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ORIGINAL PAPER

Organocatalytic SOMO reactions of copper(I)-acetylide and alkylindium compounds with aldehydes

Pavol Tisovský, Mária Mečiarová, Radovan Šebesta*

Department of Organic Chemistry, Faculty of Natural Sciences, Comenius University, Mlynská dolina CH-2, 842 15 Bratislava, Slovakia

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The derivatisation of aldehydes in their α-position is an important facet of organic synthesis. Organocatalytic radical reactions afford α-functionalised aldehydes via a SOMO activation pathway. New organo-SOMO reactions of aldehydes with copper(I)-acetylide and alkylindium reagents are detailed. These reactions proceed well under the catalysis of chiral imidazolidinones. The corresponding functionalised aldehydes were obtained with acceptable yields, but with only low enantiomeric ratios.

Keywords: organocatalysis, SOMO activation, acetylide, alkylindium

Introduction

Asymmetric organocatalysis relies on two major activation modes. The activation of electrophiles can be performed via the LUMO-lowering strategy, such as iminium salt-formation or hydrogen-bonding. On the other hand, nucleophiles can be activated through HOMO-rising, typically achieved by enamine-formation (Dalko, 2007). There is, however, a third concept, the so-called SOMO (singly-occupied molecular orbital) activation. These organo-SOMO reactions constitute a novel concept for enantioselective α-substitution of carbonyl compounds, especially aldehydes, which proceed through a radical mechanism. Aldehydes react with chiral secondary amines to give enamines, which can be readily oxidised to cation radicals. These cation radicals undergo coupling reactions with a variety of compounds, so-called somophiles, to give enantio-enriched α-substituted aldehydes (Fig. 1) (Beeson et al., 2007).

Chiral imidazolidinones were deemed the best catalysts for these transformations (MacMillan & Rendler, 2012). The oxidising agents most commonly used in SOMO reactions are $(NH_4)_2Ce(NO_3)_6$ (diammonium cerium(IV) nitrate, CAN), $Cu(OSO_2CF_3)_2$ (copper(II) trifluoromethanesulphonate, $Cu(OTf)_2$), copper(II) trifluoroacetate ($Cu(TFA)_2$), $CuCl_2$, $[Fe(phen)_3](PF_6)_3$ and $FeCl_3$.

SOMO catalysis has been applied successfully in a variety of reactions. The allylation of various aldehydes (Beeson et al., 2007) and cyclic ketones (Mastracchio et al., 2010) with π-rich olefinic silanes resulted in important chiral intermediates, including five-, six- and seven-membered carbocycles and heterocycles (Pham et al., 2011a). The reactions of SOMO-activated aldehydes with enolsilanes gave enantio-enriched γ-ketoaldehydes (Jang et al., 2007). Organocatalytic SOMO-vinylation of aldehydes yielded products with formyl- and vinyl-moieties on the stereogenic centre (Kim & McMillan, 2008). The α-arylation of aldehydes via organo-SOMO catalysis is a promising method for the synthesis of pharmacologically active molecules, e.g. (−)-tashiromin (Banwell et al., 2004), (*S*)-ketoprofen (Allen & McMillan, 2011) and other medicinal agents (Harvey et al., 2011). Chiral tetrahydronaphthalene derivatives were prepared by intramolecular SOMO α-arylation of aldehydes (Nicolaou et al., 2009; Conrad et al., 2009; Um

*Corresponding author, e-mail: radovan.sebesta@fns.uniba.sk

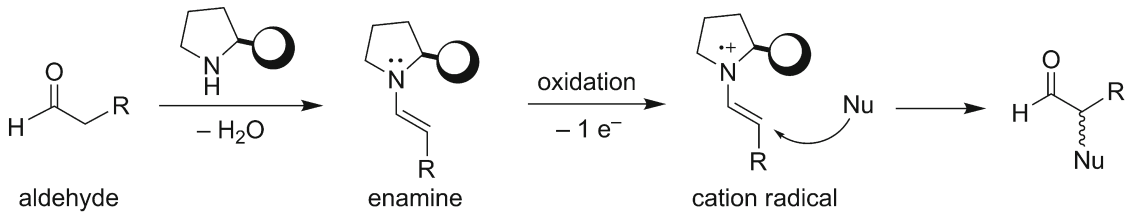


Fig. 1. SOMO-catalysed α-derivatisation of aldehydes.

