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Cite this: DOI: 10.1039/c0xx00000x

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ARTICLE TYPE

Enantioselective Addition of ArTi(O^{i}Pr)$_3$ to Aldehydes Catalyzed by a Titanium Complex of an *N*-Sulfonylated Amino Alcohol

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Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

DOI: 10.1039/b000000x

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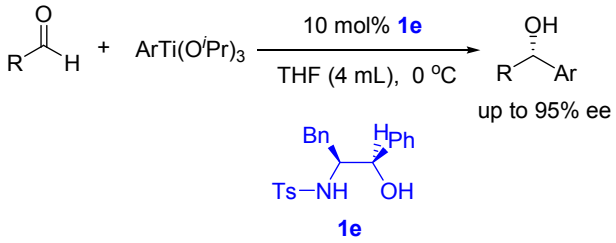


Asymmetric additions of ArTi(O^{i}Pr)$_3$ to aldehydes catalyzed by a titanium catalyst of *N*-sulfonylated amino alcohols to afford desired secondary alcohols in good yields with good to excellent enantioselectivities of up to 95% ee.

Asymmetric additions of ArTi(O^{i}Pr)$_3$ to aldehydes catalyzed by a titanium catalyst of *N*-sulfonylated amino alcohols were reported, and results showed that the chiral *N*-sulfonylated amino alcohol with two stereogenic centers could catalyzed asymmetric addition of ArTi(O^{i}Pr)$_3$ to aldehydes to afford desired secondary alcohols in good yields with good to excellent enantioselectivities of up to 95% ee.

Introduction

The enantioselective addition of aryl organometallic reagents to aldehydes provides a straightforward synthetic method for optically active diarylmethanols[1], which are key intermediates leading to bioactive compounds[2]. The use of arylzinc nucelophile for the catalytic asymmetric arylation of aldehydes has received much attention in the past two decades. A variety of arylzinc organometallic reagents, such as $ZnPh_2$[3], mixtures of $ZnPh_2/ZnR_2$ (R = Me or Et)[4], arylzinc reagents from transmetallation of arylboronic acid or arylboron with $ZnEt_2$[5], and arylzinc from *in-situ* reactions of aryl nucleophile with dialkylzinc or zinc halides[6], have been extensively employed in the titanium-catalyzed asymmetric addition for the synthesis of diarylmethanols. Recent studies have demonstrated that $AlAr_xEt_{3-x}$(THF) (x = 3 or 1)[7,8], ArMgX[9] and ArLi[10] compounds are efficient aryl sources for titanium-catalyzed asymmetric aryl addition reactions of organic carbonyls, and excess amounts of Ti(O^{i}Pr)$_4$ are required to ensure the high stereocontrol of the addition products. Mechanistic study suggested that the roles of excess Ti(O^{i}Pr)$_4$ are not only the formation of the dititanium active species bearing a chiral ligand, but also the transmetalation of an organic nucelophile from the organozinc or organoaluminum compounds to form the organotitanium reagents as the actual addition reagents[11]. Therefore, direct asymmetric additions of organotitanium reagents to organic carbonyls were the most effective method without doubt. The first catalytic asymmetric addition of RTi(O^{i}Pr)$_3$ (R = alkyl or aryl) to aldehydes was reported by Seebach and coworkers using Ti-TADDOLate catalysts at a low temperature of -78 °C[12]. Recently, we have also reported aryltitanium[13], 3-furyltitanium[14], and alkyltitanium compounds[15] as efficient nucleophiles for catalytic asymmetric addition reactions at a mild temperature of 0 °C to room temperature. To further explore aryltitanium compounds as efficient nucleophiles for catalytic reactions, we report herein the asymmetric addition of aryltitanium to aldehydes employing a series of chiral *N*-sulfonylated amino alcohols as catalysts.

