Enantioselective Michael Addition of 2-Nitropropane to Substituted Chalcones and Chalcone Analogues Catalyzed by Chiral Crown Ethers Incorporating an α-D-Glucose or an α-D-Mannose Unit

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Abstract: The chiral monoaza-15-crown-5 lariat ethers annellated to methyl-4,6-*O*-benzylidene-α-D-glucopyranoside- (**1**) or –mannopyranoside (**2**) used as phase transfer catalysts in the Michael addition of 2-nitropropane to substituted chalcones and chalcone analogues resulted in a significant asymmetric induction. The type of substituent on the chalcone molecule was found to have a significant influence on both the chemical yield and the enantioselectivity of the reaction: 24 novel chiral Michael adducts were prepared in 14-68% ee. These ee values were somewhat lower than that experienced in the case of the unsubstituted chalcone (85% ee). In the series of chalcone analogues, the 1-naphthyl Michael adduct was formed in 87% ee. Using glucose-based crown ether **1,** formation of the (+)-enantiomers was preferred, while applying mannose-based **2** as the catalyst, the (-)-enantiomers were in excess.

Keywords: Chiral crown ether, phase transfer catalysis, asymmetric Michael addition.

1. INTRODUCTION

The development of new methodologies for efficient asymmetric synthesis is of tremendous importance due to the increasing demand for optically active compounds [1]. One of the techniques of catalytic asymmetric synthesis currently attracting considerable interest is phase-transfer catalysis, in which the enantioselectivity is generated by chiral crown ether [2]. Crown ethers with carbohydrate moieties form a special group of optically active macrocycles. Over the past three decades, numerous macrocycles incorporating one or more monosaccharide units have been synthesized [3]. Inexpensive natural sugars are "green" and cheap starting materials in organic syntheses. However, until now, only a limited number of asymmetric reactions have; however, been explored in which a sugar-based crown catalyst induced the enantioselectivity [4]. The Michael reaction is one of the most important C-C bond-forming reactions, and stereoselective variants have been extensively investigated in recent years [5]. High asymmetric induction has been reported in the Michael addition of methyl phenylacetate to methyl acrylate catalyzed by carbohydrate-containing chiral crown ethers [6-10]. Recently, Itoh *et al.* published the synthesis of several α-D-glucose-based chiral macrocycles, the application of which in a Michael addition led to relatively high enantioselectivities [11].

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The hexapyranoside-based 15-crown-5 lariat ethers described earlier by us possess special complexing ability due to their flexible side-arm containing a heteroatom at the end [12]. The overall complexing ability is influenced by the steric and electronic properties of the *N*-substituent. A few of the lariat ethers have been found to be efficient phase transfer catalysts in certain type of asymmetric reactions [13]. It came to light that the glucopyranoside- and the analogous mannopyranoside-based chiral lariat ethers (**1** and **2**, respectively) are able to induce a significant asymmetric induction in the Michael addition of 2-nitropropane to chalcone [14]. Structure of the lariat ethers may be ideal as, on the one hand, the cavity of the crown entity makes possible the complexation of the cation (Na^+), while on the other hand, the flexible side-arm (that is the *N*-substituent) may bring about an additional coordination of the cation. The rigid ring system of the carbohydrate moiety annellated to the acetal ring may also be advantageous from the point of view of chiral discrimination. Earlier, we described the reaction of a few substituted chalcones [15], and their aromatic analogues [16] with 2-nitropropane in the presence of chiral crown ethers. In this paper, the asymmetric Michael reaction of additional chalcones and analogues α,β-enones with 2-nitropropane is discussed.

2. RESULTS AND DISCUSSION

The addition of 2-nitropropane to substituted chalcones and chalcone analogues was investigated under phase transfer catalytic conditions in the presence of azacrown ethers **1** and **2** (Scheme **1**). In earlier studies, these catalysts

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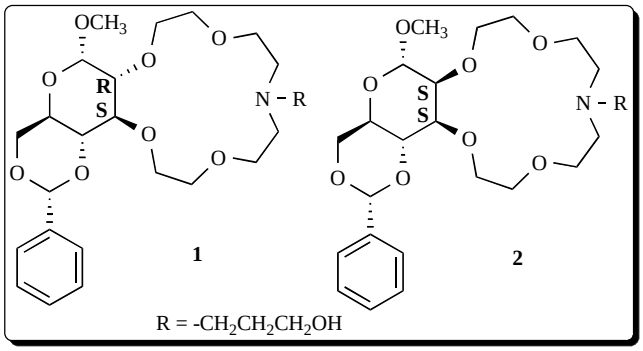
gave the best results. The α,β-unsaturated ketones were prepared according to the procedure described in the literature [17-25].