et al., 2010). SOMO-catalysed [4+2] cyclo-additions of aromatic aldehydes with styrenes and dienes provided cyclic products with high regioselectivity and stereoselectivity (Jui et al., 2010). Similarly, the [3+2] cyclo-addition of aldehydes and conjugated olefins afforded pyrrolidine derivatives under SOMO-catalysis (Jui et al., 2012). SOMO-catalysed carbo-oxidation of styrenes in the presence of cerium ammonium nitrate gave γ-nitrate-α-alkyl aldehydes, valuable building blocks of enantio-enriched butyrolactones, pyrrolidines and α-formyl homobenzylation adducts (Graham et al., 2008). Oxidative enantioselective aldehyde nitroalkylation with silyl nitronates is an efficient method for the synthesis of β-nitroaldehydes, which are versatile synthons in the synthesis of β-amino acids and 1,3-aminoalcohols (Wilson et al., 2009). The enantioselective α-benzylation of aldehydes with electron-deficient aryl and heteroaryl bromides using photoredox-organocatalysis afforded enantio-enriched α-benzyl aldehydes, which are important synthons in the synthesis of angiogenesis inhibitors (Shih et al., 2010). Enantio-enriched α-chloroaldehydes, prepared using LiCl as a chlorine source under organo-SOMO catalysis, are reactive intermediates in the synthesis of terminal aziridines, α-chloro alcohols, α-cyano alcohols, terminal epoxides, α-hydroxy acids, α-amino acids, etc. (Amatore et al., 2009). Carbonyl and carboxyl compounds with a trifluoromethyl group on the stereogenic centre at an α-position were prepared by SOMO-catalysed asymmetric α-trifluoromethylation. These compounds are versatile synthons for medicinal agents and agrochemicals synthesis (Nagib et al., 2009; Allen & McMillan, 2010; Pham et al., 2011a, 2011b). Enantioselective α-oxidation of aldehydes with TEMPO using a synergistic combination of copper and organocatalysis afforded versatile synthons for natural products and medicinal agents (Simonovich et al., 2012). Zhu et al. (2012) described the direct oxidation of 3-arylpropanals to 3-arylacroleins promoted by SOMO catalysis.

Aldehydes with alkyl, alkenyl or alkynyl chains were often prepared by multi-step synthesis with low yields. One of the intermediates in the total synthesis of (+)-frondosin A, 4-(dimethyl(phenyl)silyl)-2,2-dimethylbut-3-ynal, was prepared in a four-step process from commercially available 2-methylbut-3-yn-2-ol with an overall yield of 15 % (Barry et al., 2007). 2-Benzyl-2,4-diphenylbut-3-ynal was formed as a by-product in the synthesis of polysubstituted pyrroles from substituted alkynoles with a 10–37 % yield (Teo et al., 2013). Aldehydes with a double or triple bond were prepared by a two-step process. The first step was the reaction of epoxysilanes with organometallic reagents. The accrued diols were then oxidised with $Pb(OAc)_4$ to give the target aldehydes with an overall yield of 31–77 % (Chauret et al., 1999).

In addition, some of the resulting products could be useful for their biological properties. For instance, alkynales were used in the synthesis of fused tetrahydropyranones, which are common building blocks in biologically active molecules (Ciesielski et al., 2013).

As noted above, a variety of different somophiles have been described to date. However, very little attention has been devoted to organometallic reagents as somophiles. Accordingly, it was decided to expand the methodology of SOMO organocatalysis by applying organometallic compounds as somophiles. Using copper(I)-acetylides, a triple bond was introduced into a molecule of aldehdyde. Various organoindium compounds were used for introduction of the alkyl or alkenyl side-chain.

Experimental

All reactions were carried out in an argon inert atmosphere. Solvents were dried and purified by standard methods prior to use. FTIR spectra were obtained with Thermo Scientific Nicolet iS10 spectrometer. NMR spectra (300 MHz for ^{1}H; 75 MHz for ^{13}C) were recorded on a Varian Mercury plus instrument. Chemical shifts are referenced to the tetramethylsilane (TMS) as internal standard. Flash chromatography was performed on Merck silica gel 60. Thin-layer chromatography (TLC) was performed on Merck TLC-plates silica gel 60 F_{254}. Enantiomeric excesses were determined using HPLC on a Chiralcel OD-H, Chiralpak AD-H or Chiralpak AS-H (Daicel Chemical Industries) column using a mixture of isopropyl alcohol (IPA) and hexane as a mobile phase and detection with UV-detector at 254 nm. Copper(I) phenylacetylide (*II*) (not commercially available) was synthesised following the previously described procedure (Shi et al., 2008). Catalyst C-V was prepared using the recognised method (Samulis & Tomkinson, 2011).

