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OXIDATION OF 1,3-DICARBONYL COMPOUNDS USING (CAMPHORYLSULFONYL)OXAZIRIDINES

Franklin A. Davis,*† Hu Liu,† Bang-Chi Chen‡ and Ping Zhou‡

†Department of Chemistry, Temple University, Philadelphia, PA 19122-2585

‡ Department of Chemistry, Drexel University, Philadelphia, PA 19104

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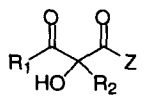
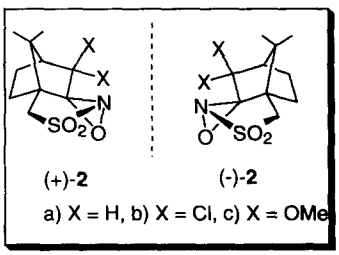
Abstract. The oxidation of 1,3-dicarbonyl compounds with (camphorylsulfonyl)oxaziridines **2** was studied in both cyclic and acyclic systems. Two reaction pathways were identified: enolate α-hydroxylation and a novel Baeyer-Villiger type oxidation. The Baeyer-Villiger oxidation product was observed only for the ketones and arises via rearrangement of an alkoxy epoxide. Synthetically useful ee's (82-95%) were observed only for enolates of β-ketoesters where the keto group is part of a 6-membered ring .

The α-hydroxy-β-dicarbonyl array **1** is a common feature of many biologically relevant molecules including the antibacterial kjellmanianone,[1] the tetracycline antibiotics,[2] indoline alkaloids such as vindoline[3] and α-acetolactate, the biological precursor of valine.[4] In addition, this moiety serves as a valuable intermediate for the asymmetric synthesis of natural products.[5] The hydroxylation of β-dicarbonyl enolates is the most direct approach to this structural unit, and a variety of oxidizing reagents have been employed. These reagents include H_2O_2, *m*-CPBA, molecular and single oxygen, and dimethyldioxirane, each of which have limitations. For example, H_2O_2 requires very high concentrations (98%) for satisfactory yields,[3] and *m*-CPBA's protic nature makes it necessary to prepare the silyl enol ether prior to oxidation.[6] With molecular[7] and single oxygen[8] the yields are often modest and they may not work with open chain substrates. While dimethyldioxirane produces **1** in high yield,[9] an asymmetric version remains undeveloped.



1
Z=OR, R



(+)-**2** (-)-**2**

a) X = H, b) X = Cl, c) X = OMe

* fdavis@astro.ocis.temple.edu (215) 204-0477 (fax)

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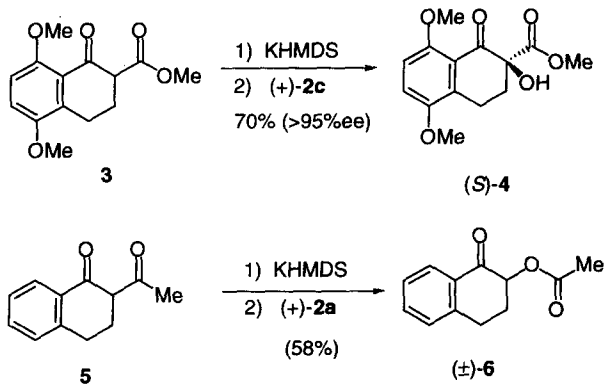
The N-sulfonyloxaziridine class of oxidizing reagents has been widely utilized for the hydroxylation of enolates to α-hydroxy carbonyl compounds.[10] With the nonracemic (camphorylsulfonyl)oxaziridines **2** these hydroxylations can be carried out with high asymmetric induction and predictable stereochemistry.[10] However, there are only a few reports of the application of these reagents to the synthesis of α-hydroxy-β-dicarbonyl compounds **1**.[1a,5] In one example treatment of potassium enolate of **3** with (+)-**2c** afforded α-hydroxy-β-ketoester **4**, a precursor of the AB-ring segment of the antitumor anthracycline antibiotic daunomycin, in 70% yield and >95% ee (Scheme 1).[5a] Unexpectedly, when the related 2-acetyl-1-tetralone (**5**) was treated in a similar fashion racemic 2-acetyloxy-1-tetralone (**6**) was formed in 58% yield. Although the isomerization of α-hydroxy-β-dicarbonyls to α-ketol esters promoted by base or heat is known,[11] methods for the direct Baeyer-Villiger type oxidation of enolizable 1,3-dicarbonyls are rare.[12,13]

Scheme 1

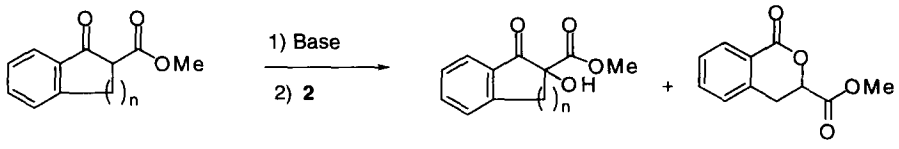


In this article, we describe details of a comprehensive study of the asymmetric hydroxylation of 1,3-dicarbonyl enolates using (camphorylsulfonyl)oxaziridines **2**.

