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Enantioselective alkynylation of aromatic and heteroaromatic aldehydes catalyzed by resin-supported oxazolidine–titanium complexes

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ABSTRACT

Highly enantioselective asymmetric addition of terminal alkynes to various aromatic and heteroaromatic aldehydes catalyzed by the readily available, low-cost, and reusable resin-supported oxazolidine **4** together with $Ti(O^iPr)_4$ provides the chiral propargylic alcohols with good to excellent yields (up to 98%) and enantioselectivities (up to 95%). The immobilized catalyst can be recovered and used for five cycles.

1. Introduction

It is well known that chiral propargylic alcohols are important intermediates for the synthesis of natural products, pharmaceuticals, and macromolecules.[1–3] The addition of acetylenes to carbonyl compounds represents the most efficient and desirable route for their synthesis.[4] Thus, the development of various chiral ligands as catalysts for the enantioselective alkynylation has gained much attention during the past years.[5] However, these homogeneous catalysts cannot be easily separated from products and hence present a serious obstacle for synthetic applications. As a consequence of the increasing demand for efficient and environmentally friendly methods, heterogenization of homogeneous catalysts by immobilizing them with liquid or solid supports has attracted a great deal of recent interest.[6] Although there have been several trials to immobilize homogeneous catalysts on solid supports, successful examples are still rare.[7] Therefore, to develop highly enantioselective and efficient chiral catalysts with broad substrate applicability and easy recyclability is still urgently needed in this field.

Degni first reported asymmetric alkynylation of benzaldehyde with L-prolinol derived chiral catalysts immobilized on polymer fibers. Although high enantioselectivities (up to 91% ee) were obtained, high loading of catalyst (1.2 equiv) and low conversions of the benzaldehyde (30–45%) prevent their scale-up possibilities.[8a] Recently, Abdi and co-workers disclosed that a polymeric Zn(salen) could catalyze enantioselective phenylacetylene addition to aldehydes and ketones. However, only 56% ee was obtained when benzaldehyde was used as the substrate.[8b] Hui and Xu have developed silica-immobilized titanium(IV) complex of β-hydroxyamide in the enantioselective alkynylation of benzaldehyde with moderate enantiomeric excesses (78% ee).[8c] Wang reported asymmetric alkynylation of ketones with polymer-supported chiral Schiff-base ligands with good enantioselectivities.[9] However, there is still a large room for improvement in terms of enantioselectivity and reusability. Recently, we described highly enantioselective alkynylation of aldehydes catalyzed by the new chiral oxazolidine **1** in combination with $Ti(O^iPr)_4$ (Fig. 1),[10a] while C_2-symmetric dioxazolidines could also catalyze the reaction in the absence of $Ti(O^iPr)_4$.[10b–d] As part of our continuing efforts toward the development of readily available, inexpensive,[11] and recyclable catalysts,[12] herein we report that the resin-supported oxazolidine(**2**–**4**)–titanium complexes could smoothly catalyze the asymmetric addition of terminal alkynes to aromatic aldehydes with high yields (up to 98%) and enantioselectivities (up to 95% ee). In addition, our catalytic system was also suitable for asymmetric

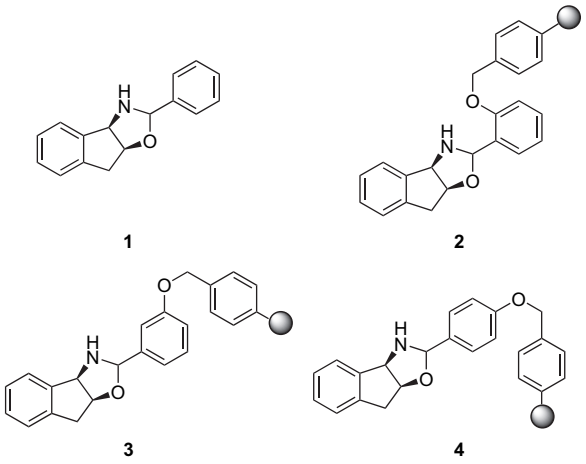

Figure 1. The evaluated chiral oxazolidine ligands in this paper.