The Michael addition was carried out in a solid-liquid two phase system; using toluene, 35 mol% of sodium *tert*-butoxide and 7 mol% of the chiral catalyst **1** or **2** at 22 °C. After obtaining the products by preparative TLC, the asymmetric inductions expressed in terms of enantiomeric excess (ee %) were determined by ^{1}H NMR spectroscopy in the presence of the chiral shift reagent (+)-Eu(hfc)$_3$.

First, we wished to study the influence of the substituents in the aromatic ring of the chalcone on the chemical and optical yields of the reaction. Table **1** contains the data obtained with substituted chalcones in the presence of catalyst **1**. As a comparison, the data obtained for the unsubstituted chalcone (Ar^1 = Ph, Ar^2 = Ph) are also shown in the Table (entry 1). In this case, the ee was 85% [4].

It can be seen from Table **1** that the yield and the enantioselectivity depend strongly on the substituents in the aromatic ring. Any kind of substituent (Cl, CH_3, NO_2, OCH_3, F, in different positions) resulted in a decrease in the optical yield (14-68% ee) as compared to the unsubstituted chalcone (85% ee). In the first place, the substituents of β-phenyl ring (Ar^2) were changed, provided that Ar^1 = Ph (entry 1-13). Regarding the position of the chloro substituent, the most significant enantiomeric excess (ee) was experienced in the case of the 3-chloro derivative **5** (56%), that was a lower value in case of the 2-chloro derivative **4** (43%) and much lower for the 4-chloro species **6** (14%). In case of methyl-, nitro- and methoxy substituents, the corresponding Michael adducts were formed in ee-s of 31-35% (**7**-**9**), 37-50% (**10**-**11**) and 34-58% (**12**-**13**), respectively. Independently of the nature of the substituents, it seems to be general that the best optical purity can be achieved in case of the *meta* position of the substituent as shown by the example of compounds **5**, **8**, **11**, and **12**. This shows that the steric effect is more considerable in position 2 than in position 3. In position 4, the electronic factors influencing the acidity of adjacent protons should be considered. In the case of the dichloro compounds even lower optical purities (for **14** an ee of 40%, while for **15** an ee of 23%) were obtained.

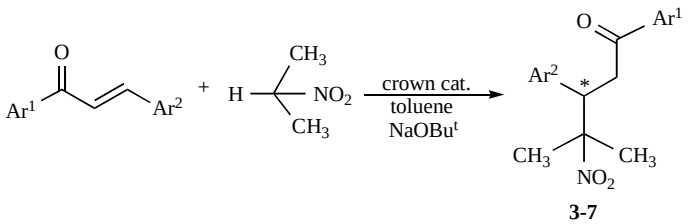
Then the effect of the substituents in the aromatic ring (Ar^1) next to the carbonyl group was studied provided that Ar^2 = Ph. It is obvious that these products (**16**-**25**) were formed in somewhat better optical yields than compounds **4**-**15**. The Michael adducts with chloro substituent (**16**-**18**), methyl substituent (**19**, **20**), methoxy substituent (**21**, **22**) and nitro substituent (**23**-**25**) were obtained in 46-68 (entry 14-16), 55-59 (entry 17-18), 51-58 (entry 19-20) and 41-58 % ee (21-23), respectively. With one exception (**22**), the best optical yields were again obtained in the case of the 3-substituted derivatives (**17**, **20**, **24**). It can also be seen that the results are quite similar, there is no such a significant difference between the above results (41-68% ee) and those experienced in the case of compounds **4**-**15** (14-58% ee). This must be due to the mere remote position of the substituent, and the steric effects are not so relevant. These substituents may influence only the reactivity of the carbonyl group. Even the presence of sterically more demanding substituents (as in **26** and **27**) did not cause a significant effect (the ee was 49 and 53%, respectively), only the chemical yields became lower (30 and 23 %, respectively).

