upon the solvent was removed under reduced pressure. The residue was extracted with C_6H_6 (50 mL), and the resultant red supernatant liquid was decanted. The red solution was concentrated to about 5 mL at which point a colorless solid precipitated. Hexane (50 mL) was added and the solution was heated to dissolve the majority of the precipitates. The solution was then decanted (60 °C) and allowed to cool slowly to room temperature affording X-ray diffraction quality, colorless crystals of **2**. Yield 0.96 g, 29.3 %. M.p.: on heating the crystals became red at 130 °C and purple at 139 °C (decomp); IR: $\tilde{\nu} = 1759$ cm^{-1} (s, Bi–H); ^{1}H NMR (400 MHz, C_6D_6): $\delta = 1.85$ (s, 12H; *o*-CH_3), 1.88 (s, 12H; *o*-CH_3), 2.24 (s, 12H; *p*-CH_3), 6.81, 6.82 (8H; *m*-Mes), 6.84 (d, $^3J_{H,H} = 7.2$ Hz, 4H; *m*-C_6H_3), 7.01 (t, $^3J_{H,H} = 7.6$ Hz, 2H; *p*-C_6H_3); ^{13}C {^{1}H} NMR (100 MHz, C_6H_6): $\delta = 21.29$ (*p*-CH_3), 21.87 (*o*-CH_3), 126.396 (*m*-C_6H_3), 128.306 (*p*-C_6H_3), 129.09 (*m*-Mes), 135.79 (*o*-Mes), 136.62 (*o*-C_6H_3), 144.3 (*i*-Mes), 150.9 (*p*-Mes), 153.2 (*i*-C_6H_3); satisfactory C,H analysis.

3: $LiAlD_4$ (0.25 g, 5.95 mmol) was added by using a solids addition tube to a solution of **1** (5.27 g, 5.8 mmol) in toluene (40 mL) at about −78 °C. The solution was allowed to warm slowly to room temperature overnight and stirring was continued for 30 h by which time the supernatant liquid had become red. This solution was filtered and the supernatant liquid was pumped to dryness. The resulting solid was extracted with hexane/toluene (3/1) (3 × 80 mL). Colorless, X-ray diffraction quality, crystals of **3** were obtained from these solutions upon cooling to −20 °C. Yield 0.52 g, 10 %. M.p.: on heating the crystals became red at 132 °C and purple at 139 °C;. IR: $\tilde{\nu} = 1260$ cm^{-1} (s, Bi–D); ^{1}H NMR (400 MHz, C_6D_6): $\delta = 1.85$ (s, 12H; *o*-CH_3), 1.88 (s, 12H; *o*-CH_3), 2.24 (s, 12H; *p*-CH_3), 6.81, 6.82 (8H; *m*-Mes), 6.84 (d, $^3J_{H,H} = 7.2$ Hz, 4H; *m*-C_6H_3), 7.01 (t, $^3J_{H,H} = 7.6$ Hz, 2H, *p*-C_6H_3); ^{13}C {^{1}H} NMR (100 MHz, C_6D_6): $\delta = 21.29$ (*p*-CH_3), 21.87 (*o*-CH_3), 126.396 (*m*-C_6H_3), 128.306 (*p*-C_6H_3), 129.09 (*m*-Mes), 135.79 (*o*-Mes), 136.62 (*o*-C_6H_3), 144.3 (*i*-Mes), 150.9 (*p*-Mes), 153.2 (*i*-C_6H_3); satisfactory C,H analysis.

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Synthesis of (*E*)-α,β-Unsaturated Esters and Amides with Total Selectivity Using Samarium Diiodide**

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The development of methods for the stereoselective formation of carbon–carbon double bonds could be considered one of the most important challenges in organic synthesis.[1] The synthesis of α,β-unsaturated esters[2] is generally achieved by C=C bond formation with Wittig,[3] Horner–Emmons,[4] Heck,[5] or Peterson[6] reactions, or with the Cope rearrangement,[7] from acetylenic compounds[8] or α-sulfanyl-ester derivatives.[9] However, in most of these papers, total control of the stereoselectivity of the carbon–carbon double bond formation remained unresolved.[3a, b, d, 4–6c, 8a, 9b,c, 10] Some methodologies are limited by their poor generality,[7, 8b, 9a, 11] and other papers describe the preparation of α,β-unsaturated esters in which the substitution pattern of the olefin is quite simple (monosubstituted or 1,2-disubstituted).[3c, 6d] Only a few examples of the synthesis of α-substituted α,β-unsaturated esters in which the C=C bond is trisubstituted have been reported.[12]

Recently, we described a stereoselective synthesis of (*Z*)-vinyl halides by treatment of O-acetylated 1,1-dihaloalkan-2-ols with samarium diiodide; this was the first general stereoselective β-elimination reaction promoted by SmI_2.[13, 14] Here we report a new methodology to obtain α,β-unsaturated esters **2** with total stereoselectivity, by treatment of the easily available 2-halo-3-hydroxyesters **1** with samarium diiodide [Eq. (1)]. We also describe preliminary results of the synthesis of related α,β-unsaturated amides.

