A Novel Darzens-Type Reaction Promoted by Tributylstannylcarbamate

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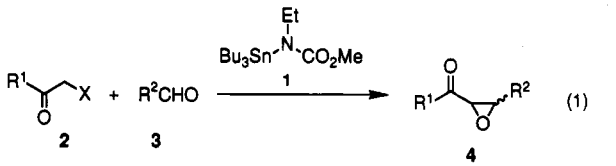
Stannylcarbamate 1 proved to be a selective agent for generating organotin(IV) enolates from α-halo ketones. Thus, a Darzens reaction was achieved under mild and neutral conditions. The reaction took place without any side reactions and even with aliphatic α-halo ketones bearing enolizable α′-hydrogens. Various types of α,β-epoxy ketones and esters were obtained in this one-pot reaction. The stereoselectivity of the reaction was influenced by changing the halogen substituent of the α-halo ketones and by additives. Moreover, the present method could be applied to γ- and δ-halo ketones as enolate precursors, and five- and six-membered cyclic compounds were obtained.

Introduction

The Darzens reaction is a versatile method for carbon–carbon bond formation which gives highly functionalized oxiranes.[1] It employs the base-induced condensation of α-halo carbonyl compounds with aldehydes for the construction of α,β-epoxy esters,[1] α,β-epoxy amides,[2] α,β-epoxy nitriles,[3] and α,β-epoxy sulfoxides.[4] On the other hand, acyl-substituted compounds, α-halo ketones, have rarely been used except when no α′-hydrogen atoms are present. Attempts to apply a Darzens-type reaction to cases where α′-hydrogens are lacking include principally aromatic α-halo ketones.[5] The reason for the unsuitability of some α-halo ketones to serve as substrates in Darzens reactions arises from the competing reactions in basic medium, such as the Favorskii rearrangement derived from the abstraction of an α′-hydrogen,[6] nucleophilic addition at the carbonyl group, and nucleophilic substitution of the halide.[7] On the basis of these facts, a Darzens reaction under neutral conditions might open a valuable route to various products without undesired side reactions. To achieve such a selective reaction, several attempts have been reported. For example, $Sn(OTf)_2$–R_3N,[8] and $Zr(O^tBu_4)$[9] were used as enolate generating agents. Although these methods effected the selective carbon–carbon bond formation by an abstraction of the α-hydrogens, the one-pot formation of epoxides did not occur.[10] However, the use of α-halo imines as enolate precursors afforded a selective Darzens reaction.[11] However, this method was not convenient because multistep reactions are required to form these substrates from α-halo ketones. These facts encouraged us to investigate an alternate method for the Darzens reaction that would involve the direct formation of epoxy ketones from α-halo ketones bearing enolizable α′-hydrogens.

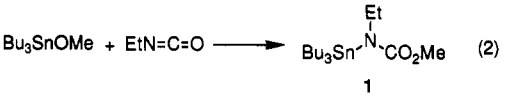
We found that *N*-tri-*n*-butylstannylcarbamate 1 acts as an effective reagent for Darzens reaction (eq 1). The



(1)

reactions proceeded under mild, neutral conditions, and novel types of cyclic compounds were prepared from various halo ketones.

Organotin(IV) enolates are often used for the formation of carbon–carbon bonds[12] because these enolates can be generated under mild and neutral conditions. Known methods for the generation of organotin(IV) enolates include transmetalation of lithium enolates,[13] hydrostannation of α,β-unsaturated ketones,[14] and transesterification of enol acetates.[15] Though intrinsically more reactive than the analogous silyl enol ethers, organotin(IV) enolates have a narrower field of applications that reflect the difficulty of handling such moisture-sensitive reagents. Hence, a convenient procedure for the generation of organotin(IV) enolates was an important problem that we needed to solve. On the basis of this background, tin compound 1 proved to be a versatile reagent for generating organotin(IV) enolates.[16] Reagent 1 was easily prepared by the addition reaction of tri-*n*-butyltin methoxide (Bu_3SnOMe) to ethyl isocyanate (EtN=C=O)[17] (eq 2).



(2)

Results and Discussion

At first, we tried the Darzens reaction of α-halo ketones 2 with aldehydes 3 in the presence of equimolar amounts of tin reagent 1.