It can be concluded that the substituents in the aromatic ring placed closer to the reaction site (Ar^2) have a more pronounced (decreasing) effect on the optical yields (as compared with compound **3**) than the substituents in the aromatic ring next to the carbonyl group (Ar^1).

Regarding the β-side, the best values were measured with 3-Cl, 3-Me and 3-OMe substituents (with ee values of 56, 55 and 58 %, respectively). The substituents in the Ar^1 ring next to the carbonyl group had a less significant effect on the optical purity. The best enantioselectivities were obtained in case of the 3-Cl, 3-Me, 2-OMe and 3-NO_2 substituents (with ee values of 68, 59, 58 and 58%, respectively).

Then the Michael addition was studied with chalcone analogue α,β-enone derivatives (Scheme **2**). The results are summarized in Table **2**. Entry 1 represents the results obtained with the unsubstituted chalcone (Y^1 = Y^2 = Ph) [4].

In the first place, the effect of different alkyl groups and naphthyl substituents was studied in place of Y^1, keeping the other substituent Y^2 as phenyl. Only a low optical purity (25% ee) was experienced in the reaction of benzylideneacetone (Y^1 = Me, entry 2), and no product was formed in case of ^{t}Bu substituent (entry 3). The best optical yield (87% ee) was achieved with the 1-naphthyl ketone (entry 4). In the case of the 2-naphthyl product (**31**), the ee



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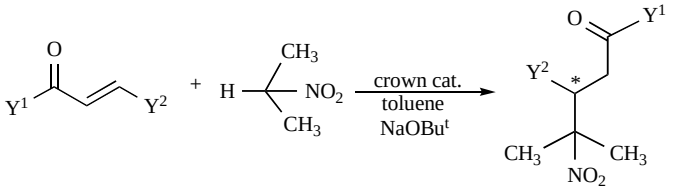
Scheme 1. Michael addition of 2-nitropropane to substituted chalcones, Ar^1 and Ar^2 listed in Table **1**.

Table 1. Asymmetric Michael Addition of 2-Nitropropane to Substituted Chalcones Mediated by Chiral Azacrown Ether 1

Entry	Product	Ar [1]	Ar [2]	Time (h)	Yield (%) [a]	$[\alpha]_D$ [b]	E.e. % [c]
1	**3**	Ph	Ph	40	55	+ 70,3	85 (*R*)[d]
2	**4**	Ph	2-Cl-Ph	17	43	+ 66,8	43 (*R*)
3	**5**	Ph	3-Cl-Ph	16	56	+ 60,0	56 (*R*)
4	**6**	Ph	4-Cl-Ph	24	60	+ 15,0	14 (*R*)
5	**7**	Ph	2-CH_3-Ph	48	29	+ 24,8	31
6	**8**	Ph	3-CH_3-Ph	23	41	+ 119,9	55
7	**9**	Ph	4-CH_3-Ph	50	58	+ 54,4	49
8	**10**	Ph	2-NO_2-Ph	20	30	+ 107,4	37 [e]
9	**11**	Ph	3-NO_2-Ph	20	43	+ 67,6	50 [e]
10	**12**	Ph	3-CH_3O-Ph	27	47	+ 53,4	58
11	**13**	Ph	4-CH_3O-Ph	52	39	+ 39,1	34
12	**14**	Ph	2,4-di-Cl-Ph	24	48	+ 53,1	40
13	**15**	Ph	2-Cl-6-F-Ph	26	18	+ 14,8	23
14	**16**	2-Cl-Ph	Ph	21	66	+ 16,9	52 (*R*)
15	**17**	3-Cl-Ph	Ph	19	64	+ 55,7	68 (*R*)
16	**18**	4-Cl-Ph	Ph	22	60	+ 60,6	56 (*R*)
17	**19**	2-CH_3-Ph	Ph	24	35	+ 22,8	55
18	**20**	3-CH_3-Ph	Ph	23	52	+ 59,8	59
19	**21**	2-CH_3O-Ph	Ph	75	35	+ 31,4	58
20	**22**	3-CH_3O-Ph	Ph	27	51	+ 54,4	51
21	**23**	2-NO_2-Ph	Ph	13	41	+ 24,3	41 [e]
22	**24**	3-NO_2-Ph	Ph	14	45	+ 38,7	58 [e]
23	**25**	4-NO_2-Ph	Ph	13	52	+ 39,6	49 [e]
24	**26**	2-$EtOCH_2O$-Ph	Ph	90	30	+ 45,4	49
25	**27**	2-*i*PrO-Ph	Ph	82	23	+ 54,7	53