Table 1. Physical and spectral data of prepared compounds

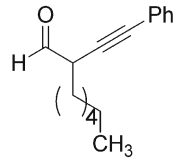
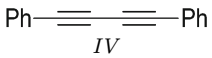
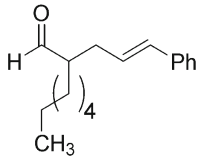
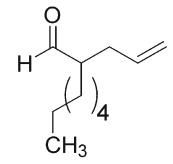
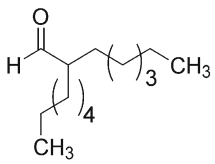
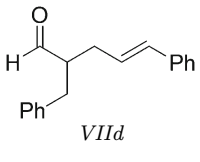
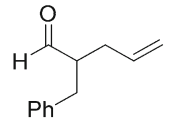
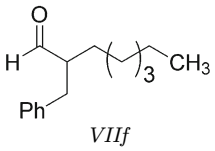
Compound	Physical and spectral data	Reference
 *IIIa*	FTIR (neat), $\tilde{\nu}$/cm^{-1}: 3435, 2960, 2933, 2860, 2112, 1728, 1490, 1416, 1380, 1071, 961, 890, 802, 757, 728, 690, 651 ^{1}H NMR (300 MHz, $CDCl_3$), δ: 9.72 (d, J = 6.4 Hz, 1H, CH═O), 7.55–7.51 (m, 2H, HC in Ph), 7.38–7.31 (m, 3H, HC in Ph), 3.61 (td, J = 7.4 Hz, J = 6.4 Hz, 1H, CH), 1.79 (dt, J = 7.4 Hz, J = 7.0 Hz, 2H, CH_2), 1.33–1.24 (m, 8H, 4 × CH_2), 0.87 (t, J = 6.9 Hz, 3H, CH_3) ^{13}C NMR (75 MHz, $CDCl_3$), δ: 200.7 (C═O), 128.5 (CH), 128.3 (CH), 122.7 (CH_q in Ph), 89.4 (C≡C), 78.6 (C≡C), 43.6 (CH), 32.3 (CH_2), 31.8 (CH_2), 28.4 (CH_2), 25.7 (CH_2), 22.7 CH_2), 14.1 (CH_3) HRMS, m/z (found/calc.): 229.1590/229.1592 ([M + H]$^+$, $C_{16}H_{21}O$) HPLC (Chiralpak OD-H; IPA/hexane (φ_r = 3 : 97); 1 mL min^{-1}; λ = 254 nm): t_R (major) = 29.13 min, t_R (minor) = 35.46 min	This article
 *IV*	FTIR (neat), $\tilde{\nu}$/cm^{-1}: 2985, 2143, 1560, 923, 756 ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.56–7.50 (m, 4H, HC in Ph), 7.39–7.29 (m, 6H, HC in Ph)	Herrmann et al. (2001)
 *VIIa*	FTIR (neat), $\tilde{\nu}$/cm^{-1}: 3318, 3023, 2920, 2855, 2362, 2340, 1596, 1495, 1465, 1379, 1262, 1029, 964, 801, 738, 691, 669, 617, 492, 419 ^{1}H NMR (300 MHz, $CDCl_3$), δ: 9.71 (d, J = 7.7 Hz, 1H, (CH═O), 7.41–7.20 (m, 5H, HC in Ph), 6.61 (d, J = 15.9 Hz, 1H, CH═CH), 6.31 (ddd, J = 4.3 Hz, J = 9.0 Hz, J = 15.9 Hz, 1H, CH═CH), 2.73 (m, 1H, CH), 2.39 (dd, J = 7.0 Hz, J = 7.0 Hz, 2H, CH_2), 1.52 (dt, J = 7.3 Hz, J = 6.6 Hz, 2H, CH_2), 1.33–1.24 (m, 8H, 4 × CH_2), 0.87 (t, J = 6.9 Hz, 3H, CH_3) ^{13}C NMR (75 MHz, $CDCl_3$), δ: 204.1 (C═O), 136.4 (CH_q in Ph), 128.5 (C═C), 128.6 (CH), 127.9 (CH), 127.8 (CH), 117.4 (C═C), 52.8 (CH), 31.8 (CH_2), 31.1 (CH_2), 29.3 (CH_2), 22.7 (CH_2), 14.1 (CH_3) HPLC (Chiralpak AD-H; IPA/hexane (φ_r = 5 : 95); 1 mL min^{-1}; λ = 254 nm): t_R (major) = 17.34 min, t_R (minor) = 20.18 min	Joosten et al. (2010)