As shown in Table I, the corresponding α,β-epoxy ketones 4 were obtained in this one-pot procedure. In these

(1) (a) Newman, M. S.; Magerlein, B. J. *Org. React. (New York)* **1949**, *5*, 413. (b) Arseniyadis, S.; Kyler, K. S.; Watt, D. S. *Org. React. (New York)* **1984**, *39*, 1.

(2) Abdel-Magid, A.; Pridgen, L. N.; Eggleston, D. S.; Lantos, I. *J. Am. Chem. Soc.* **1986**, *108*, 4595.

(3) Coutrot, P. *Bull. Soc. Chim. Fr.* **1974**, 1965.

(4) Satoh, T.; Iwamoto, K.; Sugimoto, A.; Yamakawa, K. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2109.

(5) Bansel, R. K.; Sethi, K. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1197.

(6) (a) Schamp, N.; DeKimpe, N.; Coppens, W. *Tetrahedron*, **1975**, *31*, 2081. (b) Sakai, T.; Katayama, T.; Takeda, A. *J. Org. Chem.* **1981**, *46*, 2924.

(7) Cromwell, N. H.; Bamburg, R. E. *J. Org. Chem.* **1961**, *26*, 1729.

(8) Mukaiyama, T.; Haga, T.; Iwasawa, N. *Chem. Lett.* **1982**, 1601.

(9) Sasaki, H.; Kirio, T.; Shibasaki, M. *J. Org. Chem.* **1990**, *55*, 5306.

(10) For the preparation of α,β-epoxy ketones, KF-crown ether[8] and BnLi[9] are necessary for cyclization of the formed bromohydrins.

(11) Sulmon, P.; Kimpe, N. D.; Schamp, N. *J. Org. Chem.* **1988**, *53*, 4457.

(12) For chemistry of tin, see, for example: (a) Pereyre, M.; Quintard, P. J.; Rahm, A. *Tin in Organic Synthesis*; Butterworth: London, 1987. (b) Omae, I.; *Organotin Chemistry*; *J. Organomet. Chem. Lib. 21*; Elesevier: New York, 1989.

(13) Yamamoto, Yatagai, H.; Maruyama, K. *J. Chem. Soc., Chem. Commun.* **1981**, 162.

(14) Pereyre, M.; Valade, J., *Bull. Soc. Chim. Fr.* **1967**, 1928.

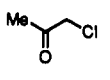
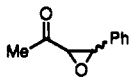
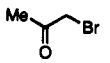
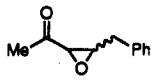
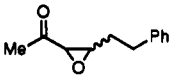
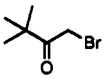
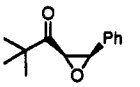
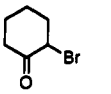
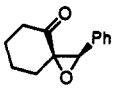
(15) Pereyre, M.; Bellegarde, B.; Mendelsohn, J.; Valade, J. *J. Organomet. Chem.* **1968**, *11*, 97.

(16) We have already published a part of the results using 1 as a communication. Shibata, I.; Yamasaki, H.; Baba, A.; Matsuda, H. *Synlett* **1990**, 490.

(17) (a) Bloodworth, A. J.; Davies, A. G. *J. Chem. Soc.* **1965**, 5238. (b) Bloodworth, A. J.; Davies, A. G.; Vasishtha, S. C. *J. Chem. Soc. C* **1967**, 1309.

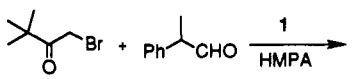
0022-3263/92/1957-6909$03.00/0

Table I. Preparation of α,β-Epoxy Ketones 4[a]

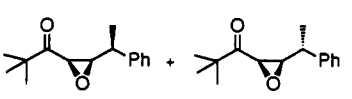
entry	α-halo ketone structure	α-halo ketone no.	aldehyde[b]	additive	time (h)	product structure	product no.	yield (%)	cis/trans ratio
1		2a	3a	-	8		4a	59	13/87
2			3a	HMPA	5			66	29/71
3		2b	3a	-	8			56	39/61
4			3a	HMPA	3			85	79/21
5		2a	3b	-	24		4b	15	4/96
6		2b	3b	HMPA	24			40	61/39
7		2a	3c	-	24		4c	43	5/95
8		2b	3c	HMPA	5			81	76/24
9		2c	3a	HMPA	6		4d	63	100/0
10		2d	3a	HMPA	24		4e	68	100/0

