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ASYMMETRIC ALKYLATION OF α-ARYL SUBSTITUTED CARBONYL COMPOUNDS BY MEANS OF CHIRAL PHASE TRANSFER CATALYSTS. APPLICATIONS FOR THE SYNTHESIS OF (+)-PODOCARP-8(14)-EN-13-ONE AND OF (-)-Wy-16,225, A POTENT ANALGESIC AGENT

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Abstract : Asymmetric induction in the alkylation (alkyl halides and enones) of α-aryl substituted ketones, esters and lactones by means of CPTC has been evaluated. The catalysts used are the bromides of N-(p-trifluoromethyl) benzyl derivatives of cinchonine, cinchonidine, dihydrocinchonine and dihydrocinchonidine. The potential of the method is illustrated by the asymmetric synthesis of (+)-podocarp-8(14)-ene-13-one (**13**) and of (-)-Wy-16,225 (**10**), a bridged aminotetralin with potent analgesic properties.

One of the main trends in the synthesis of biologically active products consists of the study of methods directed towards the formation of a single enantiomer. The synthesis of optically active molecules falls into three categories : (1) optical resolution of racemic mixtures, (2) transformation of "chiral pool" compounds and (3) asymmetric synthesis from prochiral substrates. In the last area impressive progress has been realized in the design of reactions giving high % ee and using either chiral auxiliaries or chiral catalysts . The use of chiral catalysts has, in terms of efficiency and economy, advantages when large scale production is envisaged. If moreover the catalytic process can be carried out under mild conditions (inexpensive solvents, at rt, *etc*) the method could be attractive to industrial chemists. One should furthermore bring into the balance, the degree of optical purity of the product versus other factors such as efficiency, economy and practicability. A simple method giving moderate to good enantioselectivity, combined with recrystallization to high optical purity[1] can therefore be of value. In the area of the construction of stereogenic quaternary carboncenters, the use of chiral phase transfer catalysts (CPTC) offers a potentially simple solution to the problem. Until the excellent result reported by Dolling and coworkers[2] from the Merck Sharp and Dohme Research Laboratories only few attempts[3] with discouraging low % ee (15%) have been reported. This research group performed an asymmetric methylation of the 2-phenyl-1-indanone **1** using N-(p-trifluoromethylbenzyl)cinchonium bromide (**A**) as the catalyst ; (S)-**2** was obtained with 92 % ee and in 95 % yield[2] (fig. 1).

This result encouraged us to investigate alkylations of some selected α-aryl substituted aliphatic carbonyl compounds. Dolling's result found little response in the literature and it seemed to us that it has been regarded as a special and isolated case, in which the two aromatic rings in the substrate are essential for the formation of a tight ion-pair (Fig. 1). The authors have provided evidence that the preferred conformation of the catalyst may be the one in which the quinoline ring, the C_9-O bond and the N-benzyl group are essentially coplanar; the rest of the molecule being situated behind the plane. This was also confirmed by us using force field calculations[4]. The planar anion of substrate **1**, with the negative charge delocalized in the 2-phenyl ring nicely fits on top of the catalyst. The authors invoke three interactions between catalyst **A** and anion **1** : (1) a hydrogen bond between

the C_9 hydroxyl group and the oxy-anion, (2) π-π interaction between the quinoline and dichloromethoxyphenyl rings and (3) π-π interaction between the N-benzyl and 2-phenyl rings (Fig. 1).

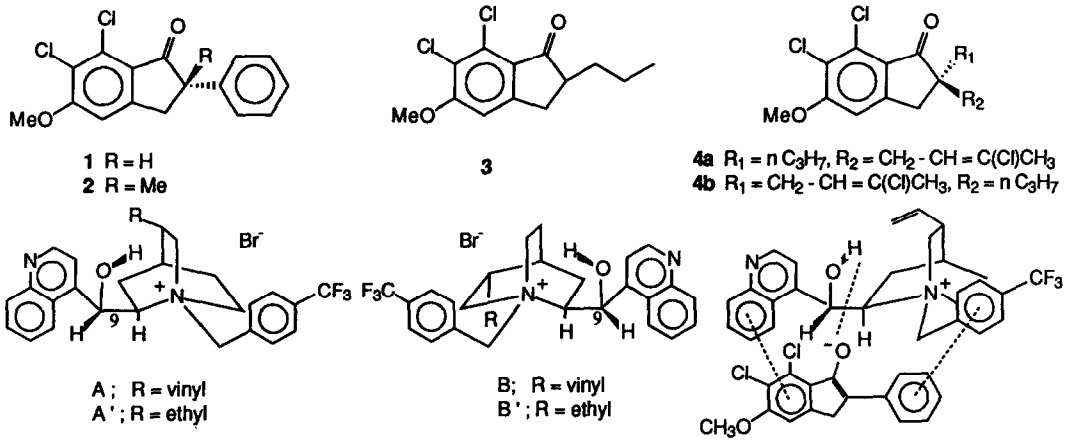


Figure 1

Alkylation from the front side (re-face) led to (S)-**2**. However during the course of our work a second example of the same laboratory involving indanone **3** has been reported ; alkylation in the presence of **A** or N-(p-trifluoromethylbenzyl)cinchonidinium bromide (**B**) gave respectively (S)-**4a** (92 % ee) and (S)-**4b** (78 % ee)[5a]. Also **A**, **B**, and **B'** mediated Michael reactions on **3** gave enantiomeric excesses between 40 and 80 %[5b].

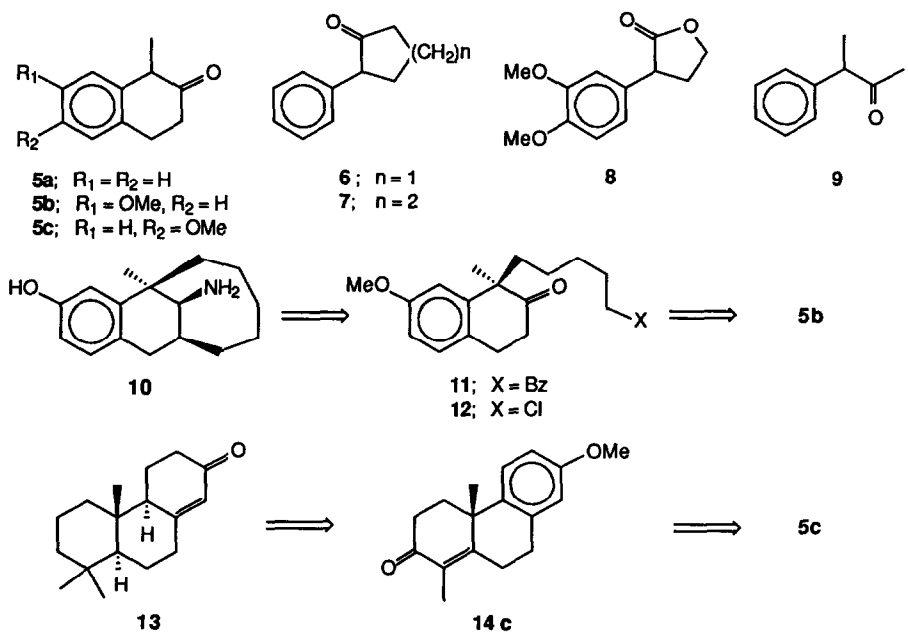


Figure 2

These results indicate that interaction (3) can be replaced by a non-bonding alkyl-π interaction. It is evident that the same rationale for ion-pairing involving cinchonidinium catalysts **B** and **B'** leads to the R enantiomer. These reactions on aromatic ketones are complementary to our work on α-aryl substituted carbonyl compounds, presented here. Comparison of the results obtained with several substrate types could enhance the knowledge on the configuration and conformation of the ion-pair involved. Next to the previously described catalysts **A**, **B** and **B'** we have also prepared and evaluated the catalyst **A'**.