[a]Based on substance isolated by preparative TLC; [b]In CH_2Cl_2 at 22 °C; [c]Determined by ^{1}H NMR spectroscopy; [d]Lit. [4]; [e]Determined by chiral HPLC.



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Scheme 2. Michael addition of 2-nitropropane to α,β-enones, Y^1 and Y^2 listed in Table **2**.

Table 2. Asymmetric Michael Addition of 2-Nitropropane to Chalcone Analogues Mediated by Chiral Azacrown Ether 1

Entry	Product	Y^1	Y^2	Time (h)	Yield (%) [a]	$[a]_D$ [b]	E.e. % [c]
1	**3**	Ph	Ph	28	53	+68,7	85 [d]
2	**28**	Me	Ph	93	34	+9,0	25
3	**29**	Bu^t	Ph	60	-	-	-
4	**30**	1-naphtyl	Ph	27	35	-8,5	87
5	**31**	2-naphtyl	Ph	76	32	+78,8	38
6	**32**	Ph	Me	118	71	-27,8	76
7	**33**	Ph	Bu^t	60	-	-	-
8	**34**	Ph	1-naphtyl	90	51	+84,1	32 [d]
9	**35**	Ph	2-naphtyl	41	19	+65,6	41
10	**36**	Bu^t	1-naphtyl	60	-	-	-

[a]Based on substance isolated by preparative TLC; [b]In CH_2Cl_2 at 22°C; [c]Determined by ^{1}H NMR spectroscopy; [d]Lit. [4].

Table 3. Asymmetric Michael Addition of 2-Nitropropane to Substituted Chalcones and Chalcone Analogues Catalyzed by Mannose-Based Crown Ether 2

Entry	Product	Ar [1]	Ar [2]	Time (h)	Yield (%) [a]	$[\alpha]_D$ [b]	E.e. % [c]
1	**3**	Ph	Ph	52	37	-74,8	92 (*S*) [d]
2	**5**	Ph	3-Cl-Ph	20	52	-54,7	51 (*S*)
3	**12**	Ph	3-CH_3O-Ph	28	49	-49,3	54
4	**17**	3-Cl-Ph	Ph	22	61	-53,3	65 (*S*)
5	**21**	2-CH_3O-Ph	Ph	70	39	-30,8	57
6	**24**	3-NO_2-Ph	Ph	16	46	-36,0	54[e]
7	**30**	1-naphtyl	Ph	32	39	-8,6	84
8	**32**	Ph	Me	106	68	-26,1	71

[a]Based on substance isolated by preparative TLC; [b]In CH_2Cl_2 at 22 °C; [c]Determined by ^{1}H NMR spectroscopy; [d]Lit. [26]; [e]Determined by chiral HPLC.

value decreased to 38%. It is worthy to mention that the sign of the optical rotation was different for the 1- and 2-naphthyl Michael adducts (**30** and **31**, respectively). Steric effect may be responsible for this phenomenon.

Varying the Y^2 substituent and keeping the other one (Y^1) as phenyl, we experienced the following. In the case of Me substituent (entry 6), product **32** was formed in 76 % ee, while with ^{t}Bu group there was no reaction at all (entry 7). Presence of the 1- and 2-naphthyl groups resulted in modest optical purities (32 % ee for **34** and 41% ee for **35**, respectively). It can be seen that if either Y^1 or Y^2 was a ^{t}Bu substituent (entry 3, 7 and 10 respectively), the Michael addition was prevented.

Then the Michael additions were carried out in the presence of mannose-based crown catalyst **2**. The results are summarized in Table **3**, where entry 1 shows the observations with chalcone as a comparison (the *S* antipode was formed in an ee of 92%) [26].