[a] Stannylcarbamate 1, 3 mmol, α-halo ketone 2, 3 mmol, aldehyde 3, 3 mmol, additive, 3 mmol, THF, 3 mL, 60 °C. [b] Benzaldehyde (3a), phenylacetaldehyde (3b), and 3-phenylpropionaldehyde (3c).

reactions, no side reactions derived from nucleophilic addition or abstraction of an α′-hydrogen took place. It was significant to note that this approach involved the first direct formation of epoxides from α-halo ketones which bear α′-hydrogens. Furthermore, it is interesting that the cis/trans ratio of products 4 was altered by changing the halogen of 2 and by the presence of HMPA. Namely, the reaction of chloroacetone (2a) with PhCHO (3a) gave *trans*-4a as a major product (entry 1), whereas the addition of HMPA slightly increased the amount of *cis*-4a (entry 2). This cis-selectivity was further increased in the reaction of bromoacetone 2b (entry 3). Moreover, the reaction of 2b in the presense of HMPA induced a remarkable change, in which *cis*-4a was obtained as the major product (entry 4). This remarkable change of stereoselectivity was also the case in the reaction of aliphatic aldehydes, 3b and 3c, to give 4b and 4c (entries 5–8), respectively. α-Bromopinacolone (2c), which bears a bulky substituent at the carbonyl group, afforded only *cis*-4d selectively (entry 9). The reaction of 2-bromocyclohexanone (2d) also provided *cis*-4e selectively. The predominant formation of *cis*-epoxy ketones is noteworthy because few examples have been reported as efficient methods to obtain *cis*-epoxy ketones in the Darzens reaction.[18] In the cis-selective reaction using 2c, Cram-selectivity was also exhibited; the reaction of aldehyde 3d that bears a chiral carbon at the α-position led to the cis-Cram isomer 4f predominantly (40% Cram:anti-Cram = 71:29) (eq 3).



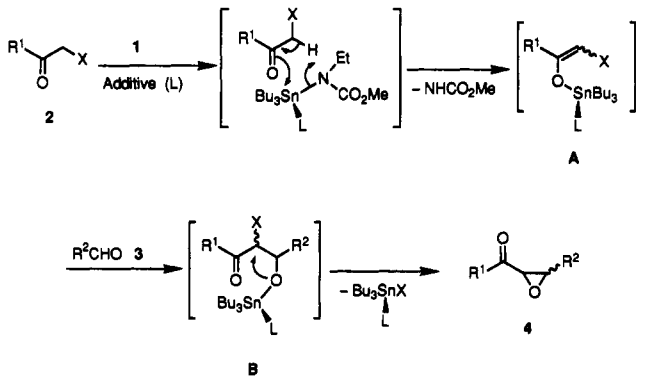
2c 3d (3)



Cram-4f *anti*-Cram-4f

(18) (a) Bachelor, F. W.; Bansel, R. K. *J. Org. Chem.* **1969**, *34*, 3600. (b) Roux-Schmitt, M. C.; Seyden-Penne, J.; Wolfe, S. *Tetrahedron* **1972**, *28*, 4965.

Scheme I



The reaction course is explained as shown in Scheme I in which the organotin enolate A is a key intermediate. Namely, stannylcarbamate 1 acts as a base and abstracts an α-hydrogen of 2 selectively to form A.[19] In the next stage, A reacts with an aldehyde 3 to afford the crossed aldol intermediate B. Finally, cyclization of B induces the formation of 4. HMPA plays an important role in the formation of 4. Since organotin compounds are reported to form complexes with HMPA,[20] the role of HMPA is explained as follows. HMPA coordinates the tin atom of 1 to increase its basicity. As a result, the effective abstraction of an α-proton to form enolate A took place. Secondly, the coordination increased the nucleophilicity of A, and this resulted in an effective reaction with an electrophile 3.[21] Finally, the coordination to the Sn atom of the alkoxide B increases the nucleophilicity of tin alkoxide.[22] The activated Sn–O bond reacts easily with the

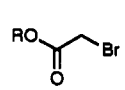
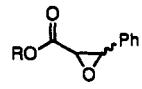
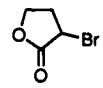
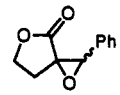
(19) One disturbing reaction is the trimerization if α-halo ketones.[19a] In our reaction, the trimer was formed quantitatively in the absence of electrophiles, which prevented the isolation of tin enolate A. (a) Tsuzuki, R.; Ishikawa, K.; Kase, M. *J. Org. Chem.* **1960**, *25*, 1009.