 *VIIb*	FTIR (neat), $\tilde{\nu}$/cm^{-1}: 3442, 2932, 2870, 1732, 1456, 1442, 1410, 1250, 1061, 930, 720, 692, 537 ^{1}H NMR (300 MHz, $CDCl_3$), δ: 9.70 (d, J = 7.3 Hz Hz, 1H, CH═O), 5.63 (ddt, J = 17.1 Hz, J = 10.5 Hz, J = 7.4 Hz, 1H, C<u>H</u>═CH_2), 4.85–4.75 (m, 2H, CH═C<u>H</u>$_2$), 2.69 (tdt, J = 7.3 Hz, J = 7.3 Hz, J = 7.0 Hz, 1H, CH), 2.41 (dd, J = 7.4 Hz, J = 7.0 Hz, 2H, CH_2), 1.51 (dt, J = 7.3 Hz, J = 6.6 Hz, 2H, CH_2), 1.41–1.28 (m, 8H, 4 × CH_2),0.86 (t, J = 7.0 Hz, 3H, CH_3) ^{13}C NMR (75 MHz, $CDCl_3$), δ: 204.5 (C═O), 135.7 (C═C), 115.7 (C═C), 52.5 (CH), 31.8 (CH_2), 31.7 (CH_2), 29.3 (CH_2), 27.8 (CH_2), 22.7 (CH_2), 14.3 (CH_3) HPLC (Chiralpak OD-H; IPA/hexane (φ_r = 5 : 95); 1 mL min^{-1}; λ = 216 nm): t_R (major) = 26.54 min, t_R (minor) = 31.27 min	Joosten et al. (2010)
 *VIIc*	FTIR (neat), $\tilde{\nu}$/cm^{-1}: 3442, 2965, 2932, 2870, 1732, 1456, 1220, 1170, 1061, 720, 503 ^{1}H NMR (300 MHz, $CDCl_3$), δ: 9.71 (d, J = 7.2 Hz, 1H, CH═O), 2.57 (dqd, J = 7.8 Hz, J = 6.2 Hz, J = 4.8 Hz, 1H, CH), 1.68–1.54 (m, 4H, 2 × CH_2), 1.33–1.27 (m, 16H, 8 × CH_2), 0.88 (t, J = 5.8 Hz, 6H, 2 × CH_3) ^{13}C NMR (75 MHz, $CDCl_3$), δ: 204.3 (C═O), 50.9 (CH), 31.8 (CH_2), 28.8 (CH_2), 26.9 (CH_2), 22.7 (CH_2), 14.2 (CH_3) GC (Lipodex E, γ-cyclodextrin, 100 °C, 122 kPa): t_R (major) = 12.5 min, t_R (minor) = 13.7 min	Kato et al. (1997)
 *VIId*	FTIR (neat), $\tilde{\nu}$/cm^{-1}: 3027, 2960, 2922, 2854, 2360, 2342, 1723, 1685, 1600, 1496, 1452, 1260, 1074, 1014, 963, 794, 737, 693, 670, 493 ^{1}H NMR (300 MHz, $CDCl_3$), δ: 9.76 (d, J = 1.8, 1H, CH═O), 7.46–7.21 (m, 10H, HC in Ph), 6.61 (d, J = 15.9 Hz, 1H, CH═C<u>H</u>Ph), 6.31 (ddd, J = 4.3 Hz, J = 9.0 Hz, J = 15.9 Hz, 1H, C<u>H</u>═CHPh), 2.87 (d, J = 7.4 Hz, 2H, CH_2), 2.84 (tdt, J = 7.4 Hz, J = 7.4 Hz, J = 7.1 Hz, 1H, CH), 2.43 (dd, J =7.1 Hz, J = 7.0 Hz, 2H, CH_2) ^{13}C NMR (75 MHz, $CDCl_3$), δ: 202.3 (C═O), 138.0 (CH_q in Ph), 136.4 (CH_q in Ph), 128.8 (C═C), 128.6 (CH), 128.5 (CH), 128.1 (CH), 127.9 (CH), 126.1 (CH), 114.8 (C═C), 54.9 (CH), 34.7 (CH_2), 30.7 (CH_2) HPLC (Chiralpak AS-H; IPA/hexane (φ_r = 3 : 97); 0.5 mL min^{-1}; λ = 254 nm): t_R (major) = 32.19 min, t_R (minor) = 43.74 min	Afewerki et al. (2012)

