

Indium triflate: a new catalyst for (4 + 2)-cycloaddition of chromone Schiff's bases

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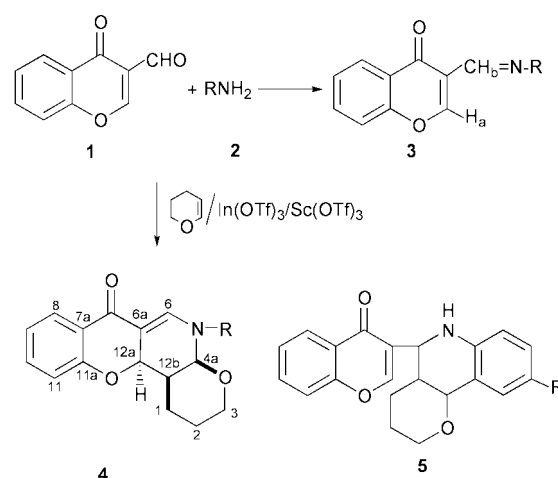
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3,4-Dihydro-2H-pyran reacts with a variety of chromone Schiff's bases **3** in the presence of indium and scandium triflates at ambient temperature and pressure to give the *endo* cycloadducts **4** regioselectively in high yields.

Indium-mediated reactions have emerged as a useful tool in organic synthesis.¹ In particular, it was found that the low reactivity of trivalent organoindium reagents can be easily increased by the formation of complexes with organolithium compounds.² The tetraorganoindates thus prepared are sufficiently reactive to take part in reactions at ambient temperature.^{2a} Allylic indates react with imides and nitriles regioselectively at the γ -carbon to give homoallylamines.^{2b} Organoindium compounds derived from dibromo-substituted active methylene compounds, such as dibromomalononitrile, and indium metal react with alkenes and carbonyl compounds to give cyclopropanes and oxiranes, depending on the nature of the reagents and substrates.³ Our interest in catalytic carbon-carbon bond formation⁴ prompted us to investigate the use of indium and scandium triflates in (4 + 2)-cycloadditions. In recent years triflates have received increasing attention both as reagents and as catalysts for organic reactions.⁵ These triflates have also been shown to be effective, water-tolerant Lewis acids in several carbon-carbon bond-forming reactions and in some cases the presence of water even improves their activity. In a recent report, indium triflate was used in hetero-Diels-Alder reactions,⁶ and scandium triflate was used in Tishchenko reduction of β -hydroxy ketones⁷ and in enantioselective Diels-Alder reactions.⁸ Herein, we report the first example of indium and scandium triflate-catalyzed (4 + 2)-cycloaddition of chromone Schiff's bases with 3,4-dihydro-2H-pyran. The reaction proceeds efficiently at ambient temperature and pressure in high yields. We selected bifunctional chromones in which an electron-withdrawing substituent at C-3 enables these substrates to act as Michael acceptors⁹ or heterodienes¹⁰ and to undergo various rearrangements on treatment with nucleophiles.¹¹

Results and discussion

The imines **3a-e** were readily obtained by allowing 3-formylchromone **1** to react with aromatic amines **2a-e** in refluxing benzene with azeotropic removal of water (Dean-Stark apparatus) and using a catalytic amount of toluene-*p*-sulfonic acid.¹² These imines **3** were prepared in good yields without the formation of any side products arising from Michael-type additions onto the carbon-carbon double bond of the chromone moiety¹³ or rupture of the chromone moiety itself. The test cycloaddition reaction was carried out by the addition of a catalytic amount of indium triflate to a solution of chromone Schiff's base **3a** and 3,4-dihydro-2H-pyran in acetonitrile at room temperature (see Experimental) (Scheme 1). The tentative structural assignment for the cycloadduct **4a** as *endo* is based on its high-resolution ¹H and ¹³C spectra. The diagnostic signal for the proton H_a in **3a**, which appeared at δ 8.65, was absent in the cycloadduct **4a**, whilst the upfield shift of this proton



Scheme 1

from δ 8.65 to 5.34 (12a-H) showed that cycloaddition had occurred at the C-2 position of the chromone unit, which clearly ruled out the possibility of any formation of product of type **5**, and also there was no evidence for the formation of any *exo* product. The observed values for the allylic coupling constants in compounds **4** are consistently \approx 1 Hz and therefore invite assignment of these products as having *endo* stereochemistry.