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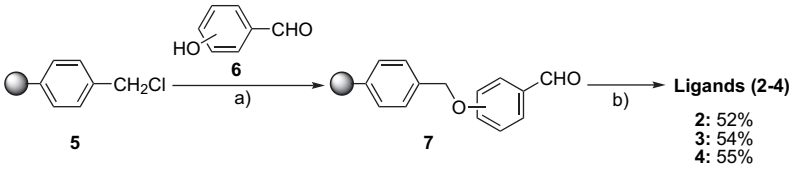


Scheme 1. Preparation of the supported chiral ligands (**2**–**4**). Reagents and conditions: (a) K_2CO_3 (2.0 mmol), 18-crown-6 (0.28 mmol), 1,4-dioxane as the solvent, Ar, 95 °C, 24 h; (b) pyridine (3.4 mmol), (1*R*,2*S*)-*cis*-1-amino-2-indanol (1.7 mmol), 1,4-dioxane as the solvent, Ar, 95 °C, 20 h.

alkynylation of heteroaromatic aldehydes and could be reused for five times after simple work-up.

2. Results and discussion

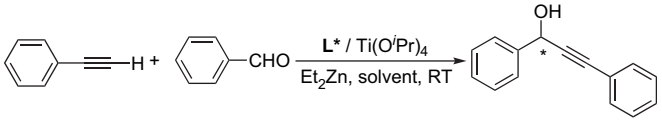
Only two simple steps were required to prepare **2**–**4** from Merrifield resin and (1*R*,2*S*)-*cis*-1-amino-2-indanol in overall yields of 52%, 54%, and 55%, respectively (Scheme 1). The resin-supported ligand **2** was initially tested as the chiral ligand in the asymmetric addition of phenylacetylene to benzaldehyde in the presence of Et_2Zn and $Ti(O^iPr)_4$ (Table 1). The addition reaction proceeded smoothly in THF at room temperature for 20 h to afford the propargylic alcohol in excellent yield (98%) and promising enantioselectivity (67% ee) (entry 1). Low ee values were obtained when the catalytic reactions were performed in toluene and dioxane (entries 2 and 3). Surprisingly, adding DIMPEG (dimethoxy polyethylene glycol, M_n=2,000)[13] as additive or reducing the reaction temperature gave lower enantioselectivities (entries 4 and 5). Increasing the amount of ligand **2** to 28 mol % gave enhanced ee (entry 6), but further increasing the amount of the ligand to 38 mol % did not lead to a further increase in ee (entry 7). Under the same conditions, the free ligand **1** gave the better enantioselectivity and yield than ligand **2** (entry 8), which suggested that generally enantioselectivity would drop after the immobilization of the ligand. In view of the structure of *ortho*-substituted ligand **2**, *meta*-substituted ligand **3** and *para*-substituted ligand **4** have been investigated in the asymmetric addition under the same conditions (entries 9 and 10).

The results showed that ligand **4** afforded the chiral propargylic alcohol with highest enantioselectivity (90% ee) (entry 10). The configuration of the propargylic alcohol product was *R* as determined by comparing with the literature.[5a,14]

Thus, entry 10 in Table 1 is identified as the optimized reaction procedure. We applied this procedure to the reaction of terminal alkynes with various aldehydes. As shown by the results summarized in Table 2, ligand **4** was employed to promote the enantioselective alkynylation of a number of aromatic aldehydes and heteroaromatic aldehydes, all of which afforded the corresponding products with high enantioselectivity (up to 95% ee). Noteworthy is that for 3-nitrobenzaldehyde as the substrate, ligand **2** gave higher ee value than that of ligand **4** (entries 10 and 11). Replacement of Et_2Zn with Me_2Zn did not give enhanced enantioselectivity (entries 15 and 16).