Results

Hydroxylation of Cyclic β-Ketoesters. Cyclic β-keto esters 2-methoxycarbonyl-1-indanone (**7a**), 2-methoxycarbonyl-1-tetralone (**7b**) and 2-methoxycarbonyl-1-benzosuberone (**7c**) were prepared in better than 75% yield by treatment of the corresponding enolates with dimethyl carbonate according to a literature procedure.[14] Typically, hydroxylations were carried out by reacting the kinetic enolates of **7**, with 1.2 equivalents of the appropriate oxaziridine **2** at -78 °C and warming to rt (Scheme 2). After quenching at -78 °C with aqueous NH_4Cl the products were isolated by preparative TLC, identified by comparison with literature values and the ee's determined by using the chiral shift reagent $Eu(hfc)_3$. The absolute configuration of **8b** was established by comparison of its CD with that of (+)-**4**. In addition to the isolated products a considerable amount of highly polar material was obtained that was not characterized. These results are summarized in Table 1.

Scheme 2



7a: n = 1
b: n = 2
c: n = 3

8 **9**

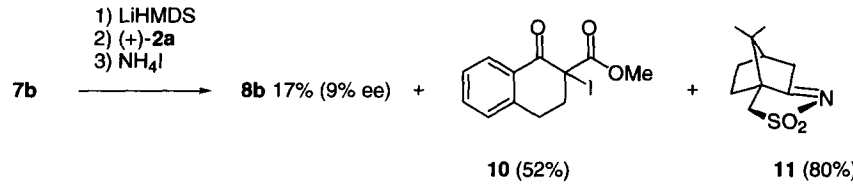
Table 1: Hydroxylation of β-ketoesters **7** using (camphorylsulfonyl)oxaziridine **2** at -78 °C to rt in THF.

entry	β-Ketoester **7**	Base	Oxaziridine **2**	Products	**8**	**9**
				% Isolated yield [% ee (config.)][a]		
1	**7a**: n = 1	LDA	(+)-**2a** (X = H)		59 [0]	< 3
2		LDA	(+)-**2b** (X = Cl)		39 [0]	2
3		LiHMDS	(+)-**2a** (X = H)		24	15
4		NaHMDS			0	24 [0]
5		KHMDS			10	64 [0]
6	**7b**: n = 2	LDA			65 [82 (*S*)]	
7		LDA	(-)-**2a** (X =H)		75 [84 (*R*)]	
8		LiHMDS	(+)-**2a** (X = H)		64 [67 (*S*)]	
9		NaHMDS			65 [76 (*S*)]	
10		KHMDS			76 [9]	
11		LDA	(+)-**2b** (X = Cl)		75 [69 (*R*)]	
12		LDA	(-)-**2b** (X = Cl)		75 [70 (*S*)]	
13		LDA	(+)-**2c** (X = OMe)		55 [5]	
14		NaHMDS	(+)-**2b** (X = Cl)		75 [51 (*R*)]	
15	**7c**: n = 3	LDA	(+)-**2a** (X = H)		62 [18]	
16		LDA	(+)-**2b** (X = Cl)		53 [11]	
17		LDA	(+)-**2c** (X = OMe)		33 [22]	
18		KHMDS			51 [0]	

a) The ee's were determined using $Eu(hfc)_3$ and the absolute configurations were determined by CD.

In earlier studies of enolate hydroxylations using **2** we advocated quenching of the enolate hydroxylation mixture with aq. NH_4I. The purpose was to reduce excess oxaziridine **2** to the (camphorylsulfonyl)imine **11** by-product facilitating isolation.[15] When this protocol was applied to the hydroxylation of **7b**, 2-methoxycarbonyl-2-iodo-1,2,3,4-tetrahydro-1-oxo-naphthalene (**10**) was isolated in 52% yield in addition to a low yield of **8b** (Scheme 3). Undoubtedly I_2, generated by oxidation of I^- by (+)-**2a**, halogenated the relatively stable β-ketoester enolate. Indeed treatment of the lithium enolate of **7b** with I_2 afforded **10** in 56% yield.