When a solution of SmI_2 in THF was added dropwise to several 2-halo-3-hydroxyesters **1** (prepared by reaction between the corresponding lithium enolates of α-haloesters and

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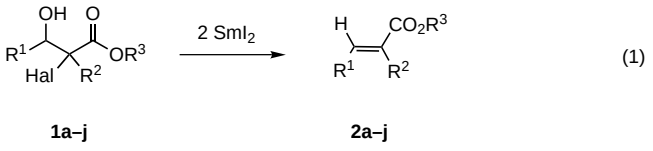


(1)

1a–j **2a–j**

Table 1. Synthesis of α,β-unsaturated esters with SmI_2 [Eq. (1)].

entry	**1**	R^1	R^2	R^3	Hal	*de* [%][a]	yield [%][b]
1	**1a**	C_7H_{15}[c]	H	Me	Cl	63	20
2	**1a**	C_7H_{15}[d]	H	Me	Cl	88	30
3	**1a**	C_7H_{15}	H	Me	Cl	>98	70
4	**1b**	C_7H_{15}	Me	Et	Cl	>98	75
5	**1c**	cyclohexyl	Me	Et	Cl	>98	90
6	**1d**	*p*-ClC_6H_4	H	*t*Bu	Cl	>98	72
7	**1e**	Ph	Bu	Et	Br	>98	86
8	**1f**	*p*-CNC_6H_4	Me	Et	Cl	>98	84
9	**1g**	*p*-$MeOC_6H_4$	Me	Et	Cl	>98	91
10	**1h**	$Me_2C{=}CH(CH_2)_2CH(Me)CH_2$	Ph	*i*Pr	Cl	>98	84
11	**1i**	MeCH(Ph)	C_6H_{13}	Et	Br	>98	87
12	**1j**	(*E*)-MeCH=CH	C_6H_{13}	Et	Br	>98	90

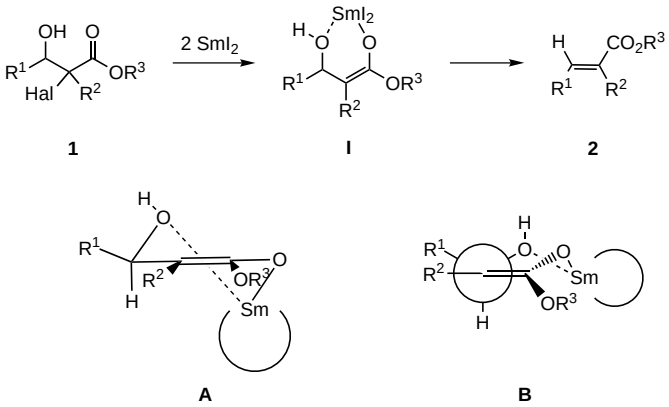
[a] Determined from crude reaction products with GC-MS. [b] Yield of isolated products. [c] Performed with Zn rather than SmI_2. [d] Performed with O-acetylated compound **1** rather than the unprotected alcohol.

aldehydes at $-78\,^{\circ}C$), the corresponding α,β-unsaturated esters **2** were isolated, after hydrolysis, with total stereoselectivity and in high yield (Table 1). The transformation was completed in a few minutes at room temperature, and addition of the SmI_2 was carried out dropwise until the blue-green color was persistent (approximately 2.1 equivalents).

The diastereoisomeric excess (*de*) was determined on the crude reaction products by ^1H NMR spectroscopy (300 MHz) and GC–MS,[15] and only a single stereoisomer was shown. When the same β-elimination reaction was carried out using Zn, a lower steroisomer ratio was obtained (entry 1). The *E* stereochemistry in the double bond C=C of α,β-unsaturated esters **2** was assigned on the basis of the value of the ^1H NMR coupling constant between the olefinic protons of compounds **2a** and **2d**[16] or by NOE experiments. In the case of compounds **2a**,[9a] **2b**,[17] **2c**,[18] **2e**,[12] and **2g**[12] comparison with the ^1H and ^{13}C NMR values described in the literature has also been carried out. It is noteworthy that although the 2-halo-3-hydroxyesters **1** were prepared and used as mixtures of diastereoisomers (roughly 1:1), the corresponding α,β-unsaturated esters **2** were obtained with total stereoselectivity.

