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# Indium/indium trichloride mediated pinacol cross-coupling reaction of aldehydes and chalcones in aqueous media: a facile stereoselective synthesis of substituted but-3-ene-1,2-diols[†]

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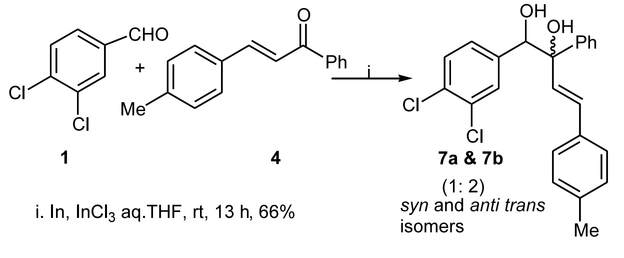
**Abstract**—A facile synthesis of substituted but-3-ene-1,2-diols by the reaction of aldehydes and chalcones mediated by indium/indium trichloride in aqueous media is described. © 2002 Published by Elsevier Science Ltd.

Ever since the pioneering work of Araki,[1] carbon–carbon bond forming reactions mediated by indium[2–4] and indium trichloride[5] have received considerable attention. The low ionization potential of indium, comparable to alkali metals, makes it a suitable reagent for single electron transfer processes. Unlike alkali metals, indium is unaffected by water, thus making it very attractive in organic synthesis, especially from the green chemistry perspective.

Recently, we have reported a facile indium mediated allylation of 1,2-diones.[6,7] In further exploration of the reactivity of indium, we examined the pinacol cross-coupling reaction of aldehydes with chalcones in the presence of indium and indium trichloride. Our preliminary results showing the facile formation of substituted but-3-ene-1,2-diols with impressive stereoselectivity are reported here. Although the pinacol coupling of aldehydes with indium under prolonged sonication is known,[8] to the best of our knowledge, there is only one report of In/InCl$_3$ mediated cross-coupling reaction of aldehydes with α,β-unsaturated ketones viz. methyl vinyl ketone and ethyl vinyl ketone and in this case, β,γ-unsaturated ketones[9] and not the pinacols are formed. It is also noteworthy that there is no report on the pinacol cross-coupling reactions of chalcones and aldehydes. The only precedent available in the literature is a Cr(II) and R$_3$SiCl mediated pinacol cross-coupling reaction of α,β-unsaturated ketones with aldehydes in which a β substituent is incompatible.[10]



**Scheme 1.**

In an initial experiment,[11] 3,4-dichlorobenzaldehyde was treated with 4-methylbenzylidene acetophenone in the presence of indium and indium trichloride in aqueous THF at room temperature to yield an isomeric mixture of 1-(3,4-dichlorophenyl)-2-phenyl-4-*p*-tolyl-but-3-ene-1,2-diols in 66% yield (Scheme 1). The products were separated by radial chromatography on a Chromatotron® and characterized by spectroscopic analysis. The structure was further confirmed by single X-ray crystallographic analysis of the *syn trans* isomer of **7** (Fig. 1).[12]

Similar results were obtained with other chalcones and aldehydes (Table 1). With benzylidene acetone and aldehydes, only one *trans*-isomer was formed whereas with other α,β-unsaturated ketones and aldehydes a mixture of *syn* and *anti trans* isomers was obtained.

In conclusion, we have uncovered a novel and efficient route to the synthesis of substituted but-3-ene-1,2-diols

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[†] This paper is dedicated to the memory of Professor Josef (Gus) Fried who passed away on August 17, 2001.

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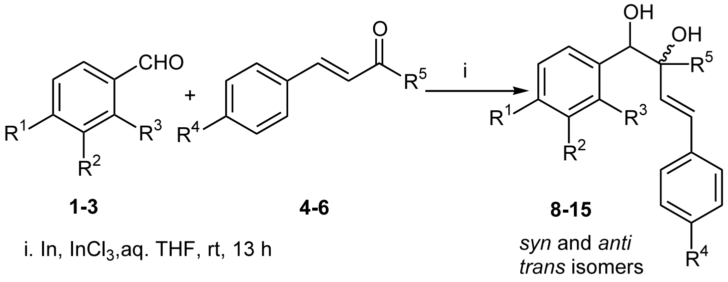
**Table 1.** Synthesis of substituted but-3-ene-1,2-diols



| Entry | Aldehyde | Chalcone | Substituents | Products[b] | Yield (%)[a] | Ratio (*syn*:*anti* ) |
|---|---|---|---|---|---|---|
| 1 | **1** | **5** | $R^1=R^2=Cl$, $R^3=R^4=H$, $R^5=Ph$ | **8** | 56 (85) | (1:2) |
| 2 | **1** | **6** | $R^1=R^2=Cl$, $R^3=R^4=H$, $R^5=Me$ | **9** | 42 (66) | (0:1) |
| 3 | **2** | **4** | $R^1=Cl$, $R^2=R^3=H$, $R^4=Me$, $R^5=Ph$ | **10** | 60 (75) | (1:2) |
| 4 | **2** | **5** | $R^1=Cl$, $R^2=R^3=R^4=H$, $R^5=Ph$ | **11** | 61 | (0.6:2) |
| 5 | **2** | **6** | $R^1=Cl$, $R^2=R^3=R^4=H$, $R^5=Me$ | **12** | 46 (63) | (0:1) |
| 7 | **3** | **4** | $R^1=R^2=H$, $R^3=Cl$, $R^4=Me$, $R^5=Ph$ | **13** | 56 (85) | (0.6:1) |
| 8 | **3** | **5** | $R^1=R^2=R^4=H$, $R^3=Cl$, $R^5=Ph$ | **14** | 42 (78) | (0.4:1) |
| 9 | **3** | **6** | $R^1=H$, $R^2=R^4=H$, $R^3=Cl$, $R^5=Me$ | **15** | 56 (75) | (0:1) |

[a] Yields based on recovered starting material are given in parentheses.