Results and discussion.

The substrates selected for this study are the tetralones **5a,b,c**[6], the non-fused α-arylketones **6**[7] and **7**[8], the lactone **8**[9] and the acyclic ketone **9**[10] (Fig. 2). It was not the intention to carry out an exhaustive comparative study of substrates and alkylating agents; the selection was made in connection with some projected target molecules. Next to the tetralones, the substrates **6**, **7** and **8** were evaluated because, in both series, the enolate anions have respectively E and Z geometries. The target molecules are the potent analgesic agent (-)-Wy-16,225 (**10**)[11], with a 5,11-methano-benzocyclodecen-13β-amine skeleton and (+)-podocarp-8(14)-en-13-one (**13**)[12], an important intermediate for the synthesis of several diterpenes.

En route to **10**, the enantioselective alkylation of **5b** with a 1,5-dihalopentane was studied with the catalyst **B**; some relevant results are shown in table 1.

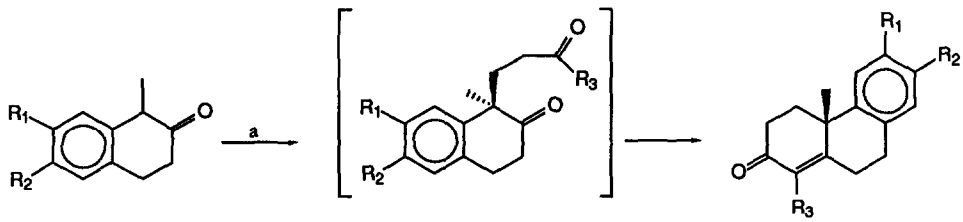
Table 1 : Enantioselective alkylation of 5b with 1,5-dihalopentane[a].

entry	reagent/eq.	solvent	cat./eq.	conc.[b]	time[c]	% Y	% ee[d]
1	dibromo/3	DIPE[e]	B/0.2	0.045	1	48	0
2	dibromo/5	pentane	B/0.1	0.07	3	40	>30
3	dibromo/3	toluene	B/0.1	0.07	2	71	>60
4	dibromo/3	benzene	B/0.1	0.045	2	74	>70
5	dichloro/10	toluene	B/0.2	0.045	10	0	-
6[f]	dibromo/2	toluene	B/0.2	0.08	3	46[g]	>50
7	dibromo/3	toluene	B/0.2	0.045	1	75	>60
8	dibromo/3	toluene	h/0.2	0.056	1	70	0

(a) under Ar, 50 % aq. NaOH at rt; (b) mol/l; (c) days; (d) determined by ^{1}H NMR in the presence of Eu(hfc)$_3$, measured on the C_1-CH_3 group. Base-line separation needed large amounts of chiral shift reagent, the resulting line-broadening made the estimation less accurate. Therefore the lower decimal value was taken as a minimum % ee; (e) iPr_2O; (f) at 0°C; (g) incomplete; (h) TEBA.

It is important to note that reactions must be carried out under complete oxygen-free conditions because of rapid oxidation at the α-position. The Dolling results indicate that the use of nonpolar solvents enhances the enantioselectivity and that toluene is the solvent of choice[2]. We observed that benzene is somewhat better (entries 3 and 4); however because of the hazard involved with this solvent on large scale, only toluene was further evaluated. Substrate concentration and amount of catalyst had little influence (entries 3 and 7); the reaction was slow at 0°C. As will be proven by the synthesis of (-)-**10** the R configuration is found for **11** (Fig. 2 and Scheme 3), hereby establishing the same ion-pair as shown in Fig. 1, thus π-π interaction of **5b** with the p-trifluoromethyl-phenyl ring of catalyst **B** (Fig. 3).

In order to investigate the asymmetric Robinson annulation, we then turned our attention to enones as the electrophiles (scheme 1 and table 2).



5a; $R_1 = R_2 = H$
5b; $R_1 = OMe$, $R_2 = H$
5c; $R_1 = H$, $R_2 = OMe$

a) see table 2

15a; $R_1 = R_2 = H$, $R_3 = Et$
15b; $R_1 = OMe$, $R_2 = H$, $R_3 = Et$
15c; $R_1 = H$, $R_2 = OMe$, $R_3 = Et$
ent-**15d**; $R_1 = H$, $R_2 = OMe$; $R_3 = Me$
15e; $R_1 = OMe$, $R_2 = H$, $R_3 = Me$

14a; $R_1 = R_2 = H$, $R_3 = Me$
14b; $R_1 = OMe$, $R_2 = H$, $R_3 = Me$
14c; $R_1 = H$, $R_2 = OMe$, $R_3 = Me$
ent-**14d**; $R_1 = H$, $R_2 = OMe$; $R_3 = H$
14e; $R_1 = OMe$, $R_2 = H$, $R_3 = H$

Scheme 1

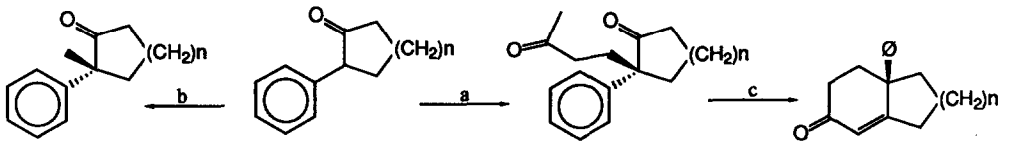
Table 2 : Enantioselective Robinson annelation of the tetralones 5a,b,c with ethyl- or methylvinylketone[a].

entry	substr.	reagent/eq.	cat.[b]	temp.°C[c]	conc.[d]	% Y	% ee[e]	prod.
1	**5c**	EVK/2	B'	-20	0.1	77	60(S)	**14c**
2	**5c**	EVK/1.5	B'	-20	0.02	75	62(S)	**14c**
3	**5c**	EVK/1.5	B'	-45	0.05	81	81(S)	**14c**
4	**5c**	EVK/1.5	B	-45	0.05	70	73(S)	**14c**
5	**5c**	EVK/1.5	A	-45	0.05	66	69(R)	ent-**14c**
6	**5c**	EVK/1.5	A'	-45	0.05	85	73(R)	ent-**14c**
7	**5c**	EVK/2	(f)	rt	0.1	86	0	±**14c**
8	**5b**	EVK/1.5	B'	-45	0.05	77	70(S)	**14b**
9	**5a**	EVK/1.5	B'	0	0.05	64	77(S)	**14a**
10	**5b**	MVK/1.5	B'	-45	0.05	50	61(S)	**14e**
11	**5c**	MVK/1.5	A'	-45	0.05	65	63(R)	ent-**14d**

(a) under Ar, in toluene, 60 % aq. KOH; (b) 0.1 eq.; (c) temp. for 1,4-addition then rt then adding of 18-Crown-6; (d) mol/l; (e) determined by ^1H NMR in C_6D_6 in the presence of $Eu(hfc)_3$, base-line separation of the substituent at C_1; (f) TEBA, 0.2 eq.