(20) Harrison, P. G. *Chemistry of Tin*; Blackie: New York, 1989.

(21) Activation of organotin enolates by HMPA has been reported. Odic, Y.; Pereyre, M. *J. Organomet. Chem.* **1973**, *55*, 273.

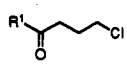
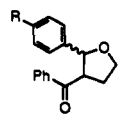
(22) We have reported the activation of a Sn–O bond by HMPA to accelerate cyclization. Shibata, I.; Baba, A.; Matsuda, H. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 4000.

Table II. Preparation of α,β-Epoxy Esters 6 from 5 and 3a[a]

entry	α-bromo ester structure	R	no.	additive	condns	product structure	R	no.	yield (%)	cis/trans ratio
1		Et	5a	HMPA	60°C, 24 h		Et	6a	15	60/40
2				Bu_4NF	-78 ~ 0°C, 24 h				81	58/42
3				LiBr	rt, 24 h				78	8/92
4		Bn	5b	Bu_4NF	-78 ~ 0°C, 24 h		Bn	6b	43	69/31
5		t-Bu	5c	Bu_4NF	-78 ~ 0°C, 24 h		t-Bu	6c	89	71/29
6			5d	Bu_4NF	-78 ~ 0°C, 24 h			6d	50[b]	

[a] Stannylcarbamate 1, 3 mmol, α-bromo ester 5, 3 mmol, PhCHO 3a, 3 mmol, additive, 3 mmol, THF, 3 mL. [b] Stereoselectivity was undefined.

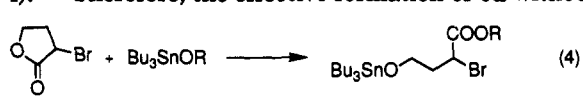
Table III. Preparation of β-Acyltetrahydrofurans 9[a]

entry	γ-chloro ketone structure	R^1	no.	R^2CHO[b]	product structure	R	no.	yield (%)	cis/trans ratio
1		Me	8a	3a		Me	9a	35	38/62
2		Ph	8b	3a		Ph	9b	38	23/77
3			8b	3e		Cl	9c	59	37/63
4			8b	3f		NO_2	9d	57	6/94

[a] Stannyliminocarbamate 7, 3 mmol, γ-chloro ketone 5, 3 mmol, aldehyde 3, 3 mmol, HMPA, 3 mmol, THF, 3 mL, 60 °C, 3 h. [b] Benzaldehyde (3a), p-chlorobenzaldehyde (3e), and p-nitrobenzaldehyde (3f).

terminal halide to give the products 4.

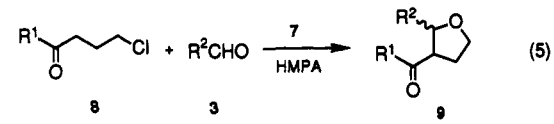
We next applied reagent 1 to reactions using α-halo esters 5 (Table II). In the reaction of 5a with 3a, α,β-epoxy esters 6a were obtained in low yield when using HMPA as an additive (entry 1). On the other hand, a remarkable effect of other additives was noted. For example, the addition of Bu_4NF instead of HMPA increased the yield of 6a even at low temperature (entry 2). These reactions were slightly cis-stereoselective. LiBr also served as an effective additive and gave high yields of the products 6a. In contrast to the reaction using Bu_4NF, LiBr afforded predominantly *trans*-6a (entry 3).[23] In this way, with suitable additives, α,β-epoxy esters were obtained in good yields. Furthermore, Table II summarizes the reactions of various types of α-halo esters 5b–5d using Bu_4NF as an additive, from which the corresponding α,β-epoxy esters (6b–6d) were obtained in good yields (entries 4–6). In particular, one of the advantages of using 1 was apparent in the formation of 6d (entry 6). Generally, organotin alkoxides and amines act as nucleophiles and induce the selective cleavage of a lactone ring at the acyl–oxygen bond. As a result, acyclic tin alkoxides are obtained in good yield (eq 4).[24] Therefore, the effective formation of 6d without