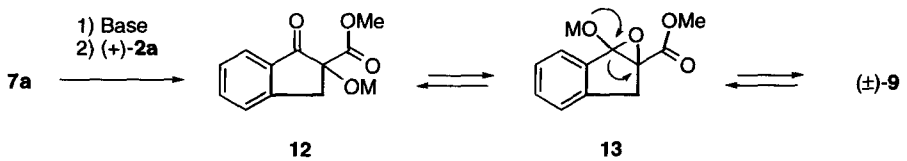
Scheme 3



For the hydroxylation of 2-methoxycarbonyl-1-indanone (**7a**) two products were obtained, the desired 2-methoxycarbonyl-2-hydroxy-2,3-dihydro-1-oxo-1H-indene (**8a**)[16] and a rearranged Baeyer-Villiger type oxidation product 3-methoxycarbonyl-3,4-dihydro-1-oxo-1H-2-benzopyran (**9**). Both compounds were racemic as indicated by chiral shift reagent experiments. As summarized in Table 1 the ratio of these products was highly dependent upon the base. With LDA **7a** gave **8a** in 59% yield (Table 1: entry 1) while at the other extreme KHMDS afforded **9** in 64% yield (Table 1: entry 5). Intermediate amounts of these products were obtained with LiHMDS and NaHMDS (Table 1: entries 3 and 4). It is noteworthy that **9** has previously been used to establish the active site structures of α-chymotrypsin[17a] and subtilisin BPN'.[17b] It was prepared in five steps with an overall yield of 7%.[17c]

The likely mechanism for the formation of **9** involves initial generation of the α-alkoxy β-ketoester anion **12** which rearranges via the alkoxy epoxide **13** (Scheme 4). Intermediates similar to **13** have been proposed for the thermal and base catalyzed rearrangement of α-hydroxy β-diketones.[11] The fact that **9** is racemic is consistent with this hypothesis. Quenching of **12** gives **8a** which is also racemic and may suggest that **8a**, **9**, **12** and **13** are in equilibrium. However, treatment of **8a** with KHMDS resulted in decomposition, whereas KH afforded **9** in 98% yield. Decomposition was the result of reaction of **9** with LDA, and with other hydride reagents recovery of starting material and decomposition occurred. Alternatively, racemic **8a** may result from a lack of chiral recognition between the enolate and oxaziridine (+)-**2a**, however, (+)-**2b** also gave racemic **8a** (Table 1: entry 2). The counter ion effect may be related to the greater ability of lithium to coordinate with the adjacent carbomethoxy group favoring **12**.

Scheme 4



Hydroxylation of the 6- and 7-membered ring systems **7b** and **7c** gave only the corresponding α-hydroxy β-ketoester **8b** and **8c**.[8b] The lack of Baeyer-Villiger rearrangement products for **7b** and **7c** compared to **7a** is most likely due to the thermodynamically unfavorable expansions of the 6 and 7-membered rings to 7- and 8-membered rings, respectively. Another possibility is that the conformations of these larger rings inhibit formation of the related alkoxy epoxide **13** species (Scheme 4).

As previously observed for the asymmetric hydroxylation of enolates, yields and asymmetric induction are highly dependent on the structure of the enolate, and the oxidant, as well as the reaction conditions.[10] An added complication with β-dicarbonyl enolates is that they can exist in several different conformations depending on the reaction conditions.[18] However, intramolecular chelation with the counterion is expected to favor a single enolate geometry. For the enolate of **7b** the best selectivity was observed for the lithium enolate generated using LDA with oxaziridine (+)-**2a** affording (-)-(*S*)-**8b** in 82-84% ee and 65-75 % yield (Table 1: entries 6 and 7). Poorer selectivity was observed for the lithium enolate generated using LiHMDS (Table 1: entry 8) as well as for the sodium and potassium enolates (Table 1: entries 9 and 10). Interestingly, the configuration of **8b** changed from S to R using (+)-(camphorylsulfonyl)oxaziridine (**2a**) and (+)-[(8,8-dichlorocamphoryl)sulfonyl]oxaziridine (**2b**), respectively, despite the fact that these reagents have the same absolute configuration (Table 1: entries 6 and 11). The absolute configurations of (-)-(*S*)-**8b** and (+)-(*R*)-**8b** were established by comparing their CD spectra to those of **4**[5a] (see experimental section). In all cases much poorer ee's, 0-22%, were observed for the 7-membered ring system, **7c** (Table 1: entries 15-18).