Table 1. (continued)

Compound	Physical and spectral data	Reference
 *VIIe*	FTIR (neat), $\tilde{\nu}$/cm^{-1}: 3032, 2983, 1724, 1602, 1498, 1454, 1442, 1409, 1211, 1081, 1031, 929, 751, 700, 691, 537, 506 ^{1}H NMR (300 MHz, $CDCl_3$), δ: 9.72 (d, J = 7.5 Hz, 1H, CH═O), 7.31–7.24 (m, 2H, HC in Ph), 7.24–7.12 (m, 3H, HC in Ph), 5.69 (m, 1H, C<u>H</u>═CH_2), 4.93 (m, 1H, CH═C<u>H</u>$_2$), 3.08 (m, 1H, CH), 2.75 (m, 2H, CH_2), 2.29 (m, 1H, CH_2), 2.10 (m, 1H, CH_2) ^{13}C NMR (75 MHz, $CDCl_3$), δ: 204.2 (C═O), 139.9 (CH_q in Ph), 135.4 (C═C), 128.9 (CH), 128.8 (CH), 126.8 (CH), 117.2 (C═C), 51.5 (CH), 37.1 (CH_2), 36.2 (CH_2) HPLC (Chiralpak AD-H; IPA/hexane (φ_r = 5 : 95); 0.75 mL min^{-1}; λ = 254 nm): t_R (major) = 23.41 min, t_R (minor) = 26.67	Zhao et al. (2011)
 *VIIf*	FTIR (neat), $\tilde{\nu}$/cm^{-1}: 3032, 2965, 2928, 1724, 1602, 1498, 1454, 1172, 1081, 1031, 751, 700, 506 ^{1}H NMR (300 MHz, $CDCl_3$), δ: 9.74 (d, J = 7.5 Hz, 1H, CH═O), 7.30–7.24 (m, 2H, HC in Ph), 7.24–7.12 (m, 3H, HC in Ph), 3.07 (m, 1H, CH_2), 2.71 (m, 1H, CH), 2.64 (m, 1H, CH_2), 1.56 (d, J = 15.5 Hz, 2H, CH_2), 1.33–1.27 (m, 8H, 4 × CH_2), 1.00–0.96 (t, J = 7.0 Hz, 3H, CH_3) ^{13}C NMR (75 MHz, $CDCl_3$), δ: 205.1 (C═O), 139.9 (CH_q in Ph), 128.9 (CH), 128.8 (CH), 126.7 (CH), 51.4 (CH), 38.1 (CH_2), 31.9 (CH_2), 31.6 (CH_2), 29.3 (CH_2), 27.6 (CH_2), 22.9 (CH_2), 14.0 (CH_3) HPLC (Chiralpak AD-H; IPA/hexane (φ_r = 5 : 95); 1 mL min^{-1}; λ = 254 nm): t_R (major) = 22.11 min, t_R (minor) = 26.63	Li et al. (2012)

General procedure for SOMO reactions with copper(I) phenylacetylide (II)

A solution of catalyst (20 mole %) in acetone (1 mL) was prepared in a flame-dried flask at –78 °C under argon atmosphere. In the following order, aldehyde (0.25 mmol), copper(I) phenylacetylide (0.5 mmol, 82 mg), $NaHCO_3$ (0.5 mmol, 42 mg), water (0.5 mmol, 8 μL), CAN (0.5 mmol, 274 mg) were added to the mixture. After purging the solution with argon for 1 min, the mixture was heated to –40 °C and stirred at this temperature for 24 h. The cold reaction mixture was poured into diethyl ether (20 mL) and filtered through a pad of SiO_2, washed with Et_2O (20 mL) and concentrated under reduced pressure. The resulting residue was purified by column chromatography (SiO_2, hexane/EtOAc (φ_r = 7 : 1)) to provide the title compound.

General procedures for synthesis of alkylindium reagent from alkyl bromide

Method A. A mixture of alkyl bromide (0.5 mmol), indium (1 mmol, 115 mg), CuCl (1 mmol, 99 mg) and dimethyl acetamide (DMA) (3 mL, analytical grade) in a 25 mL vial was stirred vigorously at 100 °C for 24 h. Next, the clear upper solution was carefully separated from the black bottom precipitate using a syringe and added to another vial charged with the catalyst (20 mole %), aldehyde (0.25 mmol) and $NaHCO_3$ (0.5 mmol, 42 mg). Water (0.5 mmol, 8 μL) and CAN (0.625 mmol, 343 mg) were added, the resulting mixture was purged with argon for 1 min and stirred at ambient temperature for 24 h. The reaction mixture was poured into Et_2O (20 mL), filtered through a pad of SiO_2, washed with Et_2O (20 mL) and concentrated under diminished pressure. The resulting residue was purified by column chromatography (SiO_2, hexane/EtOAc (φ_r = 7 : 1)) to provide the title compound.

Method B. A mixture of alkyl bromide (0.5 mmol), indium (1 mmol, 115 mg), CuCl (1 mmol, 99 mg), DMA (3 mL), catalyst (20 mole %), aldehyde (0.25 mmol), $NaHCO_3$ (0.5 mmol, 42 mg), water (0.5 mmol, 8 μL) and CAN (0.625 mmol, 342.6 mg) in a 25 mL vial was purged with argon for 1 min and placed in an ultrasound cleaning bath for 24 h. The reaction mixture was then poured into Et_2O (20 mL), filtered through SiO_2, washed with diethyl ether (20 mL), concentrated under reduced pressure and the residue was purified by column chromatography as in method A.