(4)

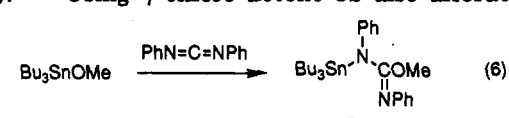
the ring cleavage indicates the low nucleophilicity of reagent 1. This new method clearly results in a selective carbon–carbon bond formation but also the one-pot preparation of α,β-epoxy ketones 4 and esters 6.

In identical fashion, we extended this one-pot procedure to a cyclization to produce β-acyltetrahydrofurans 9 by the reaction of γ-halo ketones 8 as enolate precursors (eq 5).



(5)

In the reaction of 8a with 3a, trace amounts of 9a were obtained by using stannylating agent 1, and the starting materials, 8a and 3a, were recovered. This result reflects the lower acidity of the α-hydrogen of γ-halo ketone 8 in comparison with the α-hydrogen of 2 and 5. Reagent 1 is unsuitable for the abstraction of an α-hydrogen to form an enolate. However, as shown in Table III, the desired product 9a was obtained in 35% yield by using stannyl iminocarbamate 7 instead of 1 (entry 1). This stannylating reagent (7) is easily prepared in situ from the reaction of Bu_3SnOMe with diphenylcarbodiimide (PhN=C=NPh) (eq 6).[17] Using γ-chloro ketone 8b also afforded the



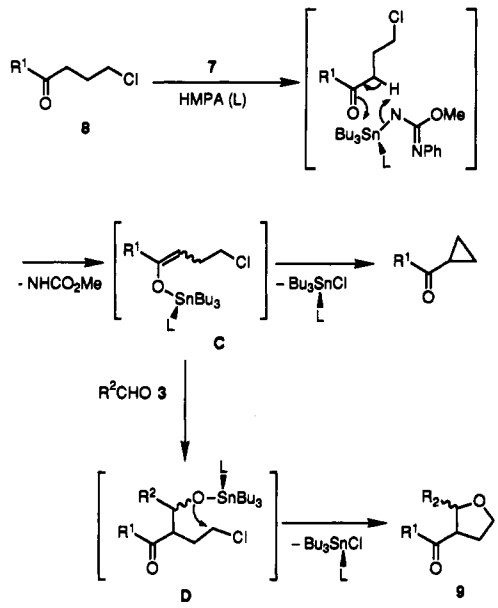
(6)

corresponding tetrahydrofuran 9b in 38% yield (entry 2). In these reactions, the thermally stable trans isomers predominated. Besides 9b, an undesired byproduct, phenyl cyclopropyl ketone, was formed in an intramolecular alkylation of 8. Introducing electron-withdrawing substituents in aldehydes 3 resulted in higher yields of the desired product. Thus, the reaction with p-chlorobenzaldehyde (3e) and p-nitrobenzaldehyde (3f) gave the corresponding cyclic compounds 9c and 9d in 59 and 57%

(23) We could not explain the role of LiBr exactly. However, recently, Takeda et al. postulated a higher-order tin compound by the activation of an organotin alkoxide with LiBr. Yamaguchi, J.; Takeda, T. *Chem. Lett.* **1992**, 423.

(24) (a) Shibata, I.; Toyota, M.; Baba, A.; Matsuda, H. *Synthesis* **1988**, 486. (b) Shibata, I.; Toyota, M.; Baba, A.; Matsuda, H. *J. Org. Chem.* **1990**, *55*, 2487. (c) Itoh, K.; Sakai, S.; Ishii, Y. *Tetrahedron Lett.* **1966**, 4941.