The oxidation of commercially available 2-methoxycarbonyl-1-oxo-cyclohexane (**14**) with (-)-**2a** was next explored and the results are summarized in Table 2 (Scheme 5). In this case, the corresponding α-hydroxy-β-ketoester intermediate was reacted with benzoyl chloride in situ to afford (*R*)-(+)-2-methoxycarbonyl-2-benzoyloxy-1-oxo-cyclohexane (**15**) in 49% yield. The ee was determined to be 86% using the chiral shift reagent Eu(hfc)$_3$. Crystallization from ethanol easily upgraded the ee of **15** to >95%. Compound **15**, previously prepared in 92 % ee in three steps using a chiral auxiliary, is a key intermediate in the synthesis of tanshidiol A.[19] However, the optical rotation of **15**, $[\alpha]^{20}_D$ +72.3 (*c* 1.2, THF) for 86% ee, was significantly higher than that previously reported for this compound, $[\alpha]^{20}_D$ +54.7 (*c* 0.1, THF) for 92% ee.[19] It is noteworthy that the configuration of (*R*)-**15** produced by (-)-**2a** is the same as that observed for **8b** (Table 1: entry 7) and for the naturally occurring antibacterial kjellmanianone.[1]

Scheme 5

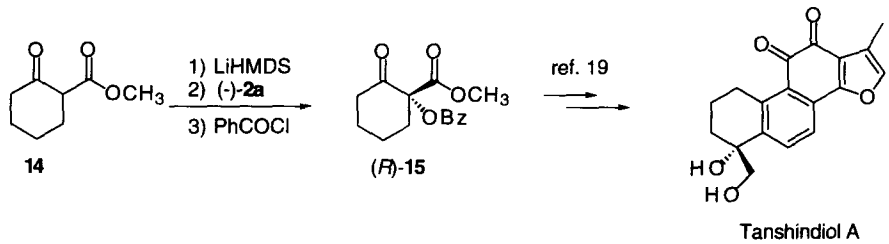


Table 2: Oxidation of the lithium enolate of **14** with **2** at -78 °C to rt.

entry	Oxaziridine	**15**, % Isolated Yield	%ee (config.)
1	(+)-**2a** (X = H)	50	84 (S)
2	(-)-**2a** (X = H)	49	86 (R)
3	(+)-**2c** (X = MeO)	32	86 (S)

The final cyclic β-ketoester studied was 2-acetyl-1-tetralone (**5**), and the results are summarized in Table 3. Earlier we had shown that potassium enolate of **5** with oxaziridine (+)-**2a** afforded racemic 2-acetyloxy-1-tetralone (**6**) in 58% yield (Scheme 1) (Table 3: entry 1).[5a] The counterion effect observed for the hydroxylation of **7** (Table 1) suggested that it may be possible to obtain the α-hydroxyl product by control of the counterion; e.g. lithium bases such as LiHMDS and LDA. However, with these bases the reaction of **5** with (+)-**2a** proved to be sluggish, requiring more than 10 h at rt for completion. Even more surprising was the isolation of 2-acetyl-1-naphthol (**16**) in 27 and 32% yield respectively (Table 3: entries 3 and 4). By using a mixed solvent of Et_2O and THF (1:1) the yield of **16** was improved to 66% (Table 3: entry 5). None of the desired α-hydroxylation product was detected.

Scheme 6

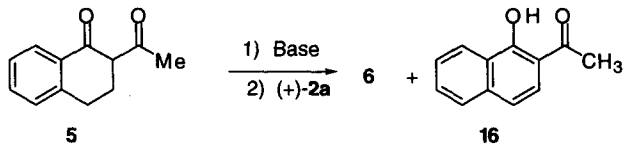


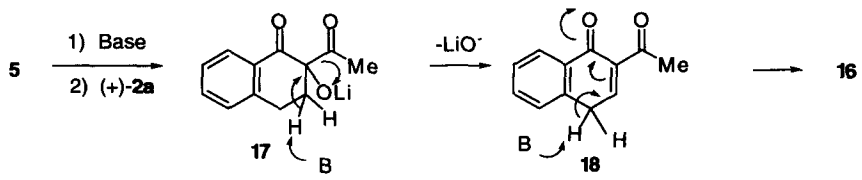
Table 3: Oxidation of **5** with (+)-**2a** in THF at rt.

Entry	Base	**6**, % yield[a]	**16**, % yield[a]
1	KHMDS	58[b]	
2	NaHMDS	20	
3	LiHMDS	4	27
4	LDA		32
5	LDA		66[c]

a) Isolated yield.
b) Ref. 5a.
c) Mixed solvent of THF and Et_2O were used.