Method C. A mixture of alkyl bromide (0.5 mmol), indium (1 mmol, 115 mg), CuCl (1 mmol, 99 mg) and THF (3 mL) in a 25 mL vial was heated in a microwave reactor at 70 °C for 2 h followed by the addition of catalyst (20 mole %), aldehyde (0.25 mmol), $NaHCO_3$ (0.5 mmol, 42 mg), water (0.5 mmol, 8 μL) and CAN (0.625 mmol, 342.6 mg). The resulting mixture was purged with argon for 1 min and stirred vigorously at ambient temperature for 24 h. The reaction mixture was poured into Et_2O (20 mL), filtered through SiO_2, washed with Et_2O (20 mL), concentrated under diminished pressure and the residue was purified by column chromatography as in method A.

Method D. A mixture of catalyst (20 mole %), alde-

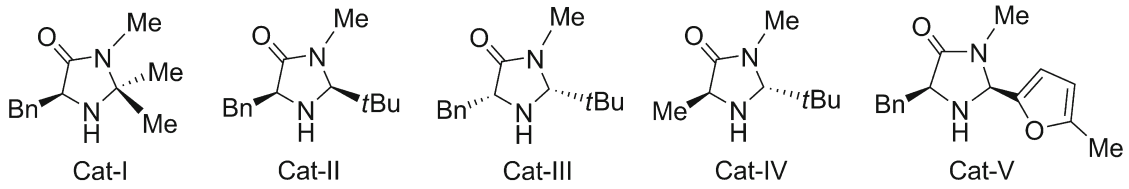


Fig. 2. Organocatalysts used in this study (*t*Bu denotes *tert*-butyl; Bn is benzyl).

Table 2. SOMO reactions of aldehyde *Ia* with copper(I) phenylacetylide (*II*)

Entry	Catalyst	Temperature/ ℃	Yield of *III*/%	Yield of *IV*/%	e.r. of *III*
1	Cat-I · HCl	–50 ℃	17	0	40 : 60
2	Cat-I · HCl	–40 ℃	61	0	58 : 42
3	Cat-I · HCl	–30 ℃	0	47	–
4	Cat-I · HCl	–20 ℃	0	54	–
5	Cat-I · HCl	+5 ℃	0	60	–
6	Cat-V	–40 ℃	10	63	50 : 50
7	Cat-I · DCA	–40 ℃	0	43	–
8	Cat-III · TFA	–40 ℃	0	56	–
9	Cat-IV · HCl	–40 ℃	0	52	–
10	Pyrrolidine	–40 ℃	0	61	–
11	Cat-I · HCl	+10 ℃	0	70	–

hyde (0.25 mmol), $NaHCO_3$ (0.5 mmol, 42 mg), water (0.5 mmol, 8 μL) and CAN (0.625 mmol, 342.6 mg) was added to a stirred mixture of alkyl bromide (0.5 mmol), indium (1 mmol, 115 mg), CuCl (1 mmol, 99 mg) and dimethyl acetamide (DMA) (3 mL) in a 25 mL vial. The resulting mixture was then purged with argon for 1 min, stirred vigorously at ambient temperature for 24 h and processed as in method C.

Results and discussion

Typically, asymmetric organocatalytic SOMO reactions are performed with various chiral imidazolidinones. The organocatalysts used in this study are depicted in Fig. 2.