Initial experiments with benzyltriethylammonium bromide (TEBA) as catalyst showed fast 1,4-addition. The subsequent aldol reaction took several hours while the β- elimination required several days under the phase transfer conditions. However the 3-step process could be completed within 12 h when 60% potassiumhydroxide was used and when 0.1 eq. 18-Crown-6 was added after 30 min (Table 2, entry 7). With the chiral catalysts the 1,4-addition was carried out at the temperatures indicated, the ring closure and β-elimination, after adding 18-Crown-6, was then allowed to proceed at room temperature (12 h). With **5b** and **5c**, the 1,4-addition was complete within 45 min. at -45°C. For the less reactive **5a** , the addition only started at 0°C (entry 9). The enantioselectivity increased substantially with higher dilution and at lower temperatures (entries 1, 2 and 3). Under identical reaction conditions, a slight but consistent superiority of the cinchonidinium-catalysts (**B**-type) over the cinchonium-catalysts (**A**-type) was observed (compare entries 3,4 with 5,6);the best enantioselectivity was found with the dihydro-catalysts **A'** and **B'**. Again the enantioselectivity observed can be explained by assuming π-π-interaction of the substrate with the p-trifluoromethyl-phenyl ring of the respective catalysts (Fig. 3a and 3b).

The results obtained with the non-fused carbonyl compounds are shown in table 3 and scheme 2.



(R) - **16**; n = 1 **6**; n = 1 (S) - **18**; n = 1 (R) - **20**; n = 1
(R) - **17**; n = 2 **7**; n = 2 (S) - **19**; n = 2 (R) - **21**; n = 2

a) see table 3, entries 6 - 8; b) see table 3, entries 1 and 2;
c) (R) - **20** : toluene, p. TosOH, 111°C (30%); (R)- **21** : id. (82%)

Scheme 2

Table 3 : Enantioselective alkylation of nonfused substrates 6, 7, 8 and 9[a].

entry	substr.	reagent[b]	cat.[c]	temp.°C	time	% Y	% ee[d]	prod.
1	**6**	MeBr	B'	rt	12 h	75	36(R)	**16**
2	**7**	MeBr	B'	rt	2 days	45	13(R)	**17**
3	**6**	MVK	B'	-20	1 h	42	78(S)	**18**
4	**6**	MVK	B'	-45	1 h	75	84(S)	**18**
5	**7**	MVK	B	-20	2.5 h	84	85(S)	**19**
6	**7**	MVK	B'	-20	2.5 h	62	87(S)	**19**
7	**7**	MVK	A	-20	2.5 h	72	74(R)	ent-**19**
8	**7**	MVK	A'	-20	2.5 h	69	78(R)	ent-**19**
9	**8**[e]	MVK	B'	-20	1 h	100	7(R)	
10	**9**	MVK	B'	rt	4 h	35	4	

(a) under Ar, in toluene, 60 % aq. KOH, conc. 0.02 mol/l; (b) 0.2 eq.; (c) 0.1 eq.; (d) determined by ^{1}H NMR in C_6D_6 in the presence of Eu(hfc)$_3$, base-line separation of the methylgroup; (e) 0.1 mol/l.

With the same substrate, methylation was slower than 1,4-addition (entries 1-4 and 2-6) and needed rt. For the 1,4-addition with cyclopentanone **6**, the yield and % ee increased substantially upon lowering the temperature (optimum at -45°C; entry 4). The cyclohexenone **7** only reacted at -20°C, very good enantioselectivities were however observed (entries 5, 6, 7 and 8). Also with these two substrates, catalysts of the **B**-type were slightly superior, again with a preference for the hydrogenated ones **A'** and **B'**. The acyclic ketone **9** was studied in order to obtain insight in the allowed degree of flexibility in a substrate; as seen in entry 10, a low % ee is found. Also the lactone **8** is not a substrate for enantioselective 1,4-additions (entry 9). Apparently the thermodynamically less stable enolate anion of **8** does not form an ion-pair with the catalyst but reacts directly with the enone as a high chemical yield is observed. Lactone **8** was originally chosen as a substrate because it could have provided an intermediate for an asymmetric synthesis of (-)-mesembrine[13].

In contrast to the tetralones, the ketones **6** and **7** gave no annulation in a one pot process. Subsequent aldol condensation of the diketones (S)-**18** and (S)-**19**, under acidic conditions[14], led to the enones (R)-**20** and (R)-**21**; the absolute configurations of the latter were determined from their CD-spectra[15]. Consequently, the precursor 1,5-diketones have the S-configuration, in agreement with the previously observed enantiospecificity. The results observed for substrates **6** and **7** are slightly better than found for the tetralones **5**. This indicates that both E and Z enolate anions can be accomodated in the tight ion-pair (Fig. 3).

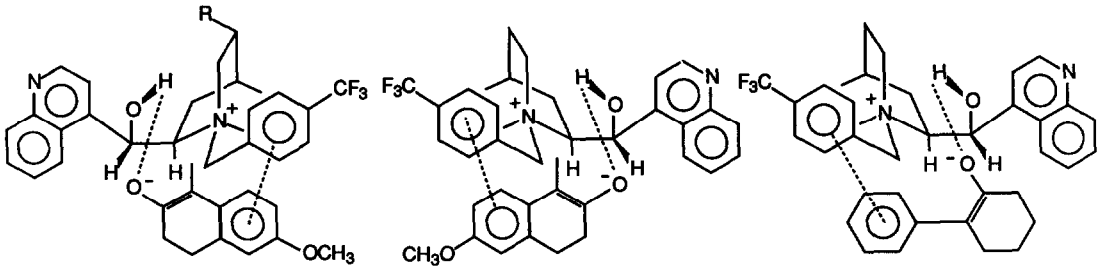
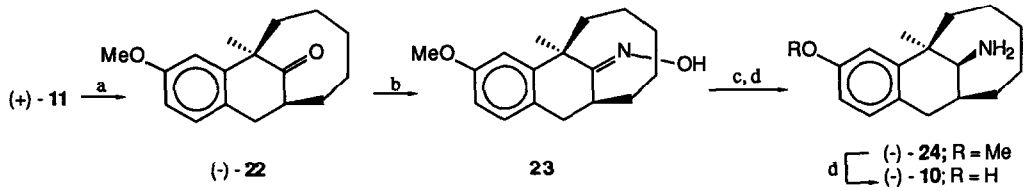


Figure 3

However the enolates of the 2-phenyl-cycloalkanones **6** and **7** are, compared to the aromatic ketone **3** (Fig.1), better nucleophiles in 1,4-additions. This indicates that π-π interaction of the substrate with the N-benzyl ring of the catalyst could be more important than with the quinoline nucleus.