A possible mechanism for the formation of **16** from **5** is illustrated in Scheme 7. We believe that hydroxylation of the enolate of **5** with (+)-**2a** affords the α-hydroxy-β-diketone **17**. However, elimination of lithium oxide gives **18** which aromatizes to **16**. A similar aromatization of 2-hydroxy-2-methyl-1-

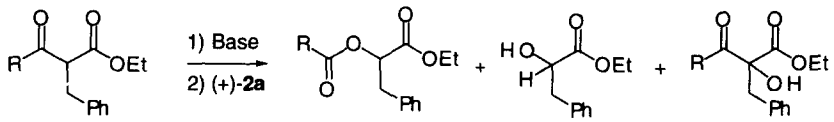
Scheme 7



tetralone to 2-methyl-1-naphthol has recently been observed on treatment with DAST.[20] Transformation of **5** to **16** has also been reported earlier by Yoshioka *et. al.* in studies of the oxidation of 1,3-dicarbonyl compounds with singlet oxygen via an initially formed α-hydroperoxy species.[8b]

Oxidation of Acyclic β-Ketoesters and β-Diesters. The hydroxylation of the enolates of ethyl 2-benzylacetoacetate (**19a**), ethyl 2-benzylbenzoylacetate (**19b**) and diethylbenzylmalonate (**19c**) by (+)-**2a** was explored to determine the effect of an acyclic structure on the Baeyer-Villiger type rearrangement (Scheme 8). These results are summarized in Table 4.

Scheme 8



19 **20** **21** **22**

a: R = CH_3
b: R = Ph
c: R = EtO

Table 4: Hydroxylation of the enolates of **19** with (+)-**2a** at -78 °C to rt in THF.

Entry	β-Dicarbonyl	Base	% Yield[a]	**20**	**21**	**22**
1	**19a** (R = Me)	LDA		3	13	39 (56% ee)[b]
2		LiHMDS		11	17	18
3		NaHMDS		50	10	
4		KHMDS		35	22	
5	**19b** (R = Ph)	LDA		28		
6		LiHMDS		37		
7		NaHMDS		65		
8		KHMDS		62		
9	**19c** (R = EtO)	LDA				90
10		LiHMDS				90
11		NaHMDS				62
12		KHMDS				68

a) Isolated yield. b) Determined using $Eu(hfc)_3$.

As observed for the cyclic β-ketoester **7a**, the lithium enolates of **19a** gave predominantly the α-hydroxylation product **22a** which was obtained in 39% yield and 56% ee (Table 4: entry 1). The sodium and potassium enolates of **19a** gave rearrangement products **20a**[21] and **21**,[22] respectively. Ethyl 3-phenyllactate (**21**) results from hydrolysis of **20a** under the reaction conditions. Neither of these products were optically active. Regardless of the counterion, ethyl 2-benzylbenzoylacetate (**19b**) gave only the Baeyer-Villiger product **20b** (Table 4: entries 5-8). This probably reflects the greater susceptibility of the ketone carbonyl to attack by the α-alkoxy anion; e.g. **12-13**. In this regard only the α-hydroxy product

22c[23] was isolated on oxidation of the enolate of **19c** (Table 4: entries 9-12) apparently reflecting the lower reactivity of the ester carbonyl to attack by the α-alkoxy anion.

Summary. Oxidation of the enolates of 1,3-dicarbonyl compounds with (camphorylsulfonyl)oxaziridine **2** were explored in both cyclic and acyclic systems. The product initially formed was the α-alkoxy anion **12** which on work-up afforded the α-hydroxy β-dicarbonyl compound or rearranged to a Baeyer-Villiger type oxidation product. This latter product, resulting from rearrangement of the alkoxy epoxide **13** formed by attack of the α-alkoxy anion **12** at the adjacent carbonyl group, was observed only for ketones. Rearrangement of the 5-membered α-alkoxy anion **12** gave lactone **9**, but similar ring expanded lactones were not observed for larger ring systems. Enolates of β-ketone esters where the keto group is part of a 6-membered ring were the only examples that gave synthetically useful ee's, on hydroxylation with oxaziridine **2**; e.g. **3**, **7b** and **14**, 82-95% ee.

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Experimental

General Procedure: Infrared spectra were recorded on Perkin-Elmer 1600 or Mattson 4020 FTIR spectrometers using sodium chloride plates for liquids and potassium bromide disks for solids. ^{1}H NMR and ^{13}C spectra were recorded in $CDCl_3$ and referenced to TMS (0.00 ppm) using Bruker 250 AM MHz, QE-300 and 500 MHz NMR spectrometers. Mass spectra were performed on a Finnigan 4000 GC/Ms at either 70 or 30 eV and recorded as m/z. High resolution mass spectra were obtained on a Fissions ZAB HF double focusing mass spectrometer. Column chromatography was performed on silica gel, Merck grade 60 (230-400 mesh) purchased from Aldrich Chemical Co. Analytical and preparative thin layer chromatography were carried out on pre-coated silica gel plates (250 and 1000 microns) purchased from Analtech Inc. TLC plates were visualized with UV light or in iodine chamber. Melting points were recorded on Mel-Temp apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 341 and 241 polarimeter. Circular dichroism spectra were obtained on a Jasco J40C Circular Dichroism Spectrophotometer. THF was freshly distilled under nitrogen from a purple solution of sodium and benzophenone. Elemental analysis was performed in the Department of Chemistry, University of Pennsylvania, Philadelphia, PA.