Actually, the products from the asymmetric addition of alkynes to heteroaromatic aldehydes are of great interest in the construction of highly functionalized organic compounds. As shown in Figure 2, 2-furyl alcohols can be transformed into 6-hydroxy-2*H*-pyran-3(6*H*)-ones, which are important structural units in biologically active molecules, through an oxidative rearrangement.[15] In addition, the thiophene ring in the resulting thienyl alcohols can be desulfurized with Raney nickel acting as a masked four-carbon synthon.[16] Recently, Pedro and co-workers discovered that terminal alkynes could enantioselectively add to furane- and thiophenecarbaldehydes in the presence of dimethylzinc and

Table 1
Asymmetric addition of phenylacetylene to benzaldehyde with supported-ligands (**2**–**4**) as ligands[a]



Entry	Ligand	[mol %]	Solvent	Yield[b] (%)	ee[c] (%)	Configuration[d]
1	**2**	20	THF	98	67	*R*
2	**2**	20	Toluene	65	63	*R*
3	**2**	20	Dioxane	90	56	*R*
4[e]	**2**	20	Toluene	63	14	*R*
5[f]	**2**	20	THF	36	67	*R*
6	**2**	28	THF	82	79	*R*
7	**2**	38	THF	83	67	*R*
8	**1**	28	THF	95	86	*R*
9	**3**	28	THF	82	83	*R*
10	**4**	28	THF	81	90	*R*

[a] All the reactions were run in THF under argon atmosphere at room temperature for 20 h. $Ti(O^iPr)_4$ was freshly distilled. Phenylacetylene/Et_2Zn/benzaldehyde/ligand/$Ti(O^iPr)_4$=2:2:0.5:0.1:0.2.
[b] Isolated yield.
[c] The enantiomeric excess was determined by chiral HPLC analysis of the corresponding products on a Chiralcel OD-H column.
[d] The absolute configuration was based on determination of the specific rotation and in comparison with the literature.
[e] DIMPEG (10 mol %) as additive.
[f] The catalytic reaction was performed at 0 °C.

Table 2
Asymmetric addition of alkynes to aromatic aldehydes promoted by ligand **4**[a]

Entry	Aldehyde	Alkyne	Yield[b] (%)	ee[c] (%)
1	Benzaldehyde	Phenylacetylene	81	90
2	4-Bromobenzaldehyde	Phenylacetylene	84	92
3	4-Bromobenzaldehyde	*p*-Tolylacetylene	81	92
4	4-Tolualdehyde	Phenylacetylene	82	90
5	4-Fluorobenzaldehyde	Phenylacetylene	86	90
6	4-Anisaldehyde	Phenylacetylene	96	87
7	4-Chlorobenzaldehyde	Phenylacetylene	87	93
8	3-Chlorobenzaldehyde	Phenylacetylene	94	91
9	2-Chlorobenzaldehyde	Phenylacetylene	93	77
10	3-Nitrobenzaldehyde	Phenylacetylene	77	87
11[d]	3-Nitrobenzaldehyde	Phenylacetylene	71	92
12	β-Naphthaldehyde	Phenylacetylene	88	94
13	β-Naphthaldehyde	*p*-Tolylacetylene	70	91
14	α-Naphthaldehyde	Phenylacetylene	82	86
15	2-Thiophenealdehyde	Phenylacetylene	98	95
16[e]	2-Thiophenealdehyde	Phenylacetylene	84	88
17	2-Thiophenealdehyde	*p*-Tolylacetylene	92	95
18	2-Furaldehyde	Phenylacetylene	76	83
19	Piperonaldehyde	Phenylacetylene	86	92
20	Piperonaldehyde	*p*-Tolylacetylene	95	90
21	2,3-Dimethoxybenzaldehyde	Phenylacetylene	84	83

[a] All the reactions were run in THF under argon atmosphere at room temperature for 20 h. $Ti(O^iPr)_4$ was freshly distilled. Phenylacetylene/Et_2Zn/benzaldehyde/ligand **4**/$Ti(O^iPr)_4$=2:2:0.5:0.14:0.28.
[b] Isolated yield.
[c] The enantiomeric excess was determined by chiral HPLC analysis of the corresponding products on a Chiralcel OD-H column.
[d] Compound**2** was used as the ligand.
[e] Me_2Zn replace of Et_2Zn.

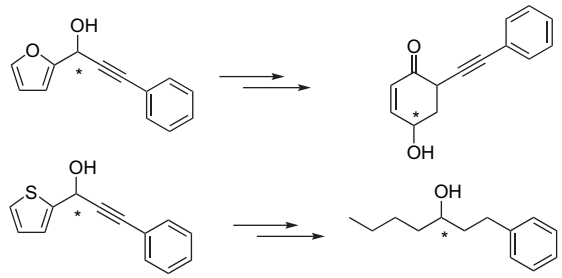


Figure 2. Known transformations of heteroaromatic propargylic alcohols.

mandelamides as chiral ligands and enantiomeric excesses up to 90% were achieved when 2-thiophenealdehyde was used as the substrate.[17] However, to our knowledge, there is no report about the reusable catalyst for the asymmetric alkynylation of 2-thiophenealdehyde till now.