Asymmetric synthesis of (-)-Wy-16.225 (10) (Scheme 3).



a) NaH, THF, Δt (86%); b) NH_2OH, MeOH, mol. sieves, 65°C(66%); c) Raney-Ni W7, NH_4OH, EtOH, H_2 (4 bar), 50°C, 2d (92%); d) BBr_3, CH_2Cl_2 (83%).

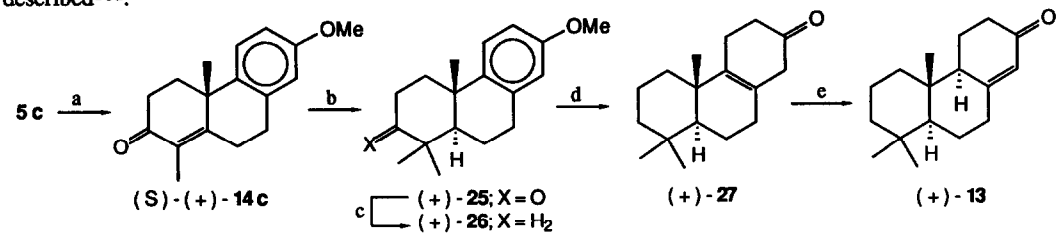
Scheme 3

The procedure followed, with some slight modifications, the one described for the racemate[16]. The alkylated tetralone (+)-**11** (Table 1, entry 3) was transformed into the crystalline tricyclic ketone (-)-**22** which was enantiomerically enriched upon recrystallization from hexane until constant rotation was reached. The enantiomeric purity could, at this stage, not be determined by chiral shift reagents. Formation of the oxime **23** and subsequent reduction afforded the amine (-)-**24** as the only epimer. At this stage the % ee was determined by the method of Mosher[17]; the MTPA-amide was shown to have a de of 98 %. The amine (-)-**24** has previously been obtained by resolution of the racemate via crystallization of the tartate salts[16]. The identical sign of rotation proves the absolute configuration of **11** (table 1, entry 3). Finally, cleavage of the aromatic methyl ether afforded the target molecule (-)-**10**.

Asymmetric synthesis of (+)-podocarp-8(14)-en-13-one (13) (Scheme 4).

Both enantiomers of the tricyclic enone **13** are important key-intermediates in the synthesis of several diterpenes of classes characterized by a 1,1,4a-trimethyl substitution in a perhydrophenanthrene or perhydronaphthalene skeleton[12]. They can be obtained as degradation products of naturally occuring diterpenes and have as such frequently been used in relay syntheses[18a]. One of the main sources of (+)-**13** is abietic acid from which it is obtained in nine steps[18b]. The (-)-**13** is obtainable from the rare *ent*-labdane diterpene,

eperuic acid[18c]. Next to several total syntheses of the racemate, one asymmetric synthesis of (+)-**13** starting from (-)-α-cyclogeranylic acid, involving a nonstereoselective Friedel-Craft cyclization step, has been described[18d].



a) toluene, 60 % aq. KOH, 0.1 eq. cat. **B'**, EVK, -45°C; then 18-Crown-6, 20°C (81 %, 81 % ee); b) Li, n.BuOH, THF, NH_3, -33°C; then MeI (57 %); c) $TosN_2H_3$, MeOH; then $NaBH_4$, i.PrOH (74 %); d) Li, t.BuOH, THF, NH_3, -33°C;then THF, pentane, 50 % aq. H_3PO_4 (82 %); e) HCl, MeOH, 65°C (75 %).

Scheme 4

The asymmmetric Robinson annulation on substrate **5c**, described in Scheme 1 and Table 2 (entry 3), afforded (+)-**14c** in 81 % ee. During purification of (+)-**14c** it was observed that in hexane/EtOAc 8:2 the racemate crystallizes out preferentially; the mother liquid contained enriched (+)-**14c** (93 % ee). Reductive methylation[19] of the enone moiety led to the trans dimethyl ketone **25** next to the cis- fused isomer (10 %) as an unseperable mixture. Both isomers were subjected to the reductive removal of the carbonyl group via the tosylhydrazone; recrystallization from methanol not only allowed to obtain pure trans-isomer but also increased the enantiomeric purity of (+)-**26** to 98 % ee. The Birch reduction and subsequent hydrolysis of the methyl enolether gave (+)-podocarp-8-en-13-one **27**. Finally, acid catalyzed isomerization led to the conjugated target molecule (+)-**13**; its formation allowed the determination of the preferred absolute configurations obtained during the chiral phase transfer catalyzed asymmetric Robinson annulation (Table 2).

The above described results obtained on α-aryl substituted ketones expand the scope of the applications of the chiral phase transfer catalysts based on the quaternized chinchona alkaloids as originally described by Dolling and collaborators. We hope to have shown that next to indanones, previously described as substrates, also selected α-aryl substituted ketones can yield 2,2-dialkyl-2-aryl ketones with comparable enantioselectivities.

EXPERIMENTAL SECTION

All reactions were carried out under argon atmosphere with magnetic stirring unless otherwise specified. "Work-up" means drying on anh. $MgSO_4$, filtration and evaporation of the solvent in vacuo. Column chromatography was performed on SiO_2. HPLC separations were performed on a Knauer 64 system with RI detection. Rf values are quoted for Merck silicagel 60 GF_{254} plates of thickness 0.25 mm. IR spectra were recorded on a Beckmann IR 4230 spectrometer, mass spectra on a Finnigan 4000 spectrometer or a HP-5988. The ^1H NMR spectra were recorded at 360 or 500 MHz (WH-Brucker), the chemical shifts are expressed in ppm relative to TMS and coupling constants in Hz. Optical rotations were measured with a Perkin-Elmer 141 polarimeter. Melting points are corrected.

(R)-(+)-7-methoxy-1-(5'-bromopentyl)-1-methyl-2-tetralone (11) (Table 1, entry 3).

To a stirred mixture of **5b** (80 mg, 0.42 mmol), N-(p-trifluoromethyl)benzylcinchonidinium bromide (**B**) (22 mg, 0.042 mmol) and 1,5-dibromopentane (290 mg, 1.26 mmol), in toluene (6 ml) was added 50 % aq. NaOH soln (0.6 ml) at 0°C. The mixture was allowed to warm up slowly to rt After two days the aqueous layer was separated and extracted (3 x) with Et_2O (10 ml). Work-up and column chromatography (hexane/EtOAc 9:1) yielded the bromide **12** (102 mg, 71 %). $[\alpha]_D^{20}$ = +37 (c = 2.0, $CHCl_3$), ee = 60 %.