2-Methoxycarbonyl-1-indanone (**7a**), 2-methoxycarbonyl-1-tetralone (**7b**) and 2-methoxycarbonyl-1-benzosuberone (**7c**) were prepared as previously reported.[14] (Camphorylsulfonyl)oxaziridines **2** were prepared as previously described.[24] Ethyl 2-benzylacetoacetate (**19a**), ethyl 2-benzylbenzoylacetate (**19b**), diethyl 2-benzylmalonate (**19c**) and 2-acetyl-1-tetralone (**5**) were purchased from Aldrich and used without further purification.

The enantiomeric purity of the α-hydroxy β-ketoesters were determined by using chiral shift reagent $Eu(hfc)_3$ in $CDCl_3$.

Oxidation of the Enolate of 2-Methoxycarbonyl-1-Indanone (7a): General Procedure: In a 25 mL oven dried two neck round-bottomed flask equipped with a magnetic stirring bar, a

rubber septum and an argon filled balloon was placed 0.07 g (0.37 mmol) of **7a** in THF (7 mL). The reaction mixture was cooled to -78 °C and KHMDS (0.80 mL, 0.40 mmol, 0.5 M in toluene) was added slowly. After 30 min a solution of 0.10 g (0.44 mmol) of oxaziridine (+)-**2a** in THF (6 mL) was added dropwise. The reaction was monitored by TLC and after 20 min at -78 °C the reaction mixture was warmed to rt. After 1 h the solution was quenched with sat. NH_4Cl solution (3 mL) at -78 °C and diluted with EtOAc (15 mL). The phases were separated, the aqueous phase was washed with EtOAc (2 x 10 mL), the combined organic phases were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. Purification by preparative TLC (Et_2O/hexane, 40: 60) afforded 0.01 g (10%) of **8a** and 0.05 g (65%) of **9**.

2-Methoxycarbonyl-2-hydroxy-2,3-dihydro-1-oxo-1H-indene (8a): mp 132-133 °C, [Lit.[16] mp 131-132 °C]; IR (KBr) cm^{-1} 3402, 1744, 1709, 1259, 1205 ; ^1H NMR ($CDCl_3$) δ 7.80 (d, 1H, *J* = 8.0 Hz), 7.70-7.65 (m, 1H), 7.49 (d, 1H, *J* = 7.5 Hz), 7.46-7.40 (m, 1H), 3.98 (bs, 1H), 3.73 (d, 1H, J = 17.5 Hz), 3.74 (s, 3H), 3.26 (d, 1H, *J* = 17.0 Hz); ^{13}C NMR ($CDCl_3$) δ 200.8, 171.9, 152.2, 136.2, 133.5, 128.0, 126.4, 125.3, 80.3, 53.4, 39.2.

3-Methoxycarbonyl-3,4-dihydro-1-oxo-1H-2-benzopyran (9): mp 85-86 °C, [Lit.[17c] mp 88-93 °C]; IR (KBr) cm^{-1} 2954, 1752, 1725, 1607, 1456, 1283, 1201; ^1H NMR ($CDCl_3$) δ 8.12 (d, 1H, *J* = 7.7 Hz), 7.60-7.53 (m, 1H), 7.46-7.39 (m, 1H), 7.26 (d, 1H, *J* = 7.3 Hz), 5.19 (t, 1H, *J* = 5.7 Hz), 3.74 (s, 3H), 3.46 (dd, 1H, *J* = 5.4 and 16.6 Hz), 3.30 (dd, 1H, *J* = 5.8 and 16.5 Hz); ^{13}C NMR ($CDCl_3$) δ 169.4, 163.3, 136.2, 134.1, 130.3, 128.2, 127.5, 124.8, 74.9, 52.9, 30.1.