The most important feature of resin-supported catalysts is their easy separation and reuse. Thus, the supported chiral catalyst **4** was taken as a representative candidate for recycling experiment under the standard conditions (Table 3). The supported catalyst was readily recovered before quenching the reaction mixture by 5% aqueous HCl. Subsequently, the recovered catalyst was washed with dioxane, MeOH, and dried under vacuum at 60 °C for 8 h for further use. The regenerated ligand thus obtained was used for the next catalytic run with the fresh supply of $Ti(O^iPr)_4$. All of the recycling experiments were performed under same conditions. It can be seen that the high catalytic capability of resin-supported oxazolidine could be retained after simple recrystallization in the successive reaction cycles. However, in the fifth reuse experiment the notable decrease of enantioselectivity was found probably due to the devastation of the catalyst.

3. Conclusion

In summary, we have developed a novel resin-supported chiral oxazolidine **4** and shown its titanium complex to be a highly efficient and easily separable catalyst in asymmetric addition of alkynes to various aromatic and heteroaromatic aldehydes. For the first time, the reusable enantioselective alkynylation of 2-thiophenealdehyde was carried out using our protocol with good to excellent yields and enantioselectivities. The immobilized catalyst can be recovered and used for five cycles. Thus, the high chemical selectivity and enantioselectivity, easily available, and low-cost catalyst, and the mild reaction conditions make this catalytic method potentially useful and could be amenable to scale-up. Work is in progress on further applications of this and related oxazolidine ligands and improvement of the recyclability of the catalyst.

Table 3
Reusability of ligand **4** for the asymmetric addition of phenylacetylene to 2-thiophenecarboxaldehyde[a]

Run	Isolated yield (%)	ee[b] (%)
1	98	95
2	93	93 (>99)[c]
3	89	90 (92)[c]
4	86	78 (91)[c]
5	80	67 (89)[c]

[a] All the reactions were run in THF under argon atmosphere at room temperature for 20 h. $Ti(O^iPr)_4$ was freshly distilled. Phenylacetylene/Et_2Zn/2-thiophenealdehyde/ligand **4**/$Ti(O^iPr)_4$=2:2:0.5:0.14:0.28.
[b] The enantiomeric excess was determined on a Chiralcel OD-H column.
[c] The ees in parentheses were determined after simple recrystallization.

4. Experimental

4.1. General experimental

All manipulations were carried out under an argon atmosphere in dried and degassed solvents. All solvents were dried and degassed by standard methods and all aldehydes, dimethylzinc, and diethylzinc were purchased from Aldrich or Acros. Melting points were determined using a melting point apparatus and are uncorrected. The reactions were monitored by thin layer chromatography (TLC). IR spectra were recorded on a Tensor 27 spectrometer in KBr with absorptions in cm^{-1}. Microanalyses were carried out on a Perkin–Elmer 2400 II instrument. NMR spectra were recorded in $CDCl_3$ on a 400 NMR spectrometer (400 MHz) with TMS as an internal reference. Optical rotations were measured with a SEPA-200 high sensitive polarimeter. Enantiomeric excess (ee) determination was carried out using a chiral OD-H column. Solvent 80:20 hexane/isopropanol; Flow rate 1 ml/min; 254 nm UV Detection. High resolution mass spectra (HRMS) were measured with EI.

4.2. Synthesis of supported 4-hydroxybenzaldehyde (7)

A mixture of Merrifield resin (2.0 mmol, 0.8 g, 2.5 mmol Cl/g), 4-hydroxybenzaldehyde (0.49 g, 4.0 mmol), potassium carbonate (0.27 g, 2.0 mmol), and 18-crown-6 (0.036 g, 0.14 mmol) in anhydrous 1,4-dioxane (30 mL) was heated at reflux under an argon atmosphere for 24 h. The product resin was collected by gravity filtration and washed thoroughly with 1,4-dioxane (40 mL) and warm distilled water (20 mL). After drying in air for 18 h, the collected resin was dried under reduced pressure for 24 h at 50 °C. IR (KBr, ν): 3025, 2924, 1701 (C=O), 1513, 1451, 1260, 1017, 699 cm^{-1}.