Similarly, other imines treated with 3,4-dihydro-2H-pyran underwent (4 + 2)-cycloaddition involving the carbon-nitrogen double bond and afforded *endo* cycloadducts in high yields. The reaction is equally effective when the cycloadditions were carried out with *in situ*-generated imines and the adducts were obtained in almost comparable yields. Furthermore the cycloaddition did not proceed when carried out without indium triflates at room temperature. Also, when indium triflate was replaced by scandium triflate and reaction attempted under identical conditions, the corresponding cycloadducts **4a-e** were obtained in 70–75% yield (Table 1) without the formation of any hetero-Diels-Alder *exo* cycloadducts **5**. All the compounds obtained were characterised by IR, mass, ¹H NMR and ¹³C NMR spectroscopy.

In conclusion, it is noteworthy that this easily reproducible technique affords various cycloadducts in just one pot at ambient temperature and pressure with excellent yields.

Experimental

Mps were determined using a Büchi melting-point apparatus and are uncorrected. IR spectra were recorded for KBr discs on a Perkin-Elmer 240C analyser. ¹H NMR spectra were recorded on 60, 90 and 300 MHz spectrometers, and chemical-shift

Table 1 In(OTf)₃ and Sc(OTf)₃-catalyzed (4 + 2)-cycloaddition of chromone imines^a

Entry	R	Product	Reaction time (t/h)	Yield (%) [Sc(OTf) ₃]
1	C ₆ H ₅	4a	8	70
2	4-MeC ₆ H ₄	4b	8	75
3	4-MeOC ₆ H ₄	4c	9	73
4	4-BrC ₆ H ₄	4d	8	70
5	4-ClC ₆ H ₄	4e	8	73
6	C ₆ H ₅ CH ₂	4f	10	0

^a Mps for products **4a–f**, and their yields in the In(OTf)₃-catalyzed cycloadditions, are given in the Experimental section.

values are recorded in δ -units (ppm) relative to Me₄Si as internal standard. The ¹³C NMR spectrum was recorded on a Bruker Avance DPX 300 machine. The imines described in this report were prepared from freshly distilled primary amines and 3-formylchromone. Solvents used were dried according to literature procedures. Light petroleum refers to the fraction with distillation range 60–80 °C.

3-(Aryliminomethyl)chromones 3

Typical procedure. Toluene-*p*-sulfonic acid (10 mg) was added to a solution of 3-formyl-1-benzopyran-4-one (1.74 g, 10 mmol) and aniline (0.93g, 10 mmol) in dry benzene (80 ml) and the resulting mixture was heated under reflux using a Dean–Stark water-trap for 30 min. The mixture was then evaporated under reduced pressure and the product [3-(phenylaminomethyl)chromone]¹⁴ **3a**, mp 153 °C, thus obtained was recrystallised from benzene–light petroleum (1 : 1) (60%); δ_{H} (60 MHz; CDCl₃) 8.65 (1H, s, H_a), 8.30 (1H, s, H_b), 6.75–7.80 (m, ArH); *m/z* M⁺, 249⁺ (Calc. for C₁₆H₁₁NO₂: C, 77.11; H, 4.42; N, 5.62. Found: C, 77.06; H, 4.40; N, 5.53%).

3-(*p*-Methylphenyliminomethyl)chromone 3b. Mp 128–129 °C, was recrystallised from benzene–light petroleum (1 : 1) (70%); δ_{H} (60 MHz; CDCl₃) 8.71 (1H, s), 8.30 (1H, s), 6.76–7.83 (8H, m, ArH), 1.98 (3H, s, CH₃); *m/z* 263 (M⁺) (Calc. for C₁₇H₁₃NO₂: C, 77.52; H, 4.94, N, 5.32. Found: C, 77.65; H, 5.1; N, 5.26%).

3-(*p*-Methoxyphenyliminomethyl)chromone 3c. Mp 153–155 °C (61%); δ_{H} (60 MHz; CDCl₃) 8.49 (1H, s), 8.25 (1H, s), 6.76–7.82 (8H, m, ArH), 3.80 (3H, s, OCH₃); *m/z* 279 (M⁺) (Calc. for C₁₇H₁₃NO₃: C, 73.14; H, 4.65; N, 5.01. Found: C, 73.19; H, 4.75; N, 5.11%).

