purified by column chromatography on silica gel to provide the allyl lactones and the pure homoallylic alcohol. In each case, the product distribution was assessed by 400 MHz ^{1}H NMR analysis of the crude residue, prior to the column purification step.

Allyl lactone 34: Yield 95%, obtained as a viscous liquid; ^{1}H NMR (500 MHz): δ = 6.00–5.89 (m, 1H; olefinic H), 5.17 (d, 1H, J = 15.0 Hz; olefinic H), 5.14 (d, 1H, J = 8.8 Hz; olefinic H), 4.35 (dd, 1H, J = 10.5, 2.0 Hz), 4.21 (dd, 1H, J = 10.7, 3.0 Hz), 3.81 (dq, 1H, J = 9.3, 7.1 Hz; OCH_2), 3.73 (s, 3H; OMe), 3.60 (s, 3H; OMe), 3.55 (dq, 1H, J = 9.3, 7.1 Hz; OCH_2), 3.00 (dd, 1H, J = 14.2, 10.7 Hz), 2.91 (dd, 1H, J = 13.9, 6.9 Hz), 2.78–2.69 (m, 1H), 2.18 (dd, 1H, J = 14.1, 3.2 Hz), 1.14 ppm (t, 3H, J = 7.1 Hz; Me); ^{13}C NMR: δ = 163.6 (O–C=O), 134.6, 117.9, 102.3, 87.9, 83.5, 79.9, 70.0, 67.2, 52.9, 52.6, 47.3, 37.4, 15.2 ppm; IR (KBr): $\tilde{\nu}$ = 2900, 1770, 1630, 1420, 1300 cm^{-1}; elemental analysis calcd (%) for $C_{14}H_{20}Cl_2O_5$: C 49.57, H 5.94; found: C 49.61, H 5.98.

Allyl lactone 35: Yield 94%, obtained as a viscous liquid; ^{1}H NMR: δ = 5.92–5.82 (m, 1H; olefinic H), 5.12–5.03 (m, 2H; olefinic H), 4.30 (dd, 1H, J = 10.8, 1.7 Hz), 4.23 (dd, 1H, J = 10.4, 3.0 Hz), 3.79 (dq, 1H, J = 9.3, 7.1 Hz; OCH_2), 3.70 (s, 3H; OMe), 3.59 (s, 3H; OMe), 3.50 (dq, 1H, J = 9.3, 7.1 Hz; OCH_2), 3.06 (dd, 1H, J = 14.2, 10.5 Hz), 2.98 (dd, 1H, J = 14.6, 7.3 Hz), 2.73–2.65 (m, 1H), 2.18 (dd, 1H, J = 14.2, 3.2 Hz), 1.10 ppm (t, 3H, J = 7.1 Hz; Me); ^{13}C NMR: δ = 163.3 (O–C=O), 134.8, 117.8, 102.5, 88.4, 84.9, 72.4 (bridgehead), 67.3, 62.6 (bridgehead), 53.11 (OMe), 53.08 (OMe), 49.1, 39.1, 15.2 ppm; IR (KBr): $\tilde{\nu}$ = 2900, 1760, 1620, 1440, 1360 cm^{-1}; elemental analysis calcd (%) for $C_{14}H_{20}Br_2O_5$: C 39.28, H 4.71; found: C 39.34, H 4.75.

Allyl lactone 36: Colorless solid, m.p. 121–122°C; ^{1}H NMR (500 MHz): δ = 7.35–7.29 (m, 5H; aromatic H), 6.03–5.93 (m, 1H; olefinic CH), 5.24–5.17 (m, 2H; olefinic CH_2), 4.52 (dd, 1H, J = 12.5, 2.0 Hz; 6-H), 3.88 (dd, 1H, J = 12.8, 6.4 Hz; 3-H), 3.84 (s, 3H; OMe), 3.66 (s, 3H; OMe), 3.06 (dd, 1H, J = 14.2, 12.7 Hz; 2-H_{exo}), 3.02–2.97 (m, 1H; allylic CH_2), 2.84–2.76 (m, 1H; allylic CH_2), 2.61 ppm (dd, 1H, J = 14.2, 6.4 Hz; 2-H_{endo}); ^{13}C NMR: δ = 164.3 (O–C=O), 134.7 (C_{13}), 134.6 (C_{10i}), 128.8, 128.3, 117.1 (C_{14}), 111.1 ($C_{7\alpha}$), 89.1 (C_6), 81.3 ($C_{4\alpha}$), 70.2 ($C_{1\alpha}$), 72.4 (bridgehead), 53.1 (C_9), 52.7 (C_8), 51.8 (C_3), 45.0 (C_2), 37.2 ppm (C_{12}); IR (KBr): $\tilde{\nu}$ = 2950, 1770, 1620, 1430 cm^{-1}; elemental analysis calcd (%) for $C_{18}H_{20}Cl_2O_4$: C 58.23, H 5.43; found: C 58.28, H 5.46.