4.2.1. Supported 3-hydroxybenzaldehyde

IR (KBr, ν): 3024, 2920, 1683 (C=O), 1599, 1492, 1452, 1028, 752, 699 cm^{-1}.

4.2.2. Supported 2-hydroxybenzaldehyde

IR (KBr, ν): 3024, 2922, 1688 (C=O), 1599, 1481, 1453, 1008, 832, 700 cm^{-1}.

4.3. Synthesis of supported-ligand 4

A mixture of supported benzaldehyde (1.7 mmol), (1*R*,2*S*)-*cis*-1-amino-2-indanol (1.7 mmol), and pyridine (3.4 mmol) in anhydrous 1,4-dioxane (30 mL) was heated at reflux under an argon atmosphere for 20 h. The product resin was collected by gravity filtration and washed thoroughly with 1,4-dioxane (40 mL) and ethanol (20 mL). After drying in air for 18 h, the collected resin was dried under reduced pressure for 24 h at 50 °C to give the immobilized ligand **4** as a yellowish powder. IR (KBr, ν): 3409 (N–H), 3023, 2919, 1602, 1509, 1492, 1452, 1224, 1165, 824, 753, 699 cm^{-1}. Elemental analysis found: C, 79.86; H, 6.58; N, 2.44. Calcd: N, 2.26. Conversion: 100%. Loading: 1.7 mmol/g.

4.3.1. Supported-ligand *3*

IR (KBr, ν): 3449 (N–H), 3024, 2921, 2360, 1599, 1585, 1491, 1451, 1260, 1154, 753, 698 cm^{-1}. Elemental analysis found: C, 79.94; H, 6.60; N, 2.59. Calcd: N, 2.26. Conversion: 100%. Loading: 1.8 mmol/g.

4.3.2. Supported-ligand *2*

IR (KBr, ν): 3419 (N–H), 3025, 2917, 1597, 1489, 1450, 227, 1018, 748, 702 cm^{-1}. Elemental analysis found: C, 82.18; H, 6.68; N, 2.13. Calcd: N, 2.26. Conversion: 100%. Loading: 1.5 mmol/g.

4.4. General procedure for the addition of phenylacetylene to aldehydes

All manipulations were carried out under an argon atmosphere using dried and degassed solvent. Ligand **4** (0.14 mmol) and $Ti(O^iPr)_4$ (0.28 mmol) were mixed in dry THF (2.0 mL) at room temperature. Then, a solution of Et_2Zn (1.0 mmol) was added. After the mixture was stirred at room temperature for 1.5 h, phenylacetylene (1.0 mmol) was added and stirring continued for another 1.5 h. The yellow solution was cooled to 0 °C and treated with aldehyde (0.5 mmol), then the resultant mixture was allowed to warm up to room temperature naturally and stirred for 20 h. After the reaction was completed, the supported ligand was obtained by simple filtration and washed with dioxane, MeOH, and dried under vacuum at 60 °C for 8 h for further use. The regenerated ligand thus obtained was used for the next catalytic run with the fresh supply of $Ti(O^iPr)_4$. The filtrate was cooled to 0 °C and quenched by 5% aqueous HCl (2 mL). The mixture was extracted with ethyl acetate (EtOAc) (2×10 mL). The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by flash column chromatography (silica gel, EtOAc/petroleum ether=1:6) to give the pure product.