3-(*p*-Bromophenyliminomethyl)chromone 3d. Mp 134–135 °C (65%); δ_{H} (60 MHz; CDCl₃) 8.70 (1H, s), 8.32 (1H, s), 6.76–7.81 (8H, m, ArH); *m/z* 328 (M⁺) (Calc. for C₁₆H₁₀BrNO₂: C, 58.57; H, 3.04; N, 4.27. Found: C, 58.61; H, 3.20; N, 4.18%).

3-(*p*-Chlorophenyliminomethyl)chromone 3e. Mp 131–133 °C (62%), recrystallised from benzene–light petroleum (1 : 1); δ_{H} (60 MHz; CDCl₃) 8.71 (1H, s), 8.32 (1H, s), 7.83–6.91 (8H, m, ArH); *m/z* 289 (M⁺) (Calc. for C₁₆H₁₀ClNO₂: C, 67.71; H, 3.55; N, 4.90. Found: C, 67.68; H, 3.48; N, 5.01%).

3-(Benzyliminomethyl)chromone 3f. Mp 120 °C (60%); δ_{H} (60 MHz; CDCl₃) 8.68 (1H, s), 8.32 (1H, s), 6.78–7.90 (9H, m, ArH), 4.22 (2H, s); *m/z* 263 (M⁺) (Calc. for C₁₇H₁₃NO₂: C, 77.57; H, 4.94; N, 5.32. Found: C, 77.69; H, 5.09; N, 5.26%).

General procedure for the reaction of chromone Schiff's bases with 3,4-dihydro-2H-pyran

In a typical case, to a solution of 3-(phenyliminomethyl)chromone **3a** (0.25 g, 1 mmol) in acetonitrile (5 ml) was added indium triflate (0.05 g, 0.1 mmol). After stirring of the mixture

for 3 min, 3-formylchromone (0.17 g, 1 mmol) and 3,4-dihydro-2H-pyran (0.084 g, 1 mmol) were added and the stirring was continued for 8 h at room temperature. After completion of the reaction (monitored by TLC), the reaction mixture was concentrated under reduced pressure and the residue was purified by TLC using dichloromethane–light petroleum (10 : 1) as develops to afford **4a** in 75% yield, mp 118–120 °C. Similarly, other imines gave the corresponding cycloadducts, isolated in 55–90% yield.

General procedure for the reaction of *in situ*-generated chromone Schiff's bases with 3,4-dihydro-2H-pyran

In a typical case, to a solution of aniline (0.093g, 1 mmol) in acetonitrile (5 ml) was added indium triflate (0.05 g, 1 mmol). After stirring of the mixture for 5 min, 3,4-dihydro-2H-pyran (0.084 g, 1 mmol) was added and the stirring was continued for 8 h at room temperature. After completion of the reaction (monitored by TLC), the reaction mixture was concentrated under reduced pressure and the residue was purified by TLC using dichloromethane–light petroleum (10 : 1) as developer to afford **4a** in 80% yield, mp 118–20 °C; δ_{H} (300 MHz; CDCl₃) 1.52–2.20 (4H, m, 1-, 2-H₂), 2.45–2.72 (1H, m, 12b-H), 3.72–4.04 (2H, m, 3-H₂), 5.34 (1H, dd, *J* 1, 4.5 Hz, 12a-H), 5.50 (1H, d, *J* 3.7 Hz, 4a-H), 6.90 (1H, d, 11-H), 7.02–7.88 (8H, m, ArH and 6-H), 8.06 (1H, dd, 8-H); ν_{max} (KBr) 1650, 1625, 1575 cm⁻¹; *m/z* 332 (M⁺) (Calc. for C₂₁H₁₉NO₃: C, 75.90; H, 5.42; N, 4.21. Found: C, 75.98; H, 5.36; N, 4.27%).

Similarly, other *in situ*-generated imines **3b–f** were treated with 3,4-dihydro-2H-pyran and underwent (4 + 2)-cycloaddition to the carbon–nitrogen double bond, affording the corresponding cycloadducts **4b–f** in high yield.