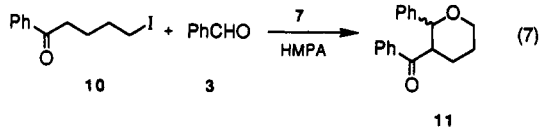
Scheme II



yields, respectively (entries 3 and 4). In this way, novel types of five-membered compounds were obtained in the one-pot procedure. The reaction path is illustrated in Scheme II.

Stannylating reagent **7** abstracts an α-proton of **8** to afford the terminally chlorinated tin enolate **C**. Next, the addition of an aldehyde **3** results in carbon–carbon bond formation to give the crossed aldol intermediate **D**. The subsequent cyclization gives cyclic product **7** and Bu_3SnCl. The undesired cyclopropyl ketone is formed by intramolecular alkylation of **C**. Competitive reactions, such as the crossed aldol reaction and the intramolecular alkylation, take place from the intermediate **C**. A lithium enolate gave an unsatisfactory result: no **9a** was obtained when LDA was used as the enolate generating agent. In the cases using the more electrophilic aldehydes such as **3e** and **3f**, enolate **C** would undergoes predominant crossed-aldol reaction instead of the intramolecular alkylation. As a result, the yields of **9** were increased.

In the last stage, we describe the formation of a six-membered ring in a β-acyltetrahydropyran **11** using a δ-halo ketone. Although product **11** was not obtained at all with δ-chloro ketone, δ-iodo isomer **10** afforded **11** in 47% yield (cis:trans = 21:79) (eq 7).



(7)

In conclusion, stannylcarbamate **1** and stannyliminocarbamate **7**, when employed as enolate generating agents, result in mild and selective Darzens reactions with high regio- and chemoselectivity. Various types of α,β-epoxy ketones and esters as well as novel types of five- and six-membered cyclic compounds were obtained in this one-pot procedure.

Experimental Section

Melting points are uncorrected. ^1H NMR and ^{13}C NMR spectra (tetramethylsilane as an internal standard) were recorded on a HITACHI R-90H (90 MHz) or a JEOL JNM-GSX-400 (400 MHz) spectrometer. Analytical GC was performed with TCD using a 2-m × 3-mm glass column packed with Silicone OV-17 on Uniport HP (5%, 60–80 mesh) or with FID using a 25-m × 0.25-mm capillary column packed with CBP-10. Column chromatography was performed on silica gel (Wakogel C-200 or C-300). Preparative TLC was carried out on silica gel plates (Wakogel B-5F).

Tri-*n*-butyltin methoxide (Bu_3SnOMe) was synthesized from bis(tributyltin) oxide [$(Bu_3Sn)_2O$] and dimethyl carbonate.[25] Ethyl isocyanate was commercial product used without further purification. Diphenylcarbodiimide was prepared according to the published method.[26] α-Halo ketones **2a–2d**, α-halo esters **5a–5d**, γ-halo ketones **8a** and **8b**, and aldehydes **3a–3f** used were commercially available. δ-Iodo ketone **10** was synthesized by Friedel–Craft acylation of benzene with δ-chloropentyl chloride, followed by halogen exchange using NaI.

***cis*-3,4-Epoxy-4-phenyl-2-butanone (4a) (General Procedure for the Preparation of α,β-Epoxy Ketones).** A representative procedure is as follows (Table I, entry 4): To a solution of Bu_3SnOMe (0.96 g, 3 mmol) in dry THF (3 mL) under N_2 atmosphere was added EtNCO (0.17 g, 3 mmol) at 0 °C. After 10 min, the IR band at 2100 cm^{-1} due to an isocyanate disappeared and a new band at 1680 cm^{-1} was detected, which indicates the formation of **1**.[17] Bromoacetone (**2b**) (0.41 g, 3 mmol), benzaldehyde (**3a**) (0.32 g, 3 mmol) and HMPA (0.54 g, 3 mmol) were added to the mixture. After heating at 60 °C for 3 h, the solvent was evaporated and the mixture was purified by chromatography on a silica gel column. Elution with hexane (200 mL) gave Bu_3SnBr. Subsequent elution with hexane/EtOAc (200 mL, 1:1 v/v) provided an almost pure mixture of *cis*- and *trans*-**4a** (0.42 g, 85% cis:trans = 79:21). Further separation of diastereomers **4a** was performed by preparative TLC with 4:1 hexane/ethyl ether. The relative stereochemistry of the diastereomers was assigned from ^1H NMR spectra by the chemical shift of the ring methine protons (δ3.4–4.5).