Comparing the data of Table **3** with those shown in Tables **1** and **2**, one can see that in respect of products **5**, **12**, **17**, **21**, **24**, **30** and **32,** the asymmetric induction was somewhat lower in the presence of mannose-based catalyst **2**, as compared to the cases, where glucose-based **1** was applied. The chemical yields were similar. As an example, adduct **5** was formed in 56 and 51% ee using catalyst **1** and **2**, respectively (Table **1**/entry 3 and Table **3**/entry 2). A similar significant decrease was experienced in the case of the other model compounds. The highest optical putity (84% ee) was achieved for the formation of product **30** (Ar^1 = 1-naphthyl, Ar^2 = Ph). In case of *trans*-crotonophenone, product **32** was obtained in a quite good optical yield (71% ee), but all of the ee values detected remained below the optical purity of 92% observed for the Michael adduct of the unsubstituted chalcone.

It seems to be general that while the glucose-based catalyst (**1**) brings about the prefered formation of the antipode with positive optical rotation (*R*), the mannose-based catalyst (**2**) promotes the formation of the other antipode (*S*). It is worth mentioning that compounds **2** and **1** differ only in the configuration of the C(2) atom of the sugar moiety. In the glucopyranoside-based **1**, position of the C(2)-O and C(3)-O groups is *trans*, while that in **2** is *cis* .

The absolute configurations were proved in the case of the new chloro-derivatives **4**-**6**, **16**-**18** by a chemical method. The chloro substituent of the aromatic ring may be easily removed by catalytic hydrogenation in the presence of Pd/C and sodium acetate to provide unsubstituted **3**, whose antipodes were already characterized [27]. The hydrogenation of compounds **4, 5, 6, 16, 17, 18,** comprising the (+)-enantiomer in excess led to product **3** with (+)-optical rotation that is of *R* configuration. Hence, the products mentioned above are also of *R* configuration. The negative sign of the optical rotation for the compounds (**5** and **17**) formed in the presence of mannose-based catalyst **2** corresponds to configuration *S***.**

It can be concluded that in the Michael addition studied, the asymmetric induction depends strongly on the nature of the Ar^1/Y^1 and Ar^2/Y^2 substituents. The Ar^1/Y^1 substituents had a more significant impact an the optical yields of the Michael adducts than the Ar^2/Y^2 substituents. The steric effect of the substituents seems to have a larger impact on the asymmetric induction than the electronic one.

3. EXPERIMENTAL

3.1. General

Melting points were taken on using a Büchi 510 apparatus and are uncorrected The compounds were crystallized from ethanol. The specific rotation was measured with the help of a Perkin-Elmer 241 polarimeter at 22 °C. NMR spectra were obtained on a Brucker 300 and a Brucker DRX-500 instrument in $CDCl_3$ with TMS as the internal standard. Mass spectra were registered from *m*-nitrobenzyl alcohol (*NOBA*) matrix on a Varian MAT312 instrument. Analytical and preparative thin layer chromatography was performed on silica gel plates (60 GF-254, Merck), while column chromatography was carried out using 70-230 mesh silica gel (Merck) using hexane–ethyl acetate, 10:1 as the eluant. Chemicals and the shift reagent $Eu(hfc)_3$ were purchased from Aldrich Chem. Co. Enantoselectivities were determined by ^{1}H NMR spectroscopy in the presence of chiral shift reagent or by chiral HPLC analysis (Chiralpak AD-H or Chiralcel OD-H, detector JASCO UV-1575, pump:PU-1580).

3.2. General Procedure for the Michael Addition of 2-Nitropropane to α,β-enones

The corresponding azacrown ether catalyst (0.10 mmol) and 0.05 g (0.50 mmol) of sodium *tert*-butoxide was added