Rf (hexane/EtOAc 8:2) : 0.33. IR (KBr) : 1700, 1610, 1575, 1495, 1450 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) : 7.09 (d, 1H, J = 8.3), 6.80 (d, 1H, J = 2.3), 6.75 (dd, 1H, J = 2.3 and 8.3), 3.28 (s, 3H), 3.30 (t, 2H, J = 6.8), 2.99 (dd, 1H, J = 2.5 and 6.0), 2.97 (d, 1H, J = 6.1), 2.68 (ddd, 1H, J = 6.6, 8.8 and 15.0), 2.56 (ddd, 1H, J = 6.0, 6.0 and 15.0), 2.11 (ddd, 1H, J = 5.5, 11.4 and 13.8), 1.74 (p, 2H, J = 7.0), 1.63 (ddd, 1H, J = 4.8, 12.1 and 13.8), 1.38 (s, 3H), 1.31 (m, 2H), 0.96 (m, 2H). MS : m/z 340 ($M^{+\cdot}$, 10), 338 ($M^{+\cdot}$, 11), 200 (5), 190 (100), 175 (7), 161 (50), 149 (9), 115 (13).

Formation of tricyclic ketone (-)-22.

A soln of (+)-**11** (613 mg, 1.8 mol) in dry THF (30 ml) was added to NaH (130 mg, 50 % dispersion, 2.7 mmol). The mixture was refluxed for 5 h. The excess NaH was destroyed by dropwise addition of water. Work-up and column chromatography (hexane/EtOAc 95:5) afforded the tricyclic ketone **22** (396 mg, 86 %).$[\alpha]_D^{20}$ = -16.6 (c = 1.10, $CHCl_3$) for 60 % ee. It was recrystallized from hexane until constant rotation (5 x); $[\alpha]_D^{20}$ = -28.5 (c = 1.05, $CHCl_3$). M.p. : 95°C. Rf (hexane/EtOAc 8:2) : 0.39. IR (KBr) : 1690, 1610, 1580, 1490, 1475 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) : 7.06 (d, 1H, J = 8.3), 6.80 (d, 1H, J = 2.6), 6.74 (dd, 1H, J = 2.6 and 8.3), 3.82 (s, 3H), 3.05 (dd, 1H, J = 5.7 and 16.0), 2.98 (dd, 1H, J = 4.6 and 16.0), 2.76 (m, 1H), 2.41 (ddd, 1H, J = 2.5, 8.2 and 14.4), 1.89 (dddd, 1H, J = 3.4, 9.1, 9.1 and 14.4), 1.74 (m, 2H), 1.56 (m, 4H), 1.36 (s, 3H), 1.30 (m, 2H). MS : m/z 258 ($M^{+\cdot}$, 100), 215 (8), 201 (22), 189 (48), 173 (22), 159 (13), 145 (10), 178 (11), 115 (17). Anal. found C, 79.03; H, 8.56 : $C_{17}H_{22}O_3$ requires C, 79.03; H, 8.58.

Formation of oxime 23.

A soln of NH_2OH was prepared by mixing the hydrochloride (655 mg, 9.42 mmol) and NaOAc (772 mg, 9.42 mmol) in MeOH (10 ml). The solids were filtered off and ketone **22** (122 mg, 0.47 mol) and 3 Å molecular sieves (20 mg) were added. After reflux for 5 h the soln was filtered and concentrated in vacuo. The residue was taken in water (10 ml) and extracted (3 x) with Et_2O (30 ml). Work-up and column chromatography (hexane/EtOAc 9:1) yielded the oxime **23** (85 mg, 66 %) in a 5 to 1 E/Z mixture. Rf (hexane/EtOAc 8:2) : 0.33. For spectral analysis, a single isomer was obtained upon crystallization from i.PrOH. (m.p. 168°C). IR (KBr) : 3400-3000, 1600, 1450, 1370, 1350 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) : 9.03 (s, 1H), 7.04 (d, 1H, J = 8.24), 6.85 (d, 1H, J = 2.6), 6.70 (dd, 1H, J = 2.6 and 8.2), 3.80 (s, 3H), 2.99 (dd, 1H, J = 7.3 and 16.0), 2.85 (dd, 1H, J = 7.7 and 16.0), 2.32 (m, 1H), 2.12 (m, 1H), 1.57 (m, 8H), 1.42 (m, 1H). MS : m/z 273 ($M^{+\cdot}$, 74), 256 (100), 202 (7), 186 (15), 174 (20), 159 (11), 120 (9), 115 (13). Anal. found C, 74.76; H, 8.46; N, 5.14 : $C_{17}H_{23}O_2N$ requires C, 74.69; H, 8.48; N, 5.12.

Formation of the amine (-)-24.

A mixture of **23** (100 mg, 0.366 mmol), NH_4OH (1 ml) and a cat. amount of freshly prepared Raney-Ni W7 in EtOH (4 ml) was kept under hydrogen at 4 bar and 50°C for 2 d. The catalyst was filtered and the solvent was removed in vacuo. Column chromatography (hexane/EtOAc/Et_3N 300:100:5) gave the pure β-amine (-)-**24** (86 mg, 92 %). The hydrochloride showed $[\alpha]_D^{rt}$ = -50.5 (c = 2.8, MeOH); lit[16] $[\alpha]_D^{25}$ = -46 (c = 3, MeOH). Rf (hexane/EtOAc/Et_3N 6:4:0.25) : 0.26. IR (KBr) : 1620, 1600, 1570, 1490, 1460, 1380 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) : 6.91 (d, 1H, J = 2.6), 6.84 (d, 1H, J = 8.3), 6.64 (dd, 1H, J = 2.6 and 8.3), 3.37 (s, 3H), 2.82 (dd, 1H, J = 5.0 and 15.6), 2.44 (dd, 1H, J = 2.4 and 15.6), 2.11 (dd, 1H, J = 2.7 and 14.4), 1.2-1.75 (m, 13H). MS : m/z 257 (100), 228 (9), 214 (12), 200 (30), 189 (49), 186 (56), 173 (49), 149 (18), 121 (15), 115 (32).

(-)-Wy-16.225 (10).

To a soln of (-)-**24** (10 mg, 0.386 mmol) in CH_2Cl_2 (0.5 ml) at -20°C, BBr_3 in CH_2Cl_2 (1 M soln, 0.120 ml, 1.16 mmol) was slowly added. The mixture was then allowed to warm up slowly to rt. After 12 h water (1 ml) was dropwise added and the mixture was further stirred for 1.5 h. The aqueous layer was separated and NH_4OH was added. Extraction with Et_2O (3 x), work-up and HPLC (hexane/EtOAc 1:1 + 0.5 % conc. aq. NH_3 soln) afforded (-)-**10** (7.8 mg, 83 %). The hydrobromide showed $[\alpha]_D^{rt}$ = -56 (c = 0.91, MeOH); lit[16] $[\alpha]_D^{rt}$ = -41.7 (c = 3, MeOH). Rf (hexane/EtOAc 1:1 + 0.5 % conc. aq. NH_3 soln) : 0.17. IR (KBr) : 3600-2600, 1630, 1600, 1580, 1500, 1460, 1440 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) : 6.78 (d, 1H, J = 8.1), 6.70 (d, 1H, J = 2.2), 6.64 (dd, 1H, J = 2.2 and 8.1), 2.76 (dd, 1H, J = 5.4 and 15.5), 2.42 (dd, 1H, J

= 2.6 and 15.5), 2.09 (dd, 1H, J = 5.2 and 13.0), 1.2-1.65 (m, 13H). MS : m/z 243 (72), 226 (12), 214 (12), 200 (13), 186 (40), 174 (50), 172 (72), 159 (36), 145 (22), 131 (22), 115 (25).