4.4.1. Retention time of the chiral products from HPLC determination

Table 2, entry 1: t_{major}=7.60 min, t_{minor}=11.56 min.
Table 2, entry 2: t_{major}=5.89 min, t_{minor}=14.65 min.
Table 2, entry 3: t_{major}=5.56 min, t_{minor}=9.92 min.
Table 2, entry 4: t_{major}=9.91 min, t_{minor}=19.97 min.
Table 2, entry 5: t_{major}=5.39 min, t_{minor}=10.68 min.
Table 2, entry 6: t_{major}=7.85 min, t_{minor}=11.65 min.
Table 2, entry 7: t_{major}=5.64 min, t_{minor}=11.93 min.
Table 2, entry 8: t_{major}=6.07 min, t_{minor}=15.83 min.
Table 2, entry 9: t_{major}=18.21 min, t_{minor}=20.86 min.
Table 2, entries 10 and 11: t_{major}=7.78 min, t_{minor}=18.16 min.
Table 2, entry 12: t_{major}=8.56 min, t_{minor}=17.57 min.
Table 2, entry 13: t_{major}=8.03 min, t_{minor}=13.78 min.
Table 2, entry 14: t_{major}=8.13 min, t_{minor}=13.12 min.
Table 2, entries 15 and 16: t_{major}=6.52 min, t_{minor}=10.38 min.
Table 2, entry 17: t_{major}=6.00 min, t_{minor}=7.65 min.
Table 2, entry 18: t_{major}=5.70 min, t_{minor}=8.63 min.
Table 2, entry 19: t_{major}=8.62 min, t_{minor}=15.40 min.
Table 2, entry 20: t_{major}=7.56 min, t_{minor}=11.81 min.
Table 2, entry 21: t_{major}=6.99 min, t_{minor}=8.68 min.

4.5. Characteristic data of the chiral products

4.5.1. 1, 3-Diphenylprop-2-yn-1-ol[14a]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62 (d, J=7.2 Hz, 2H), 7.48–7.25 (m, 8H), 5.69 (s, 1H), 2.36 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.1, 132.2, 129.2, 129.1, 128.9, 128.8, 127.2, 122.9, 89.1, 87.2, 65.6.

4.5.2. 1-(4-Bromophenyl)-3-phenylprop-2-yn-1-ol[14b]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.54–7.32 (m, 9H), 6.82 (d, J=6.0 Hz, 1H), 2.53 (d, J=6.0 Hz, 1H).

4.5.3. 1-(4-Bromophenyl)-3-p-tolylprop-2-yn-1-ol

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.55–7.49 (m, 4H), 7.36 (d, J=8.0 Hz, 2H), 7.14 (d, J=8.0 Hz, 2H), 5.65 (d, J=6.0 Hz, 1H), 2.36 (s, 3H), 2.33–2.31 (d, J=6.0 Hz, 1H).

4.5.4. 3-Phenyl-1-p-tolylprop-2-yn-1-ol

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50 (d, J=8.0 Hz, 2H), 7.47 (t, J=7.2 Hz, 2H), 7.32–7.21 (m, 5H), 5.65 (d, J=6.4 Hz, 1H), 2.37 (s, 3H), 2.24 (d, J=6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 138.7, 138.2, 132.2, 130.0, 129.0, 128.7, 127.2, 122.9, 89.4, 86.9, 65.4.

4.5.5. 1-(4-Fluorophenyl)-3-phenylprop-2-yn-1-ol[5a,14a]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62–7.07 (m, 9H), 5.69 (d, J=6.0 Hz, 1H), 2.37 (d, J=6.0 Hz, 1H).

4.5.6. 1-(4-Methoxyphenyl)-3-phenylprop-2-yn-1-ol[14a]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.55 (d, J=8.4 Hz, 2H), 7.49–7.33 (m, 4H), 6.93 (d, J=8.8 Hz, 2H), 5.65 (d, J=6.0 Hz, 1H), 3.83 (s, 3H), 2.24 (d, J=6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.1, 133.4, 132.2, 129.0, 128.7, 128.6, 122.9, 114.4, 89.4, 86.8, 65.1, 55.7.

4.5.7. 1-(4-Chlorophenyl)-3-phenylprop-2-yn-1-ol[5h]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.71–7.29 (m, 9H), 5.69 (d, J=6.0 Hz, 1H), 2.34 (d, J=6.0 Hz, 1H).

4.5.8. 1-(3-Chlorophenyl)-3-phenylprop-2-yn-1-ol[5h]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62 (s, 1H), 7.48 (t, J=7.6 Hz, 3H), 7.47 (d, J=5.6 Hz, 5H), 7.42–7.28 (m, 6H), 5.67 (d, J=5.6 Hz, 1H), 2.36 (d, J=5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.0, 135.0, 132.3, 130.4, 129.3, 129.0, 128.8, 127.4, 125.3, 122.5, 88.5, 87.5, 64.9.