Table 4. Melting Points and ^{1}H NMR Spectra of the New Michael Adducts

Comp.	Ar^2	Mp, °C	^{1}H NMR data (δ ppm, $CDCl_3$)										
			Subst.	CH_3 (s)	CH_2	CH_2	CH	Ar^1	Ar^2-H-2	Ar^2-H-3	Ar^2-H-4	Ar^2-H-5	Ar^2-H-6
4	2-Cl-Ph	oil	-	1.63; 1.65	3.45 (dd, *J* = 3.2; 17.4 Hz)	3.62 (dd, *J* = 10.5; 17.3 Hz)	4.83 (dd, *J* = 3.2; 10.4 Hz)	7.43-7.84 (m)	-	7.42 (d)	7.13-7.19 (m)		
5	3-Cl-Ph	98	-	1.55; 1.63	3.29 (dd, *J* = 3.2; 17.4 Hz)	3.62 (dd, *J* = 10.4; 17.4 Hz)	4.13 (dd, *J* = 3.2; 10.4 Hz)	7.44-7.87 (m)	7.22-7.23 (m)	-	7.22-7.23 (m)	7.12-7.14 (m)	7.22-7.23 (m)
6	4-Cl-Ph	120-122	-	1.64; 1.70	3.49 (dd, *J* = 4.5; 17.4 Hz)	3.72 (dd, *J* = 10.5; 17.2 Hz)	4.28 (dd, *J* = 3.5; 11.1 Hz)	7.42-7.83 (m)	7.24 (d)	7.41 (d)	-	7.41 (d)	7.24 (d)
7	2-CH_3-Ph	oil	2.53 (s)	1.54; 1.66	3.28 (dd, *J* = 2.9; 17.2 Hz)	3.67 (dd, *J* = 10.6; 17.2 Hz)	4.51 (dd, *J* = 2.9; 10.6 Hz)	7.41-7.84 (m)	-	7.09-7.11 (m)	7.51 (t)	7.09-7.11 (m)	7.16 (d)
8	3-CH_3-Ph	69-70	2.30 (s)	1.54; 1.62	3.26 (dd, *J* = 3.3; 17.2 Hz)	3.65 (dd, *J* = 10.2; 17.2 Hz)	4.11 (dd, *J* = 3.3; 10.2 Hz)	7.43-7.87 (m)	7.01-7.05 (m)	-	7.01-7.05 (m)	7.17 (t)	7.01-7.05 (m)
10	2-NO_2-Ph	oil	-	1.64; 1.74	3.61 (d, *J* = 6.9 Hz)	3.61 (d, *J* = 6.9 Hz)	4.81 (t, *J* = 7.0 Hz)	7.40-7.85 (m)	-	8.02 (d)	7.51 (t)	7.81-7.84 (m)	7.40 (d)
11	3-NO_2-Ph	oil	-	1.59; 1.67	3.39 (dd, *J* = 3.1; 17.7 Hz)	3.75 (dd, *J* = 10.6; 17.7 Hz)	4.29 (dd, *J* = 3.1; 10.6 Hz)	7.43-7.88 (m)	8.13 (s)	-	8.01 (d)	7.48 (t)	7.63 (d)
12	3-CH_3O-Ph	105-106	3.76 (s)	1.55; 1.,64	3.24 (dd, *J* = 3.2; 17.2 Hz)	3.66 (dd, *J* = 10.3; 17.2 Hz)	4.13 (dd, *J* = 3.2; 10.3 Hz)	7.42-7.86 (m)	6.76 (s)	-	6.77 (d)	7.19 (t)	6.82 (d)
14	2,4-diCl-Ph	amorph	-	1.61; 1.63	3.45 (dd, *J* = 3.6; 17.5 Hz)	3.59 (dd, *J* = 10.3; 17.5 Hz)	4.74 (dd, *J* = 3.6; 10.2 Hz)	7.44-7.87 (m)	-	7.45 (s)	-	7.17 (d)	7.06 (d)
15	2-Cl,6F-Ph	oil	-	1.66; 1.69	3.43 (dd, *J* = 3.5; 18.0 Hz)	3.92 (dd, *J* = 9.8; 17.9 Hz)	4.94 (dd, *J* = 3.5; 9.7 Hz)	7.44-7.90 (m)	-	6.90-7.28 (m)			-