(S)-(+)-2,3,4,4a,9,10-hexahydro-7-methoxy-1,4a-dimethyl-2-oxophenanthrene (14c) (Table 2, entry 3).

To a stirred mixture of **5c** (200 mg, 1.05 mmol) and N-(p-trifluoromethyl)benzyldihydrocinchonidinium bromide (**B'**) (56 mg, 0.105 mmol) in toluene (20 ml) at 0°C, was added a 60 % aq. KOH soln (0.53 ml). The mixture was cooled to -45°C; after 30 min ethylvinylketone (132 mg, 1.58 mmol) was added. After stirring 1 h at -45°C and 12 h stirring at rt, 18-Crown-6 (29 mg, 0.105 mmol) was added and stirring was continued for 12 h. The aqueous layer was separated and the organic phase washed with a soln of 100 mg citric acid in 2 ml water. The aqueous layers were extracted with toluene (10 ml). Work-up and HPLC (hexane/EtOAc 9:1) yielded (S)-(+)-**14c** (221 mg, 81 %). $[\alpha]_D^{23}$ = +142 (c = 2.21, $CHCl_3$), ee = 81 %. Rf (pentane/Et_2O 6:4) : 0.28. IR (KBr) : 1640, 1600, 1490, 1460, 1440, 1410 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) : 7.21 (d, 1H, J = 8.7), 6.80 (dd, 1H, J = 2.7 and 8.7), 6.65 (d, 1H, J = 2.7), 3.79 (s, 3H), 2.98 (ddd, 1H, J = 4.3, 4.8 and 15.7), 2.87 (ddd, 1H, J = 4.8, 4.8 and 14.2), 2.81 (ddd, 1H, J = 4.8, 10 and 15.7), 2.72 (ddd, 1H, J = 5.2, 14.8 and 17.6), 2.54 (ddd, 1H, J = 2.4, 4.8 and 17.6), 2.51 (dddd, 1H, J = 1, 4.2, 10 and 14.2), 2.35 (ddd, 1H, J = 2.4, 5.2 and 13), 2.03 (dddd, 1H, J = 1, 4.8, 13 and 14.8), 1.84 (s, 3H), 1.50 (s, 3H). MS : m/z 256 ($M^{+\cdot}$, 25), 241 (100), 213 (20), 185 (4), 165 (4), 153 (5), 141 (6), 115 (9). Anal. found C, 79.08; H, 7.85: $C_{17}H_{20}O_2$ requires C, 79.65; H, 7.86.
Recrystallization in hexane/EtOAc 8:2 ((1.8 g in 8 ml) gave racemic crystals. The mother liquid was concentrated in vacuo and the residue purified by HPLC (same eluent as the solvent for recrystallization) yielding (S)-(+)-**14c** (1.475 g) in 92 % ee (m.p. 65°C). $[\alpha]_D^{23}$ = +163 (c = 2.95, $CHCl_3$).3

Ent-14c (Table 2, entry 6) was prepared as described for (S)-(+)-**14c** but with N-(p-trifluoromethyl) benzyldihydrocinchonium bromide (**A'**) (yield 85 %). $[\alpha]_D^{23}$ = -128 (c = 2.32, $CHCl_3$), ee = 73 %.

(S)-(+)-2,3,4,4a,9,10-hexahydro-6-methoxy-1,4a-dimethyl-2-oxophenanthrene (14b).

As described for (+)-**14c**, **5b** gave (S)-(+)-**14b** (yield 77 %). $[\alpha]_D^{22}$ = +181 (c = 2.09, $CHCl_3$), ee = 70 %. Rf (pentane/Et_2O 6:4) : 0.43. IR (KBr) : 1655, 1600, 1750, 1495 cm^{-1}. ^1H NMR (360 MHz, C_6D_6) : 6.84 (d, 1H, J = 8.3), 6.7 (d, 1H, J = 2.6), 6.64 (dd, 1H, J = 2.56 and 8.3), 3.39 (s, 3H), 2.56 (ddd, 1H, J = 5.7, 5.7 and 15.8), 2.41 (m, 4H), 2.04 (m, 1H), 1.87 (s, 3H), 1.81 (ddd, 1H, J = 3.1, 4.8 and 13.1), 1.72 (ddd, 1H, J = 8.2, 11.2 and 11.5), 1.12 (s, 3H). MS : m/z 256 ($M^{+\cdot}$, 62), 241 (100), 225 (11), 213 (36), 119 (10), 185 (13), 171 (13), 165 (12), 153 (13), 141 (14), 128 (16), 115 (18).

(S)-(+)-2,3,4,4a,9,10-hexahydro-1,4a-dimethyl-2-oxophenanthrene (14a).

As described for (+)-**14c** but at 0°C, **5a** gave (+)-**14a** (yield 64 %). $[\alpha]_D^{22}$ = +167 (c = 1.52, $CHCl_3$), ee = 77 %. Rf (pentane/Et_2O 7:3) : 0.38. IR (KBr) : 1650, 1615, 1590, 1490, 1450, 1410 cm^{-1}. ^1H NMR (360 MHz, C_6D_6) : 7.08 (ddd, 1H, J = 1, 7.5 and 7.5), 7.01 (ddd, 1H, J = 1, 7.5 and 7.5), 6.95 (dd, 1H, J = 1 and 7.5), 6.85 (dd, 1H, J = 1 and 7.5), 2.55 (ddd, 1H, J = 4.8, 7.2 and 15.9), 2.40 (m, 4H), 2.01 (m, 1H), 1.85 (s, 3H), 1.84 (ddd, 1H, J = 2.9, 4.8 and 13.1), 1.67 (ddd, 1H, J = 7.2, 12.7 and 12.7), 1.12 (s, 3H). MS : m/z 226 ($M^{+\cdot}$, 66), 211 (100), 198 (13), 183 (59), 169 (48), 155 (27), 141 (40), 128 (33), 115 (35).

(+)-13-methoxy-podocarpa-8,11,13-trien-3-one (25).

A soln of Li (82.1 mg, 11.7 mmol) in liq. NH_3 (100 ml) was stirred for 15 min, then a soln of (S)-(+)-**14c** (1.3 g, 5.1 mmol) and n.BuOH (420 ml, 4.6 mmol) in THF (50 ml) was added over 5 min. After reflux for 2 min a soln of MeI (3.62 g, 25.5 mmol) in THF (5 ml) was added; after reflux for 2 h the solvent was removed in vacuo. The residue was taken in Et_2O (50 ml), water (10 ml) and citric acid (1 g). After stirring for 5 min the aqueous layer was separated and extracted with Et_2O (2 x 20 ml). Work-up and HPLC (hexane/EtOAc 9:1) afforded (+)-**25** (792 mg, 57 %), contaminated with 10% of the unseparable cis-isomer. Rf (hexane/EtOAc 9:1) : 0.20. IR (KBr) : 1700, 1605, 1495, 1460, 1380 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) : 7.17 (d, 1H, J = 8.7), 6.73 (dd, 1H, J = 2.7 and 8.7), 6.59 (d, 1H, J = 2.7), 3.77 (s, 3H), 2.94 (ddd, 1H, J = 2.2, 5.7 and 17.5), 2.86 (ddd, 1H, J = 7, 11 and 17.5), 2.69 (ddd, 1H, J = 7.5, 10 and 15.9), 2.58 (ddd, 1H, J = 4.0, 5.6 and 15.9), 2.46 (ddd, 1H, J = 4.0, 7.5 and 19.1), 1.92 (ddd, 1H, J = 7.6, 10 and

13.1), 1.90 (dd, 1H, J = 2.9 and 11.3), 1.8 (m, 2H), 1.28 (s, 3H), 1.16 (s, 3H), 1.14 (s, 3H). MS : m/z 272 ($M^{+\cdot}$, 53), 257 (100), 215 (65), 202 (12), 187 (7), 173 (22), 159 (15), 147 (14), 115 (11).