(*S*)-(-)-2-Methoxycarbonyl-2-hydroxy-1,2,3,4-tetrahydro-1-oxo-naphthalene (8b): mp 67-68 °C, [Lit.[8b] mp 72.5-73.5 °C]; $[\alpha]^{20}_D$ -11.3 (c, 0.55, $CHCl_3$) for 82% ee. This compound had spectral properties identical with literature values.[8b]

6-Methoxycarbonyl-6-hydroxy-6,7,8,9-tetrahydro-5-oxo-5H-benzocycloheptene (8c): oil (62%); This compound had spectral properties identical with literature values.[8b]

2-Methoxycarbonyl-2-iodo-1,2,3,4-tetrahydro-1-oxo-naphthalene (10): In a 25 mL oven dried two neck round-bottomed flask fitted with a magnetic stirring bar, a rubber septum and an argon filled balloon was placed 0.07 g (0.34 mmol) of **7b** in THF (3 mL). The reaction flask was cooled to -78 °C and 0.41 mL of LiHMDS (0.41 mmol, 1.0 M in THF) was added slowly. After 30 min a solution of 0.10 g (0.44 mmol) of (+)-**2a** in THF (6 mL) was added dropwise. The reaction was monitored by TLC and after 2 h at -78 °C the reaction mixture was quenched by addition of 3 mL of saturated aqueous NH_4I solution at -78 °C and diluted with CH_2Cl_2 (15 mL). The phases were separated and the aqueous phase was washed with CH_2Cl_2 (2 x 10 mL). The combined organic phases were washed with brine (10 mL), dried ($MgSO_4$), concentrated and the residue was purified by preparative TLC (CH_2Cl_2/Et_2O/pentane, 10:20:70) to afford 0.06 g (52%) of **10** and 0.01 g (17%) of **8b**. The ee of **8b** obtained by this method is determined to be 9% by $Eu(hfc)_3$. For iodo compound **10**: mp 113-117 °C; IR (KBr) 1741, 1669, 1237, 1213 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.11 (d, 1H, *J* = 7.9 Hz), 7.53 (t, 1H, *J* = 7.4 Hz), 7.37 (t, 1H, *J* = 7.6 Hz), 7.27 (d, 1H, *J* = 7.7 Hz), 3.85 (s, 3H), 3.08-2.99 (m, 2H), 2.76-2.64 (m, 1H), 2.60-2.49 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 188.8, 169.1, 142.2, 134.2, 129.1, 128.8, 128.6, 127.2, 54.1, 49.6, 37.7, 29.0; EIMS *m/z* (relative intensity) 330 (M^+, 7), 203 (M-I, 100), 171(88), 115 (88). Anal. calcd for $C_{12}H_{11}IO_3$: C, 43.66; H, 3.33. Found: C, 44.10; H, 3.83.

(*R*)-(+)-2-Methoxycarbonyl-2-benzoyloxy-1-oxo-cyclohexane (15): In a 25 mL oven dried two neck round-bottomed flask fitted with a magnetic stirring bar, a rubber septum and an argon filled balloon was placed 0.96 mL of LiHMDS (0.96 mmol, 1.0 M in THF) in THF (6 mL). The reaction flask was cooled to -78 °C and 0.11 g (0.71mmol) of **14** was slowly added via syringe. After 10 min a solution of 0.23 g (1.00 mmol) of (-)-**2a** in THF (6 mL) was added dropwise. After 30 min at -78 °C the solution was warmed to 0 °C for 40 min and to rt for 30 min. At this time the solution was cooled to -78 °C, 0.25 g (1.78 mmol) of benzoyl chloride was added via syringe and then warmed to 0 °C after 10 min. The solution was stirred for 2 h at this temperature, quenched with saturated aqueous NH_4Cl solution (3 mL) and diluted with EtOAc (15 mL). The organic phase was separated and the aqueous phase was washed with EtOAc (2 x 10 mL). The combined organic phases were washed with brine (10 mL), dried ($MgSO_4$) and concentrated. The crude reaction mixture was purified by preparative TLC (Et_2O/pentane, 30: 70) to afford 0.10 g (49%) of **15**; mp 64-66 °C, [Lit.[19] mp 64-65 °C]; $[\alpha]^{20}_D$ +72.3 (c, 1.2, THF) for 86% ee, [Lit.[19] $[\alpha]^{20}_D$ +54.7 (c, 0.1, THF) for 92% ee]. **15** has spectral data identical with literature values.[19] Crystallization from ethanol gave **15** in >95% ee, $[\alpha]^{20}_D$ +84.0 (c, 0.3, THF).

2-Acetyl-1-Naphthol (16): In a 25 mL oven dried two neck round-bottomed flask fitted with a magnetic stirring bar, a rubber septum and an argon filled balloon was placed 0.08 g (0.45 mmol) of **5** in Et_2O (5 mL). The reaction flask was cooled to -78 °C and 0.56 mL of LDA (0.56 mmol, 1.0 M in THF) was added slowly. After 30 min a solution of (+)-**2a** (0.13 g, 0.56 mmol) in THF (5 mL) was added dropwise, the reaction was monitored by TLC, and after 30 min it was warmed to rt. The solution was stirred for 10 h and quenched with saturated aqueous NH_4Cl solution (3 mL) at 0 °C. The reaction mixture was diluted with EtOAc (15 mL), the aqueous phase was washed with EtOAc (2 x 10 mL) and the combined organic phases were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. The crude reaction mixture was purified by preparative TLC (Et_2O/pentane, 5:95) to afford 0.06 g (66%) of **16**; mp 96-98 °C, [Lit.[25] mp 100-101 °C]. This compound has spectral properties identical with an authentic sample.