Table 5. Melting Points and ^{1}H NMR Spectra of the New Michael Adducts

Comp.	Ar^1	Mp, °C	^{1}H NMR data (δ ppm, $CDCl_3$)										
			Subst.	CH_3 (s)	CH_2	CH_2	CH	Ar^1-H-2	Ar^1-H-3	Ar^1-H-4	Ar^1-H-5	Ar^1-H-6	Ar^2
16	2-Cl-Ph	oil	-	1.51; 1,61	3.30 (dd, *J* = 3.6; 17.0 Hz)	3.60 (dd, *J* = 11.0; 17.0 Hz)	4.02 (dd, *J* = 3.6; 11.0 Hz)	-	7.02 (d)	7.33 (t)	7.19 (t)	7.34 (d)	7.14-7.28 (m)
17	3-Cl-Ph	93-94	-	1.54; 1.63	3.24 (dd, *J* = 3.3; 17.3 Hz)	3.64 (dd, *J* = 10.3; 17.3 Hz)	4.13 (dd, *J* = 3.3; 10.3 Hz)	7.81 (s)	-	7.51 (d)	7.38 (t)	7.74 (d)	7.22-7.30 (m)
19	2-CH_3-Ph	oil	2.04 (s)	1.57; 1.61	3.35 (dd, *J* = 3.7; 16.4 Hz)	3.50 (dd, *J* = 11.0; 16.4 Hz)	4.04 (dd, *J* = 3.7; 11.0 Hz)	-	7.22-7.25 (m)	7.33 (t)	7.15 (t)	7.48 (d)	7.15-7.25 (m)
20	3-CH_3-Ph	72	2.38 (s)	1.54; 1.63	3.26 (dd, *J* = 3.3; 17.2 Hz)	3.65 (dd, *J* = 10.3; 17.2 Hz)	4.15 (dd, *J* = 3.3; 10.3 Hz)	7.65 (s)	-	7.32 (d)	7.34 (t)	7.66 (d)	7.22-7.30 (m)
21	2-CH_3O-Ph	oil	3.90 (s)	1.49; 1.61	3.35 (dd, *J* = 3.8; 16.9 Hz)	3.59 (dd, *J* = 10.7; 17.0 Hz)	4.02 (dd, *J* = 3.8; 10.7 Hz)	-	6.93 (d)	6.87 (t)	7.27 (t)	7.41 (d)	7.13-7.26 (m)
22	3-CH_3O-Ph	74-75	3.79 (s)	1.53; 1.62	3.25 (dd, *J* = 3.3; 17.2 Hz)	3.66 (dd, *J* = 10.4; 17.2 Hz)	4.14 (dd, *J* = 3.3; 10.4 Hz)	7.33 (s)	-	7.07 (d)	7.34-7.36 (m)	7.46 (d)	7.22-7.31 (m)
23	2-NO_2-Ph	88-89	-	1.54; 1.59	3.26 (dd, *J* = 3.0; 17.1 Hz)	3.43 (dd, *J*= 10.8; 17.1 Hz)	4.00 (dd, *J* = 3.0; 10.8 Hz)	-	8.07 (d)	6.84 (m)	7.55 (t)	7.54 (d)	7.16-7.30 (m)
24	3-NO_2-Ph	amorph	-	1.55; 1.66	3.31 (dd, *J* = 3.1; 17.3 Hz)	3.73 (dd, *J* = 10.3; 17.3 Hz)	4.16 (dd, *J* = 3.0; 10.3 Hz)	8.67 (s)	-	8.39 (d)	7.64 (t)	8.18 (d)	7.24-7.32 (m)
25	4-NO_2-Ph	120-121	-	1.55; 1.64	3.31 (dd, *J* = 3.1; 17.3 Hz)	3.73 (dd, *J* = 10.3; 17.3 Hz)	4.12 (dd, *J* = 3.3; 10.3 Hz)	7.99 (d)	8.28 (d)	-	8.28 (d)	7.99 (d)	7.20-7.30 (m)
26	2-(ethoxy-methyl)-Ph	oil	1.25 (t); 3.75 (q); 5.31 (d)	1.50; 1.59	3.37 (dd, *J* = 3.7; 17.2 Hz)	3.64 (dd, *J* = 10.6; 17.2 Hz)	4.04 (dd, *J* = 3.6; 10.6 Hz)	-	7.15-7.26 (m)	7.38 (t)	6.92 (t)	7.15-7.26 (m)	
27	2-*i*Pr-Ph	oil	1.44 (dd); 4.71 (m)	1.52; 1.59	3.38 (dd, *J* = 3.5; 17.9 Hz)	3.75 (dd, *J* = 10.7; 17.9 Hz)	4.08 (dd, *J* = 3.4; 10.7 Hz)	-	6.92 (d)	7.37 (t)	6.84 (t)	7.35 (d)	7.18-7.28 (m)