Results and discussion

Chiral *β*-amino alcohols have widely used as chiral ligands for a variety of asymmetric syntheses[16]. Here, the asymmetric addition of PhTi(O^{i}Pr)$_3$ to 2-methoxybenzaldehyde (**2a**) were first screened using 10 mol% of the chiral *N*-sulfonylated amino alcohols **1a-1f** with one or two stereogenic centers from L-phenylalanine (Figure 1), and the results are summarized in Table

1. It was found that the ligands have a strong influence on the enantioselectivities in asymmetric phenylation reactions (entries 1-6), and only the chiral *N*-sulfonylated amino alcohols **1e** with two stereogenic centers showed high enantioselectivity (entry 5). In our previous mechanistic study, we have demonstrated that the dititanium complex that simultaneously beared the chiral directing ligand and the phenyl nucleophile was an active species in the crucial and final step of the catalytic addition reaction of organic carbonyl compounds[13b]. The chiral *N*-sulfonylated amino alcohols **1e** with two stereogenic centers showed high enantioselectivity probably due to the above reason. The investigations for the choice of the solvent showed that THF is the best one (entries 5, 7-10). The enantioselectivities of product **4a** is nearly invariable with reduction of the temperature of reaction (entry 13). In order to suppress the racemic background reactions that would lower the enantioselectivities, further study showed that substrate in 1 mL THF was added dropwise to the catalytic solution to afford **4a** in excellent enantioselectivity of 95% ee (entry 14).

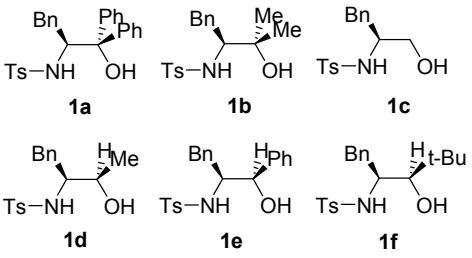
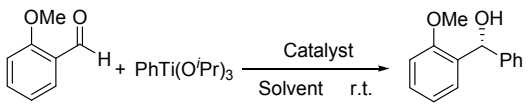


Figure 1. Different chiral *N*-sulfonylated amino alcohols

Table 1. Optimizations of asymmetric $PhTi(O^iPr)_3$ additions to 2-methoxybenzaldehyde [a]



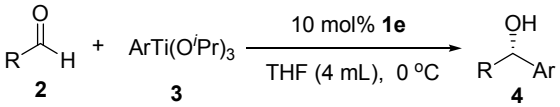
2a **3a** **4a**

Entry	Ligand	$PhTi(O^iPr)_3$ (equiv)	Solvent	Temp (°C)	Conv. (%)[b]	*ee* (%)[c]
1	**1a**	1.4	THF	r.t.	97	3 (*R*)
2	**1b**	1.4	THF	r.t.	97	rac
3	**1c**	1.4	THF	r.t.	92	4 (*R*)
4	**1d**	1.4	THF	r.t.	97	22 (*R*)
5	**1e**	1.4	THF	r.t.	100	88 (*R*)
6	**1f**	1.4	THF	r.t.	92	4 (*R*)
7	**1e**	1.4	toluene	r.t.	100	75 (*R*)
8	**1e**	1.4	hexane	r.t.	100	66 (*R*)
9	**1e**	1.4	CH_2Cl_2	r.t.	100	82 (*R*)
10	**1e**	1.4	Et_2O	r.t.	100	75 (*R*)
11	**1e**	1.6	THF	r.t.	100	85 (*R*)
12	**1e**	1.2	THF	r.t.	93	88 (*R*)
13[d]	**1e**	1.4	THF	0	100	89 (*R*)
14[e]	**1e**	1.4	THF	0	100	95 (*R*)

[a] 2-$MeOC_6H_4CHO$ (0.50 mmol), Ligand (0.05 mmol), THF (4 mL), equiv of $PhTi(O^iPr)_3$ is relative to 2-$MeOC_6H_4CHO$. [b] Conversions based on ^1H NMR spectra. [c] The *ee* values were determined by HPLC, and the absolute configuration of **4a** was determined by comparison with optical rotation of known compounds. [d] Reaction time: 10 min. [e] 2-$MeOC_6H_4CHO$ (0.50 mmol) in 1 mL THF was added to the catalytic solution dropwise over 20 min; then reacted another 10 min.