4.5.9. 1-(2-Chlorophenyl)-3-phenylprop-2-yn-1-ol[10c]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.84 (d, J=7.6 Hz, 1H), 7.47 (t, J=7.6 Hz, 2H), 7.42–7.28 (m, 6H), 6.05 (d, J=4.8 Hz, 1H), 2.36 (d, J=4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 138.4, 133.3, 132.2, 130.2, 129.1, 128.9, 128.8, 127.7, 122.7, 88.1, 87.1, 62.8.

4.5.10. 1-(Naphthalen-3-yl)-3-phenylprop-2-yn-1-ol

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 (s, 1H), 7.91–7.85 (m, 3H), 7.73 (d, J=8.4 Hz, 1H), 7.51–7.33 (m, 7H), 5.87 (d, J=6.0 Hz, 1H), 2.40 (d, J=6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 138.4, 133.7, 132.3, 129.1, 128.8, 128.7, 128.2, 126.8, 126.0, 125.1, 122.8, 89.2, 87.4, 65.7.

4.5.11. 1-(Naphthalen-4-yl)-3-phenylprop-2-yn-1-ol[14a]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.38 (d, J=8.4 Hz, 1H), 7.94–7.86 (m, 3H), 7.61–7.48 (m, 5H), 7.47–7.32 (m, 3H), 6.36 (d, J=4.4 Hz, 1H), 2.43 (d, J=5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 136.1, 134.5, 132.3, 131.1, 129.9, 129.2, 129.1, 128.8, 127.0, 126.4, 125.7, 125.2, 124.4, 122.9, 89.0, 87.8, 63.9.

4.5.12. 1-(Thiophen-2-yl)-3-phenylprop-2-yn-1-ol[5s]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.51 (d, J=6.8 Hz, 2H), 7.35–7.00 (m, 6H), 5.91 (s, 1H), 2.46 (d, J=6.8 Hz, 1H).

4.5.13. 1-(Thiophen-2-yl)-3-p-tolylprop-2-yn-1-ol[5s]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40–7.26 (m, 3H), 7.15–7.13 (m, 2H), 7.02–6.97 (m, 2H), 5.89 (d, J=6.0 Hz, 1H), 2.44 (d, J=6.0 Hz, 1H), 2.36 (s, 3H, CH_3).

4.5.14. 1-(Furan-2-yl)-3-phenylprop-2-yn-1-ol[5s]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50–7.45 (m, 3H), 7.34–7.33 (m, 3H), 6.53 (d, J=2.8 Hz, 1H), 6.39 (s, 1H), 5.69 (d, J=6.0 Hz, 1H), 2.44 (d, J=6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.3, 143.5, 132.2, 129.2, 128.7, 122.5, 110.9, 108.3, 86.6, 86.1, 59.0.

4.5.15. 1-(Benzo[d][1,3]dioxol-5-yl)-3-phenylprop-2-yn-1-ol

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.48–7.26 (m, 7H), 5.99 (s, 2H), 5.61 (s, 1H), 6.82 (d, J=5.6 Hz, 1H) 2.26 (d, J=6.0 Hz, 1H).

4.5.16. 1-(Benzo[d][1,3]dioxol-5-yl)-3-p-tolylprop-2-yn-1-ol

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37 (d, J=8.0 Hz, 2H), 7.14–7.07 (m, 4H), 6.82 (d, J=8.0 Hz, 1H), 5.99 (s, 2H), 5.60 (d, J=5.6 Hz, 1H), 2.38 (s, 3H), 2.25 (d, J=6.0 Hz, 1H).

4.5.17. 1-(2,3-Dimethoxyphenyl)-3-phenylprop-2-yn-1-ol[5i]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.46–7.44 (m, 2H), 7.31–7.29 (m, 3H), 7.17 (d, J=8.0 Hz, 1H), 7.09 (t, J=8.0 Hz, 1H), 6.92 (d, J=8.4 Hz, 1H), 5.80 (s, 1H), 3.91 (s, 3H), 3.89 (s, 3H), 3.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.2, 147.1, 135.2, 132.1, 128.9, 128.7, 124.8, 123.1, 120.1, 113.3, 89.8, 86.2, 62.5, 61.6, 56.3.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.08.003.

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