***cis*-4a**: wax; IR (neat) 1250, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.84 (s, 3 H), 3.80 (d, 1 H, J = 4.9 Hz, CHPh), 4.34 (d, 1 H, J = 4.9 Hz, CHC=O), 7.29–7.38 Hz (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 27.8, 57.9, 61.2, 126.5, 128.4, 128.5, 133.1, 203.3; HRMS calcd for $C_{10}H_{10}O_2$ 162.0681, found 162.0708.

***trans*-4a**: mp 48–50 °C; IR (KBr) 1250, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.20 (s, 3 H, CH_3C=O), 3.49 (d, 1 H, J = 2.0 Hz, CHPh), 4.00 (d, 1 H, J = 2.0 Hz, CHC=O), 7.25–7.38 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 24.8, 57.8, 63.5, 125.7, 128.7, 129.1, 135.1, 204.1; HRMS calcd for $C_{10}H_{10}O_2$ 162.0681, found 162.0655.

***cis*-3,4-Epoxy-5-phenyl-2-pentanone (*cis*-4b)**: wax; IR (neat) 1240, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.27 (s, 3 H, CH_3C=O), 2.74 (dd, 1 H, J = 6.4 and 14.7 Hz, one of CH_2Ph), 2.98 (dd, 1 H, J = 6.4 and 14.7 Hz, one of CH_2Ph), 3.46 (td, 1 H, J = 6.4 and 4.9 Hz, CHBn), 3.66 (d, 1 H, J = 4.9 Hz, CHCO=O), 7.19–7.36 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 28.6, 33.9, 58.6, 58.7, 127.0, 128.4, 128.8, 136.5, 203.8; HRMS calcd for $C_{11}H_{12}O_2$ 176.0837, found 176.0845.

***trans*-3,4-Epoxy-5-phenyl-2-pentanone (*trans*-4b)**: wax; IR (neat) 1240, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.04 (s, 3 H, CH_3), 2.93 (dd, 1 H, J = 5.9 and 15.2 Hz, one of CH_2Ph), 2.99 (dd, 1 H, J = 4.9 and 15.2 Hz, one of CH_2Ph), 3.24 (d, 1 H, J = 2.0 Hz, CHC=O), 3.31 (ddd, 1 H, J = 2.0, 4.9, and 5.9 Hz, CH), 7.23–7.36 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 24.3, 37.9, 57.9, 59.6, 127.1, 128.8, 129.1, 135.8, 205.6; HRMS calcd for $C_{11}H_{12}O_2$ 176.0837, found 176.0839.

***cis*-3,4-Epoxy-6-phenyl-2-hexanone (*cis*-4c)**: wax; IR (neat) 1250, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.74–1.82 (m, 1 H, one of CH_2Bn), 1.88–1.96 (m, 1 H, one of CH_2Bn), 2.05 (s, 3 H, CH_3), 2.67–2.75 (m, 1 H, one of CH_2Ph), 2.82–2.89 (m, 1 H, one of CH_2Ph), 3.24 (td, 1 H, J = 6.3 and 4.9 Hz, CH), 3.55 (d, 1 H, J = 4.9 Hz, CHC=O), 7.16–7.30 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 28.1, 29.0, 32.4, 58.0, 58.8, 126.3, 128.5, 128.6, 140.1, 203.8; HRMS calcd for $C_{12}H_{14}O_2$ 190.0994, found 190.1000.

***trans*-3,4-Epoxy-6-phenyl-2-hexanone (*trans*-4c)**: wax; IR (neat) 1250, 1719 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.90–1.98 (m, 2 H, CH_2Bn), 2.01 (s, 3 H, CH_3), 2.72–2.88 (m, 2 H, CH_2Ph), 3.09 (td, 1 H, J = 2.0 and 5.9 Hz, CH), 3.17 (d, 1 H, J = 2.0 Hz, CHC=O), 7.17–7.33 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 25.6, 33.1, 34.5, 58.6, 61.0, 127.4, 129.4, 129.7, 141.5, 206.7; HRMS calcd for $C_{12}H_{14}O_2$ 190.0994, found 190.1018.