[b] Traces of chalcone coupled products are also formed.

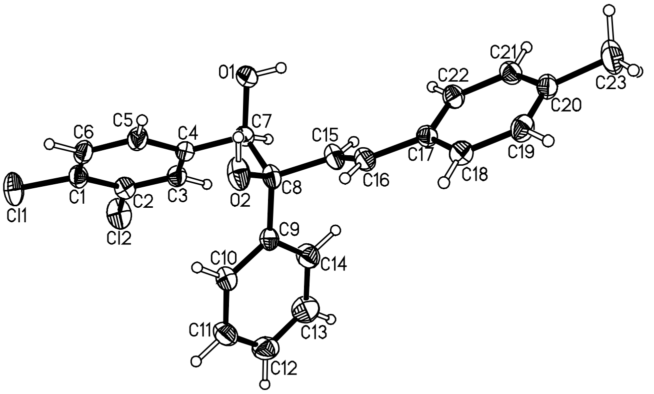


**Figure 1.** X-Ray structure of the *syn* isomer of **7**.

via In/$InCl_3$ mediated pinacol cross-coupling reactions of aldehydes with chalcones. The mild reaction conditions and the stereoselectivity of the process are noteworthy. Further work in this area is in progress.

## Acknowledgements

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11. Typical experimental procedure: To a stirred mixture of aldehyde (1 mmol), indium trichloride (1 mmol), indium (2 mmol) in THF:$H_2O$ (1:1), chalcone (1 mmol) was added and continued at rt for 13 h. After the addition of a few drops of 2N HCl, the reaction mixture was stirred for 15 min and extracted three times with ethyl acetate. The combined organic phase was washed with brine and dried over anhydrous sodium sulphate. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel followed by radical chromatography on a Chromatotron® to afford the pure products.
    Spectral data for **7**:
    *syn* Isomer: colorless solid. Recrystallized from dichloromethane–hexane mixture. Mp: 150–152°C. IR (KBr) $\nu_{max}$: 3467, 3346, 3016, 2921, 1647, 1512, 1452, 1371, 1182, 1135, 1034, 980, 845, 690 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$) $\delta$: 2.27 (s, 3H), 4.89 (d, $J=4.6$ Hz, 1H), 5.46 (s, 1H, exchangeable by $D_2O$), 5.75 (d, $J=4.7$ Hz, 1H, exchangeable by $D_2O$), 6.46 (d, $J=16$ Hz, 1H), 6.91 (d, $J=16$ Hz, 1H), 7.02–7.46 (m, 12H). $^{13}C$ NMR ($CDCl_3$) $\delta$: 21.30, 79.22, 79.33, 126.14, 126.63, 127.12, 127.64, 128.17,

129.28, 129.41, 129.91, 130.65, 131.18, 133.48, 137.94, 138.80, 141.77. Elemental analysis calcd: C, 69.18; H, 5.05. Found: C, 68.66; H, 5.58%.

*anti* Isomer: colorless solid. Recrystallized from dichloromethane–hexane mixture. Mp: 120–123°C. IR (KBr) $\nu_{max}$: 3380, 3272, 3022, 2921, 1647, 1512, 1472, 1371, 1209, 1067, 1027, 980, 791, 697 $cm^{-1}$. $^1H$ NMR ($CDCl_3$) $\delta$: 2.32 (s, 3H), 2.77 (s, 2H, exchangeable by $D_2O$), 4.91 (s, 1H), 6.36 (d, $J=16$ Hz, 1H), 6.54 (d, $J=16$ Hz, 1H), 6.82–6.85 (m, 1H), 7.06–7.38 (m, 11H). $^{13}C$ NMR ($CDCl_3$) $\delta$: 21.26, 79.45, 79.62, 126.53, 126.66, 127.12, 127.95, 128.37, 128.65, 129.34, 129.87, 131.58, 131.81, 133.62, 137.75, 138.93, 142.39. Elemental analysis calcd: C, 69.18; H, 5.05. Found: C, 69.17; H, 5.38%.

12. Crystal data for *syn* isomer of **7**: $C_{23}H_{20}Cl_2O_2$, $Mr=399.29$, monoclinic space group $P2_{1/n}$, $a=16.0585(3)$ Å, $b=5.7572(1)$ Å, $c=21.1947(3)$ Å, $\beta=100.997(1)°$, $Z=4$, $V=1923.51(6)$ Å$^3$, $D_{(calcd)}=1.379$ Mg/m$^3$, $F(000)=832$, $T=180(2)$ K. Crystallographic data for this compound has been deposited at the Cambridge Crystallographic Data Centre as CCDC 195501.