Homoallylic alcohol 37: Colorless solid, m.p. 96–98°C; ^{1}H NMR: δ = 7.34–7.24 (m, 5H; aromatic H), 6.10–5.96 (m, 1H; olefinic H), 5.27–5.10 (m, 2H; olefinic H), 4.44–4.40 (m, 1H; carbinol H), 3.89 (dd, 1H, J = 14.3, 6.0 Hz; H_5), 3.64 (s, 3H; OMe), 3.52 (s, 3H; OMe), 3.33 (s, 3H; OMe), 3.22–3.15 (m, 2H), 2.55–2.47 (m, 1H), 2.36 (dd, 1H, J = 14.0, 6.4 Hz; allylic CH_2), 2.21 ppm (dd, 1H, J = 13.9, 6.1 Hz; 4-H_β); ^{13}C NMR: δ = 167.6 (O–C=O), 135.5, 134.6, 128.5, 128.3, 117.1 (C_{14}), 111.1 ($C_{7\alpha}$), 85.8 (carbinol C), 82.5, 73.6, 53.0 (OMe), 52.8 (OMe), 52.7 (OMe), 52.4 (C_5), 43.2 (C_2), 36.8 ppm (allylic CH_2); IR (KBr): $\tilde{\nu}$ = 2900, 1700, 1620, 1430 cm^{-1}; elemental analysis calcd (%) for $C_{19}H_{24}Cl_2O_5$: C 56.59, H 6.00; found: C 56.77, H 5.79.

X-ray crystallographic analysis: The crystal structures of **3b**, **4b**, and **37** were determined from single-crystal X-ray diffraction data. Data were collected at room temperature on a Bruker SMART 1000 CCD-based diffractometer using graphite-monochromated $Mo_{K\alpha}$ radiation (λ = 0.71073 Å). The structures were solved with the aid of WinGX Version 1.64.04, an integrated system of windows programs for the solution, refinement, and analysis of single-crystal X-ray diffraction data by Louis J. Farrugia, Department of Chemistry, University of Glasgow (1997–2002).[20] The structure was initially solved with SIR-97 and then refined with SHELX-97, which are incorporated in WinGX. The structure was refined by full-matrix least-squares methods on F^2. The hydrogen atom positions were initially determined on the basis of geometrical considerations and were refined with a riding model. Non-hydrogen atoms were refined with anisotropic displacement parameters. CCDC-227642 (**3b**), CCDC-227641 (**4b**), and CCDC-227643 (**37**) 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: (+44) 1223-336033; or e-mail: deposit@ccdc.cam.ac.uk).

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

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

[3] a) B. C. Ranu, *Eur. J. Org. Chem.* **2000**, 2347–2356; b) M. R. Pitts, J. R. Harrison, C. J. Moody, *J. Chem. Soc. Perkin Trans. 1* **2001**, 955–977, and references therein.

[4] N. Kalyanam, G. V. Rao, *Tetrahedron Lett.* **1993**, *34*, 1647–1648.

[5] B. C. Ranu, S. K. Guchhait, A. Sarkar, *Chem. Commun.* **1998**, 2113–2114.

[6] a) B. C. Ranu, J. Dutta, S. K. Guchhait, *J. Org. Chem.* **2001**, *66*, 5624–5626; b) B. C. Ranu, J. Dutta, S. K. Guchhait, *Org. Lett.* **2001**, *3*, 2603–2605.
[7] C. J. Moody, M. R. Pitts, *Synlett* **1998**, 1028–1029.
[8] F. A. Khan, B. Prabhudas, *Tetrahedron* **2000**, *56*, 7595–7599.
[9] F. A. Khan, J. Dash, N. Sahu, S. Gupta, *Org. Lett.* **2002**, *4*, 1015–1018.
[10] a) F. Kido, H. Kitahara, A. Yoshikoshi, *J. Org. Chem.* **1986**, *51*, 1478–1481; b) S.-I. Murahashi, T. Saito, H. Hanaoka, Y. Murakami, T. Naota, H. Kumobayashi, S. Akutagawa, *J. Org. Chem.* **1993**, *58*, 2929–2930; c) E. Piers, J. Renaud, *J. Org. Chem.* **1993**, *58*, 11–13; d) T. Money, *Studies in Natural Product Chemistry, Vol. 4* (Ed.: Atta-ur-Rahman), Elsevier, Amsterdam, **1989**, p. 625.
[11] a) U. Schräpler, K. Rühlmann, *Chem. Ber.* **1964**, *97*, 1383; b) T. Mori, T. Nakahara, H. Nozaki, *Can. J. Chem.* **1969**, *47*, 3266–3269.
[12] a) E. J. Bailey, D. H. R. Barton, J. Elks, J. F. Templeton, *J. Chem. Soc.* **1962**, 1578–1591; b) W. Adam, M. Müller, F. Prechtl, *J. Org. Chem.* **1994**, *59*, 2358–2364.
[13] R. Hayakawa, T. Sahara, T. Shimizu, *Tetrahedron Lett.* **2000**, *41*, 7939–7942, and references therein.
[14] a) A. Clerici, O. Porta, *J. Org. Chem.* **1985**, *50*, 76–81; b) M. Yamada, T. Horie, M. Kawai, H. Yamamura, S. Araki, *Tetrahedron* **1997**, *53*, 15685–15690.
[15] W. Reusch, R. LeMahieu, *J. Am. Chem. Soc.* **1964**, *86*, 3068–3072.
[16] J. C. Lee, Y. S. Jin, J.-H. Choi, *Chem. Commun.* **2001**, 956–957.
[17] F. A. Khan, B. Prabhudas, J. Dash, N. Sahu, *J. Am. Chem. Soc.* **2000**, *122*, 9558–9559.
[18] F. A. Khan, B. Prabhudas, J. Dash, *J. Prakt. Chem.* **2000**, *342*, 512–517.
[19] F. A. Khan, J. Dash, N. Sahu, Ch. Sudheer, *J. Org. Chem.* **2002**, *67*, 3783–3787.
[20] L. J. Farrugia, WINGX suite, *J. Appl. Crystallogr.* **1999**, *32*, 837–838.

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