Next, we explored the scope of the asymmetric addition of $PhTi(O^iPr)_3$ to aldehydes using the best performing ligand **1e**, and the results are listed in Table 2. Regardless of the electronic nature or the steric effect of the substituent on the aryl groups, asymmetric phenyl additions to aromatic aldehydes afforded diarylmethanols in high yields. However, a steric effect of the substrates on the enantioselectivities of products was observed. The addition reactions of aromatic aldehydes with an *ortho*-substituent gave the corresponding products in the enantioselectivities of ≥ 90% ee except for 2-nitrobenzaldehyde (85% ee, entry 15) and 1-naphthylaldehyde (86% ee, entry 18). The addition reactions of aromatic aldehydes with a *para*-substituent showed a slight lower enantioselectivities than those with an *ortho*-substituents. However, The addition reaction of heteroaromatic 2-furaldehyde furnished product **4t** in good yield with a enantioselectivity of 78% ee (entry 20), and the addition reaction of α,β-unsaturated (E)-cinnamaldehyde afforded **4u** in a good enantioselectivity of 84% ee (entry 21). Different to our previous catalytic system[7a], the addition reaction of $PhTi(O^iPr)_3$ to aliphatic aldehydes afforded the corresponding products in moderate enantioselectivities of 56 to 76% *ee* (entries 22-24). The additions of aryl nucleophiles of $ArTi(O^iPr)_3$ (Ar = *p*-tolyl, 4-$MeOC_6H_4$, 4-ClC_6H_4, 4-$F_3CC_6H_4$, and 2-naphathyl) to aldehyde were also studied, affording aryl addition products in excellent enantioselectivities for electron-donating aryltitanium reagents (entries 25-26 and 35) but in moderate enantioselectivities for electron-withdrawing aryltitanium reagents (entries 27-28, and 34). For *ortho*-substituted aryl titanium reagents $ArTi(O^iPr)_3$ (Ar = 1-naphathyl, *o*-tolyl, *o*-anisyl and *o*-chlorophenyl), the low enantioselectivities were obtained (entries 30-33). Especially, the *racemic* diarylmethanols **4d'** and **4a'** were obtained for the bulky aryl titanium reagent (entries 31-32). For *ortho*-substituted aryl titanium reagents, the low enantioselectivities were obtained, probably because the steric hindrance made aldehydes' coordination to titanium metal in *Re*-face and *Si*-face equality of opportunities.

Table 2. Asymmetric $ArTi(O^iPr)_3$ addition to aldehydes catalyzed by the titanium catalyst of *N*-sulfonylated amino alcohol[a]



2 **3** **4**

Entry	Substrate	$ArTi(O^iPr)_3$	Product	Yield (%)[b]	ee (%)[c]
1	2-$MeOC_6H_4CHO$	Ph	**4a**	93	95 (R)
2	3-$MeOC_6H_4CHO$	Ph	**4b**	92	86 (R)
3	4-$MeOC_6H_4CHO$	Ph	**4c**	95	92 (R)
4	2-MeC_6H_4CHO	Ph	**4d**	97	91 (R)
5	3-MeC_6H_4CHO	Ph	**4e**	93	90 (R)
6	4-MeC_6H_4CHO	Ph	**4f**	83	84 (R)
7	2-ClC_6H_4CHO	Ph	**4g**	91	90 (R)
8	3-ClC_6H_4CHO	Ph	**4h**	94	90 (R)
9	4-ClC_6H_4CHO	Ph	**4i**	96	80 (R)
10	2-BrC_6H_4CHO	Ph	**4j**	98	90 (R)
11	3-BrC_6H_4CHO	Ph	**4k**	90	86 (R)
12	4-BrC_6H_4CHO	Ph	**4l**	92	82 (R)
13	2-FC_6H_4CHO	Ph	**4m**	90	90 (R)
14	4-$F_3CC_6H_4CHO$	Ph	**4n**	95	77 (R)
15	2-$O_2NC_6H_4CHO$	Ph	**4o**	91	90 (R)
16	3-$O_2NC_6H_4CHO$	Ph	**4p**	93	76 (R)
17	4-$O_2NC_6H_4CHO$	Ph	**4q**	89	72 (R)
18	1-naphthaldehyde	Ph	**4r**	93	86 (R)
19	2-naphthaldehyde	Ph	**4s**	96	82 (R)
20	Furan-2-carbaldehyde	Ph	**4t**	90	78 (R)
21	Cinnamaldehyde	Ph	**4u**	91	84 (S)
22	Isobutyraldehyde	Ph	**4v**	85	76 (S)
23	Pivalaldehyde	Ph	**4w**	88	56 (S)
24	Cyclohexane-carbaldehyde	Ph	**4x**	96	73 (S)
25	C_6H_5CHO	4-$OMeC_6H_4$	**4c'**	86	90 (S)
26	C_6H_5CHO	4-MeC_6H_4	**4f'**	89	87 (S)
27	C_6H_5CHO	4-ClC_6H_4	**4i'**	91	62 (S)
28	C_6H_5CHO	4-$CF_3C_6H_4$	**4n'**	59	53 (S)
29	C_6H_5CHO	2-naphthyl	**4s'**	93	77 (S)
30	C_6H_5CHO	1-naphthyl	**4r'**	51	12 (S)
31	C_6H_5CHO	2-MeC_6H_4	**4d'**	57	*rac*
32	C_6H_5CHO	2-$MeOC_6H_4$	**4a'**	64	3 (S)
33	C_6H_5CHO	2-ClC_6H_4	**4g'**	55	52 (S)
34	2-$OMeC_6H_4CHO$	4-ClC_6H_4	**4y**	89	72 (S)
35	2-$OMeC_6H_4CHO$	4-MeC_6H_4	**4z**	91	93 (S)