This proposed methodology to obtain α,β-unsaturated esters is general, and R^1, R^2, and R^3 can be varied widely. Aliphatic (linear, branched, or cyclic), unsaturated, or aromatic (electron rich or deficient) aldehydes could be used to introduce different R^1 groups. Substitution at the C2 position could also be changed using different α-haloesters (again, aliphatic and aromatic groups are allowed). The stereoselectivity and yield were also unaffected by the presence of bulky groups R^3 on the carboxyl ester (entries 6 and 10), in contrast to the Wittig olefination reaction.[10] Although not only chloro- but also bromohydroxyesters can be used as the starting material (entries 7, 11, and 12), the elimination reaction has mainly been carried out using α-chloro-β-hydroxyesters, which are more accessible than the equivalent bromo derivatives.[19]

The observed stereochemistry of products **2** may be explained by assuming a chelation-control model (Scheme 1). Thus, metalation and removal of the halogen generates the enolate intermediate **I**. Chelation of the oxophilic Sm^{III} center with the oxygen atom of the alcohol group produces a six-membered ring and increases the ability of the hydroxyl group



Scheme 1. Mechanistic proposal for the synthesis of (*E*)-α,β-unsaturated esters **2** through intermediate **I**. **A** is the proposed transition state model, **B** is a Newman projection of **A** through atoms C2 and C3. Hal = Cl, Br.

as a leaving group.[20] Indirect support for this is provided by the lower stereoselectivity obtained with an O-acetylated starting compound (entry 2). Tentatively, we propose a transition state model **A** with an equatorial R^1 group (to avoid interactions with the samarium coordination sphere). As depicted in **B**, R^1 and R^2 show a *cis* relationship. Consequently, elimination from **A** affords (*E*)-α,β-unsaturated esters. Synthesis of **2** with total stereoselectivity from a mixture of diastereoisomers of **1** could be explained by an epimerization of the $C(R^2)$ carbon center after the reaction of **1** with SmI_2, affording the diastereoisomer with the appropriate conformation for coordination of the samarium center with the alcohol oxygen.

Different behavior was observed when esters **1** derived from ketones instead of aldehydes and α-chloroesters were used. In addition to the α,β-unsaturated ester analogue of **2** the corresponding β-hydroxyester was obtained. In this case, coordination of samarium(III) with the hydroxyl oxygen could be disfavored by the higher substitution of the β-carbon, with hydrolysis of the samarium enolate by the hydroxyl group preferred to the elimination.[21]

Attempts have been made towards extending this methodology to the synthesis of α,β-unsaturated amides. Treatment of 2-chloro-3-hydroxyamides **3** (obtained from the lithium enolate of α-chloroamides with different aldehydes) with a solution of SmI_2 in THF at room temperature [Eq. (2)] afforded, in a few minutes, the corresponding α,β-unsaturated amides **4** with total *E* stereoselectivity[22] in high yield (Table 2). Generalization of this synthesis of (aliphatic and aromatic) α,β-unsaturated amides is currently under examination.

In conclusion, an easy, simple, and general methodology, promoted by samarium diiodide, has been developed to

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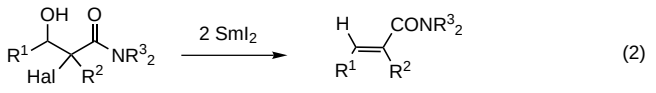

(2)

3a–c **4a–c**

Table 2. Synthesis of α,β-unsaturated amides with SmI_2 [Eq. (2)].

entry	**4**	R^1	R^2	R^3	Hal	*de* [%][a]	yield [%][b]
1	**4a**	C_7H_{15}	H	Et	Cl	> 98	89
2	**4b**	Ph	H	Et	Cl	> 98	90
3	**4c**	MeCH(Ph)	H	Et	Cl	> 98	82

[a] Determined from crude reaction products with GC-MS. [b] Yield of isolated products.

synthesize α,β-unsaturated esters and amides with total *E* stereoselectivity from the easily available 2-halo-3-hydroxy-esters or amides.

Experimental Section

A solution of SmI_2 (1 mmol) in THF (12 mL) was very slowly added dropwise, under a nitrogen atmosphere, to a stirred solution of halohydroxyester **1** (0.4 mmol) in THF (2 mL) at room temperature, until the reaction mixture turned permanently blue. The reaction mixture was quenched with aqueous HCl (1M, 5 mL). Standard work-up and filtration through a pad of Celite provided pure α,β-unsaturated esters **2** (> 98 %).

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Investigations of Lipid – Protein Interactions on Monolayers of Chain-Substituted Phosphatidylcholines**

Ursula Dahmen-Levison,* Gerald Brezesinski, Helmuth Möhwald, Jens Jakob, and Peter Nuhn

Polarization-modulated infrared reflection absorption spectroscopy (PM-IRRAS, Figure 1) is a versatile method for studying the hydrolysis of long-chain lipids at the air/water interface and the influence of phase separations on the activity of proteins.[1, 2] Our investigations using this method were performed on phospholipase A_2 (PLA_2). PLA_2 cleaves selectively the *sn*-2 ester linkage of phospholipids, leading to a fatty acid and a lysophospholipid. PLA_2 plays an important role in the arachidonyl cascade, since arachidonyl is the main group found in the 2-position at the glycerol of the phospholipids in mammal cells. PLA_2 is an interfacially active enzyme, whose activity is strongly dependent on the physical-chemical structure of the substrate, which makes it very difficult to develop inhibitors. The investigations at the air/water inter-

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