(+)-13-methoxy-podocarpa-8,11,13-triene (26).

A soln of (+)-**25** (600 mg, 2.2 mmol) and tosylhydrazine (450 mg, 2.4 mmol) in MeOH (3 ml) was refluxed for 1 h. The solvent was removed in vacuo and the residue taken in i.PrOH (6 ml), and sodiumborohydride (125 mg, 3.3 mmol) was added in 3 portions. The mixture was refluxed for 4 h , brought to rt and MeOH (1 ml) was carefully added. After evaporation of the solvent in vacuo the residue was taken in toluene (10 ml) and water (10 ml). The aqueous phase was separated and extracted with toluene (2x). Work-up and column chromatography (hexane/EtOAc 9.5:0.5) and HPLC (hexane/Et_2O 98:2) yielded (+)-**26** (422 mg, 74 %) accompanied by 10% cis-isomer. Recrystallization from MeOH gave pure (+)-**26** (251 mg) in 98 % ee. m.p. : 85°C; rac. 75°C. $[\alpha]_D^{21}$ = +52.6 (c = 2.00, $CHCl_3$); lit[18d] $[\alpha]_D^{rt}$ = +53.9. Rf (pentane/Et_2O 9:1) : 0.62. IR (KBr) : 1610, 1580, 1500, 1450, 1375 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) : 7.17 (d, 1H, J = 8.7), 6.70 (dd, 1H, J = 2.4 and 8.7), 6.57 (d, 1H, J = 2.4), 3.77 (s, 3H), 2.92 (ddd, 1H, J = 2, 7.0 and 17.7), 2.84 (ddd, 1H, J = 7.4, 11.2 and 17.7), 2.26 (dddd, 1H, J = 1.3, 3, 3.5 and 12.9), 1.87 (dddd, 1H, J = 2, 2.2, 7.4 and 13.2), 1.74 (ddddd, 1H, J = 3.5, 3.5, 13.5, 13.6 and 13.8), 1.70 (dddd, 1H, J = 7.0, 11.2, 12.6 and 13.2), 1.60 (ddddd, 1H, J = 3, 3.7, 4, 4.0 and 13.8), 1.48 (dddd, 1H, J = 1.3, 3.5, 4 and 13.3), 1.37 (ddd, 1H, J = 3.7, 12.9 and 13.5), 1.32 (dd, 1H, J = 2.2 and 12.6), 1.22 (ddd, 1H, J = 4.0, 13.3 and 13.6), 1.77 (s, 3H), 0.95 (s, 3H), 0.93 (s, 3H). MS : m/z 258 ($M^{+\cdot}$, 33), 243 (100), 187 (11), 173 (26), 161 (20), 147 (30), 115 (9).

(+)-podocarp-8-en-13-one (27).

To a soln of (+)-**26** (200 mg, 0.775 mmol), t.BuOH (5 ml) and THF (5 ml) in refluxing liq. NH_3 (10 ml), Li (54.3 mg, 7.75 mmol) was added in 3 portions. After 2 h water (0.5 ml) was added and after removal of the solvent in vacuo the residue was taken in THF (10 ml), pentane (10 ml) and water (20 ml). The aqueous layer was separated, the organic layer washed with water (2 ml) and 50 % aq. H_3PO_4 (2 ml) was added. The mixture was stirred at rt for 3 h. Work-up and column chromatography (hexane/EtOAc 95:5) gave (+)-podocarp-8-en-13-one **27** (156 mg, 82 %). $[\alpha]_D^{30}$ = +173 (c = 2.3, $CHCl_3$); lit[18d] $[\alpha]_D^{30}$ = +176 (c = 2.28, $CHCl_3$). Rf (pentane/Et_2O 9:1) : 0.33. IR (KBr) : 1720, 1630, 1610, 1460, 1440 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) : 2.73 (d, 1H, J = 20.7), 2.66 (d, 1H, J = 20.7), 2.38 (m, 4H), 1.96 (m, 2), 1.78 (dddd, 1H, J = 1.3, 3.3, 3.4 and 12.8), 1.72 (dddd, 1H, J = 2, 2.9, 5.3 and 13.2), 1.62 (ddddd, 1H, J = 3.4, 3.5, 13, 13 and 13.7), 1.49 (dddd, 1H, J = 7.4, 10.6, 12.8 and 13.2), 1.49 (ddddd, 1H, J = 3.3, 3.4, 3.7, 4.3 and 13.7), 1.42 (dddd, 1H, J = 1.3, 3.4, 3.5 and 13), 1.17 (dd, 1H, J = 1.5 and 12.8), 1.16 (ddd, 1H, J = 4.3, 13 and 13), 1.08 (ddd, 1H, J = 3.8, 13 and 13), 1.02 (s, 3H), 0.90 (s, 3H), 0.86 (s, 3H). MS : m/z 246 ($M^{+\cdot}$, 45), 231 (52), 161 (33), 149 (32), 135 (36), 124 (63). Anal. found C, 82.65; H, 10.13 : $C_{17}H_{26}O$ requires C, 82.87; H, 10.64.

(+)-podocarp-8(14)-en-13-one (13).

A soln of (+)-**27** (47 mg, 0.192 mmol) and 37 % aq. HCl (0.6 ml) in MeOH (1.5 ml) was refluxed for 1 h. After dilution with water (3 ml) the mixture was extracted twice with Et_2O (10 ml). The combined organic layers were washed with sat. $NaHCO_3$ soln. Work-up and column chromatography and HPLC (hexane/EtOAc 8:2) yielded enone (+)-**13** (35 mg, 75 %). m.p : 54°C; rac. 90°C. $[\alpha]_D^{26}$ = +38.6 (c = 1.10, $CHCl_3$); lit[18d] $[\alpha]_D^{26}$ = +39 (c = 1.10, $CHCl_3$). Rf (pentane/Et_2O 9:1) : 0.09. IR (KBr) : 1660, 1615, 1465, 1370 cm-1. ^1H NMR (500 MHz, $CDCl_3$) : 5.87 (t, 1H, J = 2.2), 2.85 (ddd, 1H, J = 1.8, 4.8 and 15.6), 2.39 (dddd, 1H, J = 0.6, 4.5, 4.5 and 15.9), 2.28 (m, 1H), 2.20 (ddd, 1H, J = 5.50, 13.8 and 15.9), 2.07 (m, 1H), 1.99 (dddd, 1H, J = 4, 5.5, 5.5 and 13.5), 1.73 (m, 3H), 1.47 (m, 4H), 1.21 (ddd, 1H, J = 5.0, 12.6 and 12.6), 1.16 (dd, 1H, J = 2.7 and 12.6), 1.10 (ddd, 1H, J = 4.9, 12.3 and 12.3), 0.92 (s, 3H), 0.87 (s, 3H), 0.80 (s, 3H). MS : m/z 246 ($M^{+\cdot}$, 17), 231 (6), 149 (33), 137 (67), 123 (75), 110 (100).