[a] Substrate/**1e**/$ArTi(O^iPr)_3$ = 0.50/0.05/0.70 mmol, substrates in 1 mL THF was added dropwise over 20 min; reaction time (30 min) including the addition time of the substrate to the catalytic solution. [b] Isolated yield. [c] The *ee* values were determined by HPLC.

Based on our previous mechanistic study, the phenyl group of arylaldehyde pointing toward the same side of the bridging oxygen donor of the chiral ligand, predominantly giving the intermediate **A** for a *Re*-face addition of the nucleophile to aldehydes[11e].

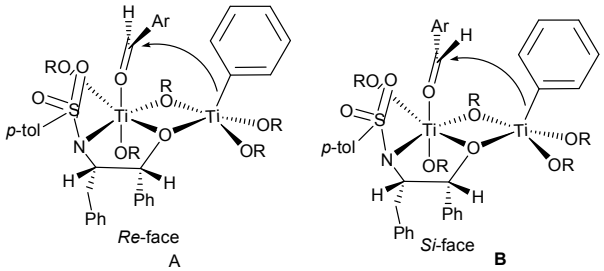


Figure 2. (a) The *Re*-face addition of the phenyl nucleophile to arylaldehyde; (b) The *Si*-face addition of Ph to arylaldehyde**.**

Conclusion

In summary, the asymmetric aryl additions of $ArTi(O^iPr)_3$ to aldehydes employing a series of *N*-sulfonylated amino alcohols were examined. Results showed that the chiral *N*-sulfonylated amino alcohol with two stereogenic centers could catalyzed asymmetric addition of $ArTi(O^iPr)_3$ to aldehydes to afford the desired optically active diarylmethanols in good yields with good to excellent enantioselectivities of up to 95% ee.

Experimental section

General Methods.

All syntheses and manipulations were carried out under a dry nitrogen atmosphere using standard Schlenk techniques or in a glovebox. Solvents were dried by refluxing for at least 24 h over P_2O_5 (dichloromethane) or sodium/benzophenone (THF, *n*-hexane or toluene) and were freshly distilled prior to use. $ArTi(O^iPr)_3$ was prepared according to the literature procedure[17]. The chiral *N*-sulfonylated amino alcohols **1a**, **1e** and **1f** were prepared according to the literature procedure[18]. ^1H NMR spectra were obtained with a Varian Mercury-400 (400 MHz) spectrometer, and ^{13}C NMR spectra were recorded with the Varian Mercury-400 (100.70 MHz). ^1H and ^{13}C chemical shifts were measured relative to TMS as the internal reference.

Synthesis of chiral *N*-sulfonylated amino alcohol 1b-1d.