Table 6. Melting Points and ^{1}H NMR Spectra of the New Michael Adducts

Comp.	Y^1	Y^2	Mp, °C	^{1}H NMR data (δ ppm, $CDCl_3$)							
				CH_3 (s)	CH_2	CH_2	CH	Y^2-H-2,6	Y^2-H-3,5	Y^2-H-4	Napht-H-1-8
30	1-naphtyl	Ph	oil	1.51; 1,62	3.35 (dd, *J* = 3.7; 16.5 Hz)	3.66 (dd, *J* = 10.8; 16.5 Hz)	4.15 (dd, *J* = 3.6; 10.8 Hz)	7.17-7.24 (m)			7.36-7.45 (m, H-3,6,7); 7.69-7.92 (m, H-2,4,5,8)
31	2-naphtyl	Ph	133-134	1.55; 1.65	3.39 (dd, J = 3.3; 17.0 Hz)	3.80 (dd, *J* = 10.4; 17.0 Hz)	4.22 (dd, *J* = 3.3; 10.8 Hz)	7.20-7.26 (m)			7.51-7.55 (m, H-6,7); 7.79-7.92 (m, H-3,4,5,8); 8.38 (s, H-1)
35	Ph	2-naphtyl	143-144	1.58; 1.68	3.36 (dd, *J* = 3.2; 17.3 Hz)	3.80 (dd, *J* = 10.4; 17.3 Hz)	4.33 (dd, *J* = 3.1; 10.4 Hz)	7.86 (d)	7.42 (t)	7.53 (t)	7.38-7.46 (m, H-3,6,7); 7.68 (s, H-1); 7.76-7.79 (m, H-4,5,8)

to a solution of 1.44 mmol of α,β-enone and 0.3 mL (3.36 mmol) of 2-nitropropane in 3 mL of dry toluene. The mixture was stirred at room temperature under argon. After a reaction time of 13 to 106 h, toluene (7 mL) and water (10 mL) were added and the mixture was stirred for several minutes. The organic phase was washed with water and dried (Na_2SO_4). The crude product obtained after evaporating the solvent was purified by preparative *TLC* (silica gel, hexane – ethyl acetate, 10:1 as the eluant) to give the Michael adducts (**4**-**32**) in a pure form.

The reaction times, yields, optical rotation and ee% values of the new Michael adducts are listed in Tables **1**-**3**, while the melting points and ^{1}H NMR spectral parameters are shown in Tables **4**-**6**.

Physical and spectroscopycal data of compounds **3**, **9**, **13**, **18**, **28** and **32** are not included in the Tables, as those were identical with the characteristics described in the literature (**3**, [4], **9**, **13, 18** [15], **28** [28] and **32** [29]. The optical rotations measured were included in all case.

3.3. Hydrogenation of Compounds Consisting Chloro-Substituent

A solution of the Michael adduct (**4-6**, **16-18)** (0.9 mmol), sodium acetate (0.1 g, 1.22 mmol) and Pd/C (10%, 100 mg) in methanol (5 mL) was stirred under an atmosphere of H_2 (1 atm) at room temperature for 14 h. The reaction mixture was filtered and the filtrate was concentrated. The residue was purified by crystallization to give **3** as a solid (0.24 g, 80%); mp 146-148 ^{o}C; $([\alpha]_D^{20}$ = +80.8 (c 1, CH_2Cl_2) for the pure (+)-(*R*)-enantiomer). ^{1}H NMR ($CDCl_3$) δ ppm:1.54 (s, 3H), 1.63 (s, 3H), 3.70 (dd, 1H, J_{gem} = 17.6, 3.1 Hz), 4.09 (dd, 1H, J_{gem} = 17.6, 10.0 Hz) 4.15 (dd, 1H), 7.18-7.32 (m, 5H, CHPhH), 7.42 (t, 2H, COPhH-m), 7.53 (t, 1H, COPhH-p), 7.85 (d, 2H, COPhH-o); MS (EI) m/z 298 $(M+H)^+$.

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