The investigation commenced with a reaction of octanal (*Ia*) with copper(I) phenylacetylide (*II*) under various conditions. Copper(I) phenylacetylide (*II*) is insoluble in dimethoxyethane (DME), THF and MeCN, hence the reaction did not proceed in these solvents. The only suitable solvent for the reaction was acetone with CAN as an oxidant and $NaHCO_3$ as a base. The stability of compound *II* under the reaction conditions was also evaluated and no decomposition of this compound was observed after 24 h. The reaction of *Ia* with *II* using catalyst Cat-I · HCl at –50 ℃ afforded product *IIIa* with only a 17 % yield. Increasing the reaction temperature to –40 ℃ resulted in enhancing the yield of product *IIIa* to 61 %. Unfortunately, these reactions proceeded with practically no enantioselectivity (Table 2, entries 1 and 2). Further increases in the reaction temperature to –30 ℃, –20 ℃ and 5 ℃ incurred a change of reaction mechanism and only the product of homo-coupling (*IV*) was isolated with a 47–60 % yield (Table 2, entries 3–5). The reaction at ambient temperature resulted in a complex mixture of products. The reaction of aldehyde *Ib* with copper(I) phenylacetylide (*II*) at –40 ℃ again afforded only the homo-coupling product *IV* with a 62 % yield. Using catalyst Cat-V at –40 ℃, product *IIIa* was isolated with a 10 % yield as a racemic mixture and product *IV* was isolated with a 63 % yield (Table 2, entry 6). The reaction with aldehyde *Ib* under the same reaction conditions did not proceed. Both product *IIIa* as well as product *IV* were absent in the reaction mixture. When catalysts Cat-I · DCA (DCA = dichloroacetic acid), Cat-III · TFA (TFA = trifluoroacetic acid), Cat-IV · HCl, as well as pyrrolidine were used at –40 ℃ in the reactions of *Ia* with *II*, product *IIIa* was again absent in the reaction mixture and only the product of homo-coupling *IV* was isolated with a 43–61 % yield (Table 2, entries 7–10). In respect of the radical mechanism of these reactions, an attempt was made to improve their course using ultrasonic irradiation. However, sonication of the reaction mixture of *Ia* with *II* using Cat-I · HCl as a catalyst at 10 ℃ for 8 h in an ultrasonic cleaning bath (20 kHz) resulted in the formation of only the homo-coupling product *IV* with a 70 % yield (Table 2, entry 11).

In addition, organo-SOMO reactions of aldehydes with organoindium compounds were studied. These somophiles were prepared from the corresponding halides, indium powder and CuCl (methods A and C) then used in reactions with aldehydes. Alternatively, these reactions were performed as a one-pot process (methods B and D) (Fig. 4).

A reaction of octanal (*Ia*) with separately prepared alkylindium *VIa* in DMA using catalyst Cat-I · HCl af-

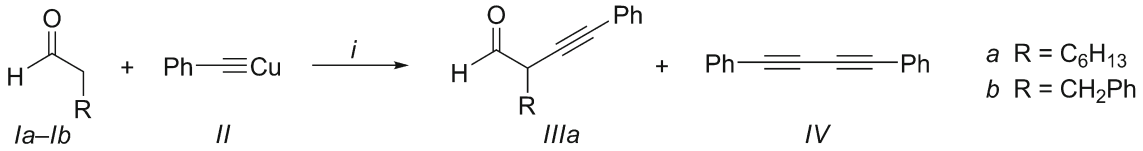


Fig. 3. SOMO reactions of aldehydes *Ia*, *Ib* with copper(I) phenylacetylide (*II*). Reaction conditions: *i*) organocatalyst (20 mole %), CAN, $NaHCO_3$, H_2O, acetone, 24 h.

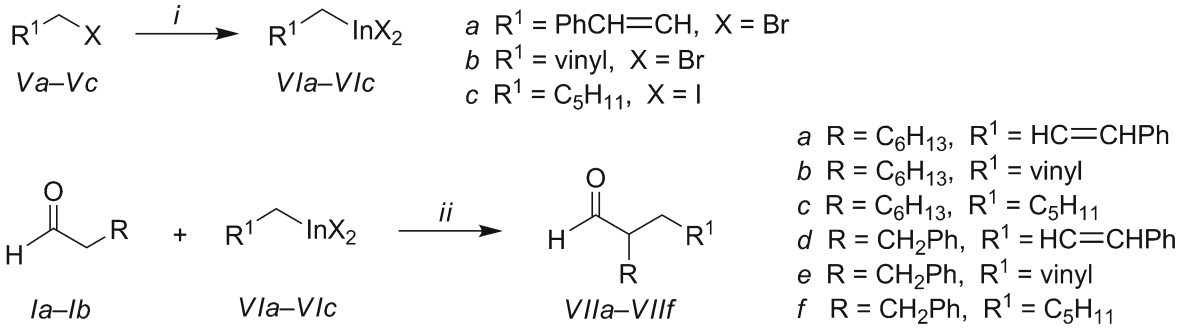


Fig. 4. SOMO reactions of aldehydes *Ia*, *Ib* with organoindium compounds *VIa–VIc*. Reactions conditions: *i*) In, CuCl; *ii*) organocatalyst (20 mole %), CAN, $NaHCO_3$, H_2O, solvent.