A solution of *p*-tolylsulphonyl chloride (0.95 g, 5.00 mmol) in CH_2Cl_2 (20 mL) was added to a cold (0 °C) solution of the corresponding chiral amino alcohol (5.00 mmol) and Et_3N (2.1 mL, 15 mmol) in CH_2Cl_2 (20 mL). The reaction mixture was

allowed to warm to room temperature and stirred overnight. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and washed with 1 N HCl (2-5 mL), saturated aqueous $NaHCO_3$ (3-10 mL), and brine (3-10 mL). The organic layer was dried over anhydrous $MgSO_4$, concentrated under reduced pressure, and recrystallized from EA/Hexane to afford the chiral *N*-sulfonylated amino alcohols **1b-1d.**

(*S*)-3-(*p*-Toluenesulfonylamino)-2-methyl-4-phenyl-2-butanol (1b). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-6.89 (m, 9H, *Ph* and *Ph*(SO_2NH)), 5.30 (s, 1H, N*H*), 3.46 (m, 1H, C*H*N), 2.95 (m, 2H, PhCH_AH_B, O*H*), 2.43 (m, 1H, PhCH_AH_B), 2.35 (s, 3H, CH_3), 1.29 (s, 3H, (CH_3)$_2$CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.6, 137.7, 137.1, 129.4, 129.0, 128.3, 126.6, 126.1, 72.8, 64.7, 37.4, 27.7, 25.5, 21.4 ppm.

(*S*)-3-phenyl-2-(*p*-Toluenesulfonylamino)-1-propanol (1c). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61-6.95 (m, 9H, *Ph* and *Ph*(SO_2NH)), 5.74 (d, *J* = 7.2 Hz, 1H, N*H*), 3.61(m, 1H, CH_AH_BOH), 3.53-3.45 (m, 2H, CH_AH_BOH, C*H*N) 2.75 (m, 2H, PhCH_AH_B, O*H*), 2.63 (m, 1H, PhCH_AH_B), 2.35 (s, 3H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ 143.0, 137.0, 129.5, 129.0, 128.3, 126.8, 126.2, 63.7, 56.8, 37.4, 21.3 ppm.

(2*R*,3*S*)-3-(*p*-Toluenesulfonylamino)-4-phenyl-2-butanol (1d). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44-6.88 (m, 9H, *Ph* and *Ph*(SO_2NH)), 5.39 (d, *J* = 7.6 Hz, 1H, N*H*), 3.97 (m, 1H, PhC*H*OH), 3.42 (m, 1H, C*H*N), 2.72 (m, 1H, PhCH_AH_B), 2.56 (m, 1H, PhCH_AH_B), 2.36 (s, 3H, CH_3), 1.23 (d, *J* = 6.4 Hz, 3H, CH_3CHOH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.9, 137.0, 136.5, 129.4, 128.9, 128.4, 126.8, 126.2, 68.9, 60.6, 35.4, 21.4, 18.2 ppm.

General Procedure for the Asymmetric Aryl Addition of Aldehydes.

Under a dry nitrogen atmosphere, **1e** (0.019 g, 0.05 mmol) and ArTi(O^iPr)$_3$ (0.70 mmol) were mixed in dry THF (4 mL) at 0 °C. After stirring for 30 min, and an aldehyde (0.50 mmol) in THF (1 mL) was added dropwise to the resulting solution over 20 min at 0 °C. The mixture was allowed to react for 10 min at this temperature, and then quenched with 2 M NaOH. The aqueous phase was extracted with ethyl acetate (3 × 10 mL), dried over $MgSO_4$, filtered and concentrated. The residue was purified by column chromatography to give the secondary alcohol. Enantiomeric excesses of products were determined by HPLC using suitable chiral columns from Daicel.

(2-Methoxyphenyl)phenylmethanol (4a)[5a]. $[\alpha]^{25}_D$ = +47.84 (c 1.08, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.21 (m, 7H, *Ar*), 6.94-6.85 (m, 2H, *Ar*), 6.03 (s, 1H, C*H*O), 3.77 (s, 3H, OCH_3), 3.12 (br, 1H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6, 143.2, 131.9, 128.6, 128.1, 127.7, 127.1, 126.5, 120.7, 110.6, 72.1, 55.3 ppm.

(3-Methoxyphenyl)phenylmethanol (4b)[4b]. $[\alpha]^{25}_D$ = -15.23 (c 1.16, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.18 (m, 6H, *Ar*), 6.88-6.91 (m, 2H, *Ar*), 6.77-6.69 (m, 1H, *Ar*), 5.69 (s, 1H, C*H*O), 3.71 (s, 3H, OCH_3), 2.77 (br, 1H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 145.4, 143.6, 129.4, 128.3, 127.4, 126.4, 118.8, 112.8, 112.0, 75.9, 55.0 ppm.