Enone (R)-(+)-21 (Tabel 3, entry 6).

To a stirred mixture of **7** (348 mg, 2 mmol) and N-(p-trifluoromethyl)benzyldihydrocinchonidinium bromide (**B'**) (106 mg, 0.2 mmol), in toluene (20 ml), a 60 % aq. KOH soln (1 ml) was added. After 5 min the mixture was cooled to -20°C and methylvinylketone (260 mg, 4 mmol) was slowly added during 30 min and stirring was continued for 30 min. The aqueous layer was separated and the organic layer was washed (2 x) with a soln of citric acid (100 mg) in water (2 ml). The combined aqueous layers were extracted with toluene

(2 x, 10 ml). Work-up and column chromatography and HPLC (hexane/EtOAc 8:2) afforded (+)-**19** (264 mg, 56 %). $[\alpha]_D^{19}$ = +157 (c = 2.64, $CHCl_3$), ee = 87 %. Rf (pentane/Et_2O 6:4) : 0.25. IR (KBr) : 1700, 1590, 1575, 1490, 1445 cm^{-1}. ^1H NMR (360 MHz, C_6D_6) : 7.09 (m, 2H), 7.01 (m, 1H), 6.94 (m, 2H), 2.14 (m, 5H), 1.93 (m, 2H), 1.60 (s, 3H), 1.42 (m, 1H), 1.27 (m, 2H). MS : m/z 226 ($M^{+\cdot}$, 10), 151 (10), 145 (51), 129 (17), 117 (13), 115 (18).
A soln of (+)-**19** (50 mg, 0.221 mmol; ee 87 %) and p-TsOH (10 mg) in toluene (20 ml) was refluxed for 1 h with azeotropic removal of water. The organic layer was extracted (2x) with sat.aq. $NaHCO_3$ soln (2 x, 20 ml) which was then extracted with toluene (10 ml). Work-up and column chromatography and HPLC (hexane/EtOAc 9:1) yielded enone (+)-**21** (38 mg, 82 %). Rf (hexane/ether 6:4) : 0.39. CD : $\Delta\varepsilon_{232}$ = +24.32, $\Delta\varepsilon_{203}$ = +7.26 (c = 0.960 mmol/l, MeCN). $[\alpha]_D^{20}$ = +214 (c = 1.9, $CHCl_3$). IR (KBr) : 1665 1615, 1490, 1440 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) : 7.36 (m, 2H), 2.25 (m, 3H), 6.11 (s, 1H), 2.62 (m, 1H), 2.33 (m, 2H), 2.12 (m, 3H), 1.96 (m, 1H), 1.80 (m, 1H), 1.60 (m, 2H), 1.49 (m, 1H), 1.30 (m, 1H). MS : m/z 226 ($M^{+\cdot}$, 100), 211 (12), 198 (49), 184 (90), 169 (91), 155 (33), 141 (94), 128 (41).

Enone (R)-(+)-20 (Table 3, entry 4).

As described for (+)-**21** via (+)-**18**. (+)-**18**; $[\alpha]_D^{20}$ = +56.9 (c = 1.95, $CHCl_3$), ee = 84 %. Rf (pentane/Et_2O 6:4) : 0.22. IR (KBr) : 1730, 1710, 1595, 1580, 1490 cm^{-1}. ^1H NMR (360 MHz, C_6D_6) : 7.29 (m, 2H), 7.12 (m, 2H), 7.02 (m, 1H), 2.22 (m, 1H), 2.11 (m, 1H), 2.04 (m, 1H), 1.87 (m, 3H), 1.47 (m, 1H), 1.47 (s, 1H), 1.35 (m, 3H). MS : m/z 230 ($M^{+\cdot}$, 6), 202 (17), 144 (22), 131 (77), 129 (16), 117 (14). (+)-**21**; $[\alpha]_D^{21}$ = +162 (c = 1.3, $CHCl_3$). CD : $\Delta\varepsilon_{220}$ = +11.28, $\Delta\varepsilon_{200}$ = +20.06 (c = 0.872 mmol/l, MeCN). Rf (pentane/Et_2O 6:4) : 0.40. IR (KBr) : 1670, 1595, 1580, 1490, 1450, 1420 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$) : 2.27 (m, 5H), 6.13 (s, 1H), 2.64 (m, 2H), 2.38 (m, 2H), 2.15 (m, 2H), 1.97 (m, 1H), 1.75 (m, 2H), 1.42 (m, 1H). MS : m/z 212 ($M^{+\cdot}$, 8), 184 (55), 170 (100), 155 (25), 141 (26), 128 (31), 115 (28).

N-(p-trifluoromethyl)benzyldihydrocinchonium bromide (A').

A mixture of dihydrocinchonine (1 g, 3.42 mmol), p-trifluoromethylbenzyl bromide (980 mg, 4.1 mmol) and i.PrOH (0.261 ml) in dichloromethane (20 ml) was refluxed for 2 d. The precipitate was filtered and recrystallized from n.BuOH (2 x, 20 ml), yielding catalyst **A'** (1.25 g, 69 %). m.p. : 260°C (decomp.). $[\alpha]_D^{20}$ = +129 (c = 2.0, MeOH). Rf ($CHCl_3$/MeOH/acetone/aq. 25 % NH_3 60:20:20:1)) : 0.56. IR (KBr) : 3240-3080, 2940, 2860, 1610, 1580, 1560, 1500, 1450, 1415 cm^{-1}. ^1H NMR (500 MHz, CD_2Cl_2) : 8.80 (d, 1H, J = 4.4), 8.27 (d, 1H, J = 8.2), 7.83 (m, 4H), 7.60 (d, 1H, J = 7.7), 7.44 (d, 1H, J = 7.9), 7.00 (t, 1H, J = 7.1), 6.90 (t, 1H, J = 7.1), 6.71 (d, 1H, J = 5.7), 6.46 (m, 1H), 6.26 (d, 1H, J = 11.9), 5.41 (d, 1H, J = 11.9), 4.16 (m, 1H), 4.06 (t, 1H, J = 9.0), 3.97 (t, 1H, J = 11.8), 3.20 (t, 1H, J = 11.1), 2.63 (q, 1H, J = 11.0), 2.06 (t, 1H, J = 12.5), 1.79-1.57 (m, 3H), 1.47 (m, 2H), 0.82 (t, 3H, J = 6.9), 0.71 (m, 1H). Anal. found C, 59.69; H, 5.50; N, 5.00 : $C_{27}H_{30}O_1N_2Br_1F_3$ requires C, 60.57; H, 5.65; N, 5.23.

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