Table 3. SOMO reactions of aldehydes with organoindium compounds

Entry	Aldehyde	$RInX_2$	Catalyst	Method[a]	Product	Yield/%	e.r.
1	*Ia*	*VIa*	Cat-I · HCl	A	*VIIa*	60	57 : 43
2	*Ia*	*VIa*	Cat-I · HCl	B (12 h)	*VIIa*	40	47 : 53
3	*Ia*	*VIa*	Cat-I · HCl	B (12 h)	*VIIa*	32	50 : 50
4	*Ia*	*VIb*	Cat-IV · HCl	B (24 h)	*VIIb*	12	50 : 50
5	*Ia*	*VIb*	Cat-I · HCl	C	*VIIb*	34	–
6	*Ia*	*VIc*	Cat-I · HCl	D	*VIIc*	0	–
7	*Ia*	*VIc*	Cat-I · HCl	B (24 h)	*VIIc*	32	50 : 50
8	*Ia*	*VIc*	Cat-II	D	*VIIc*	40	50 : 50
9	*Ia*	*VIc*	Cat-II	B (24 h)	*VIIc*	28	48 : 52
10	*Ib*	*VIa*	Cat-II	A	*VIId*	41	42 : 58
11	*Ib*	*VIa*	Cat-II	B (24 h)	*VIId*	52	50 : 50
12	*Ib*	*VIb*	Cat-II	A	*VIIe*	34	50 : 50
13	*Ib*	*VIb*	Cat-II	B (24 h)	*VIIe*	17	53 : 47
14	*Ib*	*VIc*	Cat-II	A	*VIIf*	30	56 : 44
15	*Ib*	*VIc*	Cat-II	B (24 h)	*VIIf*	–	–

a) Method A: preparation of RCH_2InX_2 at 100 °C for 24 h; reaction of RCH_2InX_2 with aldehyde at ambient temperature for 48 h; method B: one-pot reaction for 12 h or 24 h under ultrasonic irradiation; method C: preparation of RCH_2InX_2 at 70 °C under microwave irradiation for 2 h; reaction of RCH_2InX_2 with aldehyde at ambient temperature for 24 h; method D: one-pot reaction at ambient temperature for 24 h.

forded product *VIIa* with a 60 % yield (Table 3, entry 1). When this reaction was performed as a one-pot process under ultrasonic irradiation, the yield of product *VIIa* declined to 40 % with catalyst Cat-I · HCl and to 32 % with catalyst Cat-IV · HCl (Table 3, entries 1–3). The products were obtained as virtually racemic mixtures. Product *VIIb* was obtained with a 12 % yield as a racemic mixture using catalyst Cat-I · HCl when the reaction mixture was irradiated in an ultrasonic cleaning bath for 24 h. A somewhat better yield (34 %) of compound *VIIb* was obtained when the reaction of *Ia* with somophile *VIb* (prepared under microwave irradiation at 70 °C for 2 h) proceeded in THF with Cat-I · HCl (Table 3, entries 4 and 5). The one-pot reaction of hexyl iodide, metallic indium, CuCl and *Ia* using Cat-I · HCl as the catalyst did not proceed at ambient temperature for 24 h (method D). Only the starting material was detected in the reaction mixture. When this reaction proceeded under ultrasonic irradiation (method B) for 24 h, the product was isolated with a 32 % yield as a racemate. The reaction of hexyl iodide, indium, CuCl and *Ia* with catalyst Cat-II under standard conditions afforded product *VIIc* with a 40 % yield. In contrast with the reaction with Cat-I · HCl, sonication of the reaction mixture for 24 h

decreased the yield slightly to 28 % (Table 3, entries 6–9).

The reaction of *Ib* with *VIa* using catalyst Cat-II (method A) afforded compound *VIId* with a 41 % yield. A better yield (52 %) of the aldehyde *VIId* was achieved by a one-pot reaction under ultrasonic irradiation for 24 h (method B) (Table 3, entries 10 and 11). Unlike with *VIa*, the reaction of *Ib* with *VIb* afforded 34 % of the product *VIIe* using method A and only 17 % of the product *VIIe* was achieved after the one-pot reaction (method B) (Table 3, entries 12 and 13). Compound *VIIf* was obtained after the reaction of aldehyde *Ib* and organoindium *VIc* with a 30 % yield (method A), but the reaction did not proceed under ultrasonic irradiation as a one-pot process (Table 3, entries 14 and 15).

Conclusions

Copper(I) phenylacetylide was demonstrated to be a rather poor SOMO-phile, because it has a distinct propensity for homo-coupling under SOMO reaction conditions. However, under proper conditions, the product of its SOMO reaction, 2-(2-phenylethynyl)octanal (*IIIa*) can be isolated with a 61 % yield using imidazolidinone catalyst, Cat-I · HCl. The reactions of various aldehydes with organoindium compounds gave α-alkylated aldehydes with fair yields (up to 60 %) but with only low enantiomeric purities. The application of ultrasonic irradiation improved the reaction course in some cases.

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