(4-Methoxyphenyl)phenylmethanol (4c)[5a]. $[\alpha]^{25}_D$ = +0.93 (c 1.08, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.25 (m, 7H, *Ar*), 6.87-6.81 (m, 2H, *Ar*), 5.81 (d, *J* = 2.0 Hz, 1H, C*H*O), 3.79 (s, 3H, OCH_3), 2.19 (d, *J* = 3.2 Hz 1H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9, 144.0, 136.1, 128.4, 127.8, 127.3, 126.3, 113.8, 75.7, 55.2. ppm.

(2-Tolyl)phenylmethanol (4d)[5h]. $[\alpha]^{25}_D$ = -2.70 (c 1.11, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47-7.45 (m, 1H, *Ar*), 7.32-7.10 (m, 8H, *Ar*), 5.88 (s, 1H, C*H*O), 2.55 (br, 1H, O*H*), 2.18 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.8, 141.4, 135.2, 130.4, 128.3, 127.4, 127.3, 127.0, 126.2, 126.0, 73.2, 19.3 ppm.

(3-Tolyl)phenylmethanol (4e)[19]. $[\alpha]^{25}_D$ = +2.63 (c 1.14, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.05 (m, 9H, *Ar*), 5.69 (s, 1H, C*H*O), 2.60 (br, 1H, O*H*), 2.29 (s, 3H, CH_3), ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.2, 144.1, 138.4, 128.73, 128.68, 128.6, 127.8, 127.5, 126.8, 124.0, 76.5, 21.8 ppm.

(4-Tolyl)phenylmethanol (4f)[5a]**.** $[\alpha]^{25}_D$ = +16.35 (c 1.04, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.09 (m, 9H, *Ar*), 5.69 (s, 1H, C*H*O), 2.51 (s, 1H, O*H*), 2.29 (s, 3H, CH_3), ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.3, 141.3, 137.5, 129.5, 128.7, 127.7, 126.9, 126.8, 76.3, 21.4 ppm.

(2-Chlorophenyl)phenylmethanol (4g)[5f]. $[\alpha]^{25}_D$ = +15.26 (c 1.07, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58-7.56 (m, 1H, *Ar*), 7.36-7.17 (m, 8H, *Ar*), 6.17 (s, 1H, C*H*O), 2.60 (br, 1H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.2, 140.9, 132.4, 129.5, 128.7, 128.4, 128.0, 127.7, 127.0, 126.9, 72.6 ppm.

(3-Chlorophenyl)phenylmethanol (4h)[18]. $[\alpha]^{25}_D$ = -29.36 (c 1.09, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.20 (m, 9H), 5.68 (s, 1H, C*H*O), 2.63 (br, 1H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.7, 143.1, 134.3, 129.6, 128.6, 127.8, 127.5, 126.5, 124.5, 75.5 ppm.

(4-Chlorophenyl)phenylmethanol (4i)[5a]. $[\alpha]^{25}_D$ = -12.50 (c 1.04, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.26 (m, 9H, *Ar*), 5.76 (s, 1H, C*H*O), 2.48 (br, 1H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.4, 142.1, 133.2, 129.3, 128.6, 127.8, 126.5, 116.6, 75.5 ppm.

(2-Bromophenyl)phenylmethanol (4j) [5a]. $[\alpha]^{25}_D$ = +24.64 (c 2.34, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50-7.48 (m, 2H, *Ar*), 7.31-7.20 (m, 7H, *Ar*), 7.08-7.05 (m, 1H, *Ar*), 6.04 (s, 1H, C*H*O), 3.02 (s, 1H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.3, 142.0, 132.6, 128.9, 128.4, 128.3, 127.8, 127.6, 126.9, 122.6, 74.5 ppm.

(3-Bromophenyl)phenylmethanol (4k)[5g]. $[\alpha]^{25}_D$ = -29.70 (c 1.01, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49-7.48 (m, 1H, *Ar*), 7.35-7.10 (m, 8H, *Ar*), 5.63 (s, 1H, C*H*O), 2.85 (d, *J* = 5.6 Hz, 1H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.9, 143.0, 130.4, 129.9, 129.4, 128.6, 127.8, 126.5,125.0, 122.5, 75.4 ppm.