Adduct **4b** in 78% yield, mp 62–63 °C; δ_{H} (90 MHz, CDCl₃) 1.25–1.37 (3H, s), 1.53–2.17 (4H, m, 1-, 2-H₂), 2.47–2.71 (1H, m, 12b-H), 3.72–4.04 (2H, m, 3-H₂), 5.33 (1H, dd, 12a-H), 5.54 (1H, d, 4a-H), 6.90 (1H, d, 11-H), 7.10–7.85 (7H, m, ArH and 6-H), 8.08 (1H, dd, 8-H); ν_{max} (KBr) 1650, 1625, 1575 cm⁻¹; *m/z* 347 (M⁺) (Calc. for C₂₂H₂₁NO₃: C, 76.08; H, 6.05; N, 4.03. Found: C, 76.12; H, 6.12; N, 4.10%).

Adduct **4c** in 75% yield, mp 58–59 °C δ_{H} (300 MHz, CDCl₃) 1.72–1.73 (4H, m, 1-, 2-H₂), 2.64–2.69 (1H, m, 12b-H), 3.29–3.48 (2H, m, 3-H₂), 3.80 (3H, s, OCH₃), 5.38–5.40 (1H, dd, *J* 1, 4.5 Hz, 12a-H), 5.61–5.63 (1H, d, *J* 3.7 Hz, 4a-H), 6.88–7.76 (8H, m, ArH and 6-H), 7.94 (1H, dd, 8-H); δ_{C} (CDCl₃) 18.82 (C-2), 23.71 (C-1), 36.36 (C-12b), 55.45 (OCH₃), 61.58 (C-3), 73.71 (C-12a), 81.80 (C-13), 103.20 (C-6a), 114.27 (C-4a), 117.38 (C-8), 121.50 (C ϕ), 122.73 (C ϕ), 123.26 (C-7a), 123.73 (C-9), 127.00 (C-10), 127.40 (C ϕ), 134.09 (C-11), 134.99 (C ϕ), 157.41 (C-6), 160.44 (C ϕ), 179.53 (C=O).

Adduct **4d** in 90% yield, mp 201–202 °C; δ_{H} (90 MHz, CDCl₃) 1.61–2.25 (4H, m, 1-, 2-H₂), 2.48–2.8 (1H, m, 12b-H), 3.75–4.1 (2H, m, 3-H₂), 5.34 (1H, dd, 12a-H), 5.62 (1H, d, 4a-H), 6.96 (1H, d, 11-H), 7.20–8.1 (7H, m, ArH and 6-H), 8.20 (1H, dd, 8-H); ν_{max} (KBr) 1650, 1625, 1575 cm⁻¹; *m/z* 412 (M⁺) (Calc. for C₂₁H₁₈B₂NO₃: C, 61.16; H, 4.36; N, 3.39. Found: C, 61.10; H, 4.21; N, 3.46%).

Adduct **4e** in 85% yield, mp 210–212 °C; δ_{H} (90 MHz, CDCl₃) 1.63–2.30 (4H, m, 1-, 2-H₂), 2.50–2.85 (1H, m, 12b-H), 3.80–4.40 (2H, m, 3-H₂), 5.4 (1H, dd, 12a-H), 5.65 (1H, d, 4a-H), 6.98 (1H, d, 11-H), 7.22–8.1 (7H, m, ArH and 6-H), 8.22 (1H, dd, 8-H); ν_{max} (KBr) 1650, 1625, 1575 cm⁻¹; *m/z* 367 (M⁺) (Calc. for C₂₁H₁₈ClNO₃: C, 68.66; H, 4.90; N, 3.81. Found: C, 68.62; H, 4.98; N, 3.76%).

Adduct **4f** in 55% yield (oil), δ_{H} (90 MHz, CDCl₃) 1.60–2.27 (4H, m, 1-, 2-H₂), 2.46–2.74 (1H, m, 12b-H), 3.78–4.31 (4H, m, 3-H₂ and CH₂), 5.36 (1H, dd, 12a-H), 5.63 (1H, d, 4a-H), 7.02 (1H, d, 11-H), 7.24–8.11 (8H, m, ArH and 6-H), 8.20 (1H, dd, 8-H); ν_{max} (KBr) 1650, 1625, 1570 cm⁻¹; *m/z* 347 (M⁺) (Calc. for C₂₂H₂₁NO₃: C, 76.08; H, 6.05; N, 4.03. Found: C, 76.14; H, 6.12; N, 4.06%).

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