General Procedure for the Oxidation of Acyclic β-Dicarbonyl Enolates: Ethyl 2-Benzylacetoacetate (19a): In a 25 mL oven dried two neck round-bottomed flask fitted with a magnetic stirring bar, a rubber septum and an argon filled balloon was placed 0.16 g (0.72 mmol) of **19a** in THF (7 mL). The reaction flask was cooled to -78 °C and 0.79 mL of LDA (0.79 mmol, 1.0 M in THF) was slowly added. After 30 min a solution of 0.20 g (0.86 mmol) of (+)-**2a** in THF (3 mL) was added dropwise. The reaction mixture was monitored by TLC and after 20 min the solution was warmed to rt. After completion of the oxidation (typically 1.5 h), the reaction mixture was quenched by addition of saturated aqueous NH_4Cl solution (3 mL) at -78 °C and diluted with EtOAc (15 mL). The aqueous phase was washed with EtOAc (2 x 10 mL) and the combined organic phases were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. The crude mixture was purified by preparative TLC (Et_2O/hexane, 20:80) to afford 0.005 g (3%) of **20a**, 0.02 g (13%) of **21**[22] and 0.07 g (39%) of **22a**.

Ethyl α-acetyloxy-β-phenylpropionate (20a)[21]**:** oil; IR (neat) cm^{-1} 2983, 1749, 1374, 1234, 1081; ^1H NMR ($CDCl_3$) δ 7.30-7.15 (m, 5H), 5.16 (dd, 1H, *J* = 4.8 and 8.4 Hz), 4.14 (q, 2H, *J* = 7.2 Hz), 3.20-3.02 (m, 2H), 2.05 (s, 3H), 1.19 (t, 3H, *J* = 7.2 Hz) ; ^{13}C NMR ($CDCl_3$) δ 170.2, 169.6, 135.9, 129.3, 128.4, 126.9, 73.0, 61.3, 37.3, 20.5, 14.0; HRMS calcd for $C_{13}H_{17}O_4$ (m+H) 237.1127, found 237.1129. Anal. calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.78. Found: C, 66.32; H, 6.93.

(+)-Ethyl α-acetyl-α-hydroxy-β-phenylpropionate (22a): $[\alpha]^{20}_D$+18.9 (c, 0.78, $CHCl_3$) for 56% ee. This compound has spectral properties identical with literature values.[9]

Ethyl 2-benzyloxy-β-phenylpropionate (20b): oil; IR (neat) cm^{-1} 1720, 1260; ^1H NMR ($CDCl_3$) δ 8.05-7.25 (m, 10H), 5.41 (dd, 1H, *J* = 4.1 and 6.2 Hz), 4.20 (q, 2H, *J* = 8.7 Hz), 3.28 (m, 2H), 1.22 (t, 3H, *J* = 8.7 Hz); ^{13}C NMR($CDCl_3$) δ 169.4, 165.7, 133.2, 129.7, 129.3, 128.4, 128.3, 126.9, 73.9, 61.9, 37.6, 14.1; HRMS calcd for $C_{18}H_{19}O_4$ (m+H) 299.1283, found 299.1282. Anal. calcd for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08. Found: C, 72.12; H, 5.90.

Diethyl benzyl hydroxymalonate (22c):[23] oil, IR (neat) cm^{-1} 3495, 1739, 1278, 1231; ^1H NMR ($CDCl_3$) δ 7.26-7.24 (m, 5H), 4.23 (q, 4H, *J* = 7.5 Hz), 3.79 (bs, 1H), 3.35 (s, 2H), 1.27 (t, 6H J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 169.8, 134.6, 130.3, 128.0, 127.0, 79.1, 62.4, 40.3, 13.9.

Determination of absolute configuration of 8b by circular dichroism (CD): All spectra were recorded in methanolic solutions of the samples in a 1 cm path length quartz cell. Δε values were corrected for 100% ee of the samples. λ_{max}(nm) (Δε): (*R*)-**8b**: 312 (+0.41), 354 (-0.32); (*R*)-**4**: 345 (+0.32), 383 (-0.18); (*S*)-**8b**: 311 (-0.49), 355 (+0.26); (*S*)-**4**: 343 (-0.32), 380 (+0.17).

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