(4-Bromophenyl)phenylmethanol (4l)[5a]. $[\alpha]^{25}_D$ = -15.45 (c 1.10, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43-7.41 (m, 2H, *Ar*), 7.33-7.19 (m, 7H, *Ar*), 5.71 (s, 1H, C*H*O), 2.51 (br, 1H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$):δ 143.2, 142.6, 131.5, 128.6, 128.2, 127.8, 126.5, 121.3, 75.5 ppm.

(2-Fluorophenyl)phenylmethanol (4m)[5h]. $[\alpha]^{25}_D$ = -9.82 (c 0.95, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47-6.94 (m, 9H, *Ar*), 6.03 (s, 1H, C*H*O), 2.82 (s, 1H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.0, 158.5, 142.6, 130.9, 130.8, 129.4, 129.0, 128.9, 128.4, 127.6, 127.5, 126.3, 124.2, 115.3, 115.2, 115.1, 69.8 ppm.

(4-Trifluoromethylphenyl)phenylmethanol (4n)[2c]. $[\alpha]^{25}_D$ = -26.30 (c 1.09, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55-

7.54 (m, 2H, *Ar*), 7.44-7.42 (m, 2H, *Ar*), 7.33-7.21 (m, 9H, *Ar*), 5.75 (s, 1H, C*H*O), 2.74 (br, 1H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.4, 143.0, 129.4, 128.7, 128.0, 126.61, 126.59, 125.45, 125.39, 125.35, 125.31, 125.28, 122.8, 75.6 ppm.

(2-Nitrophenyl)phenylmethanol (4o)[20]. $[\alpha]^{25}_D$ = +82.24 (c 1.07, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (dd, *J* = 8.0 Hz and 1.2 Hz, 1H, *Ar*), 7.72 (dd, *J* = 8.0 Hz and 0.8 Hz, 1H, *Ar*), 7.63-7.59 (m, 1H, *Ar*), 7.45-7.40 (m, 1H, *Ar*), 7.36-7.11 (m, 5H, *Ar*), 6.39 (s, 1H, C*H*O), 2.85 (br, 1H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2, 141.4, 138.4, 133.4, 129.3, 128.5, 128.4, 128.0, 126.9, 124.6, 71.4 ppm.

(3-Nitrophenyl)phenylmethanol (4p)[21]. $[\alpha]^{25}_D$ = -42.31 (c 1.04, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25-8.24 (m, 1H, *Ar*), 8.08-8.05 (m, 1H, *Ar*), 7.68-7.66 (m, 1H, *Ar*), 7.48-7.43 (m, 1H, *Ar*), 7.36-7.24 (m, 5H, *Ar*), 5.86 (s, 1H, C*H*O), 2.85 (br, 1H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2, 145.7, 142.7, 132.4, 129.3, 128.8, 128.2, 126.6, 122.3, 121.2, 75.2 ppm.

(4-Nitrophenyl)phenylmethanol (4q)[16b]. $[\alpha]^{25}_D$ = -57.02 (c 1.14, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13-8.10 (m, 2H, *Ar*), 7.52-7.50 (m, 2H, *Ar*), 7.35-7.28 (m, 5H, *Ar*), 5.85 (d, *J* = 2.0 Hz 1H, C*H*O), 2.88 (br, 1H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.8, 147.2, 142.8, 128.8, 128.2, 127.0, 126.6, 123.5, 75.3 ppm.

Naphthalen-1-yl-phenylmethanol (4r)[5a]. $[\alpha]^{25}_D$ = +38.36 (c 1.06, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98-7.95 (m, 1H, *Ar*), 7.83-7.76 (m, 2H, *Ar*), δ 7.57-7.55 (m, 1H, *Ar*), δ 7.45-7.19 (m, 8H, *Ar*), 6.43 (s, 1H, C*H*O), 2.55 (s, 1H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.1, 138.7, 133.9, 130.6, 128.7, 128.43, 128.39, 127.6, 127.0, 126.1, 125.5, 125.3, 124.5, 123.9, 73.5 ppm.

Naphthalen-2-yl-phenylmethanol (4s)[4b]. $[\alpha]^{25}_D$ = -9.90 (c 1.01, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81-7.71 (m, 4H, *Ar*), 7.46-7.17 (m, 8H, *Ar*), 5.87 (s, 1H, C*H*O), 2.64 (br, 1H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.5, 141.0, 133.1, 132.8, 128.4, 128.2, 128.0, 127.6, 127.5, 126.6, 126.1, 125.9, 124.9, 124.7, 76.2 ppm.

Furan-2-yl-phenylmethanol (4t)[4b]. $[\alpha]^{25}_D$ = +6.23 (c 1.07, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41-7.29 (m, 6H), 6.28 (dd, *J* = 2.0, 1.6 Hz, 1H), 6.07 (d, *J* = 1.6, 0.8 Hz) 5.75 (s, 1H), 2.79 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.9, 142.4, 140.7, 125.6, 128.3, 127.9, 126.5, 110.1, 107.3, 69.9 ppm.

(*E*)-1,3-Diphenyl-prop-2-en-1-ol (4u)[4b]. $[\alpha]^{25}_D$ = -9.91 (c 0.37, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48-7.16 (m, 10H), 6.60-6.56 (m, 1H), 6.33-6.27 (m, 1H), 5.26-5.24 (m, 1H), 2.91 (br, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7, 136.4, 131.5, 130.3, 128.5, 128.4, 127.59, 127.55, 126.5, 126.4, 126.3, 74.8 ppm.

2-Methyl-1-phenyl-propan-1-ol (4v)[4b]. $[\alpha]^{25}_D$ = -26.07 (c 1.01, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.26 (m, 5H, *Ph*), 4.37-4.35 (m, 5H, C*H*Ph), 1.97-1.95 (m, 1H, C*H*$(CH_3)_2$), 1.83 (s, 1H, O*H*), 1.01-0.99 (m, 3H, C*H*$_3$), 0.80-0.78 (m, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.6, 128.2, 127.4, 126.5, 80.0, 77.3, 77.0, 76.7, 35.2, 19.0, 18.2 ppm.

2,2-Dimethyl-1-phenyl-propan-1-ol (4w)[4b]. $[\alpha]^{25}_D$ = -17.13 (c 1.07, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.29 (m, 5H, Ph), 4.40 (d, *J* = 2.8 Hz, 1H, C*H*O), 1.87 (d, *J* = 2.8 Hz, 1H, O*H*), 0.92 (s, 9H, C*H*$_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1, 127.6, 127.5, 127.2, 82.3, 35.6, 25.9 ppm.

Cyclohexyl-phenyl-methanol (4x)[3b]. $[\alpha]^{25}_D$ = -20.92 (c 1.02, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.24 (m, 5H, Ph), 4.33 (d, *J* = 7.2 Hz, 1H, C*H*O), 1.96-0.89 (m, 11H, O*H* and Cy) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.6, 128.1, 127.3, 126.6, 79.3, 44.9, 29.2, 28.8, 26.4, 26.0, 25.9 ppm.

(4-Chlorophenyl)(2-methoxyphenyl)methanol (4y). $[\alpha]^{25}_D$ = +44.34 (c 1.06, CH_2Cl_2). ^{1}H NMR (400 MHz, CDCl3): δ 7.29-7.18 (m, 6H, *Ar*), 6.93-6.83 (m, 2H, *Ar*), 5.96 (s, 1H, C*H*O), 3.75 (s, 3H, OC*H*$_3$) ppm. ^{13}C NMR (100 MHz, CDCl3): δ 156.4, 141.8, 132.6, 131.4, 128.8, 128.1, 127.8, 127.5, 120.8, 110.7, 71.4, 55.3 ppm.

(4-Methylphenyl)(2-methoxyphenyl)methanol (4z)[22]. $[\alpha]^{25}_D$ = +40.56 (c 1.20, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25-7.19 (m, 4H, *Ar*), 7.10-7.08 (m, 2H, *Ar*), 6.93-6.82 (m, 2H, *Ar*), 5.99 (s, 1H, C*H*O), 3.75 (s, 3H, OC*H*$_3$), 3.08 (s, 1H, O*H*), 2.30 (s, 1H, C*H*$_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6, 140.3, 136.6, 132.0, 128.7, 128.5, 127.6, 126.4, 120.6, 110.6, 71.8, 55.3, 21.0 ppm.

Acknowledgments

Financial support under the grant number of NSC 99-2113-M-005-005-MY3 from the National Science Council of Taiwan, Republic of China is appreciated.

Notes and references

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† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

‡ Footnotes should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.

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