2,2-Dimethyl-*cis*-4,5-epoxy-5-phenyl-3-pentanone (4d): mp 71–72 °C; IR (KBr) 1265, 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (s,

(25) Davies, A. G.; Palan, P. R.; Vasishtha, S. C. *Chem. Ind.* **1967**, 229.
(26) Monagle, J. J. *J. Org. Chem.* **1962**, *27*, 3851.

9 H, CH_3), 4.22 (d, 1 H, J = 4.9 Hz, CH), 4.33 (d, 1 H, J = 4.9 Hz, CH), 7.26–7.34 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 25.9, 43.2, 58.8, 59.8, 126.7, 128.1, 128.5, 133.1, 206.2; MS m/z 204 (M^+). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.43; H, 7.90. Found: C, 76.67; H, 7.83.

2-Oxa-4-oxo-1-phenylspiro[2.5]octane (4e): mp 68–70 °C; IR (KBr) 1250, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.72–2.40 (m, 8 H, CH_2), 4.07 (s, 1 H, CHPh), 7.25–7.35 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 25.0, 26.6, 35.6, 43.1, 65.4, 69.9, 126.3, 128.2, 128.4, 133.2, 203.2; MS m/z 202 (M^+). Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.19; H, 6.98. Found: C, 76.94; H, 6.95.

2,2-Dimethyl-*cis*-4,5-epoxy-*erythro*-6-phenyl-3-heptanone (Cram-4f). This compound was isolated by TLC as a mixture with ***anti*-Cram-4f** (Cram:anti-Cram = 3:2): wax; IR (neat) 1260, 1719 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (s, 9 H, CH_3), 1.48 (d, 3 H, J = 7.0 Hz, CH_3), 2.66–2.77 (m, 1 H, CHMe), 3.43 (q, (dd, 1 H, J = 4.4 Hz, CH of epoxide), 3.89 (d, 1 H, J = 4.4 Hz, CHC=O), 7.06–7.35 (m, 5 H); HRMS calcd for $C_{15}H_{20}O_2$ 232.1463, found 232.1457.

2,2-Dimethyl-*cis*-4,5-epoxy-*threo*-6-phenyl-3-heptanone (*anti*-Cram-4f). This compound was isolated by TLC as a mixture with **Cram-4f** (Cram:anti-Cram = 3:2): wax; IR (neat) 1260, 1719 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (d, 3 H, J = 10 Hz, CH_3), 1.30 (s, 9 H, CH_3), 2.66–2.77 (m, 1 H, CHMe), 3.30 (q, 1 H, J = 4.9 Hz, CH of epoxide), 4.03 (d, 1 H, J = 4.9 Hz, CHC=O), 7.06–7.35 (m, 5 H); HRMS calcd for $C_{15}H_{20}O_2$ 232.1463, found 232.1443.

***cis*-Ethyl 1,2-Epoxy-2-phenylpropanoate (6a) (General Procedure for the Preparation of α,β-Epoxy Esters).** A representative procedure is as follows (Table II, entry 2): To a solution of Bu_3SnOMe (0.96 g, 3 mmol) in dry THF (3 mL) under N_2 atmosphere was added EtNCO (0.17 g, 3 mmol) at 0 °C. After 10 min, the mixture was cooled to −78 °C, and α-bromo ester **5a** (0.50 g, 3 mmol), benzaldehyde (**3a**) (0.32 g, 3 mmol), and Bu_4NF (1M THF solution, 3 mL) were added. The mixture was allowed to warm to 0 °C and to stir overnight. The solvent was evaporated, and the mixture was purified by chromatography on a silica gel column, eluting with hexane/EtOAc (1:1 v/v). An almost pure mixture of *cis*- and *trans*-**6a** was obtained (0.47 g, 81%, cis:trans = 58:42). Further purification was performed by preparative TLC with 4:1 hexane/ethyl ether. The relative stereochemistry of diastereomers was assigned from ^1H NMR spectra by the chemical shift of the ring methine protons (δ3.4–4.2).

***cis*-6a.** This compound was isolated by TLC as a mixture with *trans*-**6a** (cis:trans = 3:2): wax; IR (neat) 1205, 1742 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (t, 3 H, J = 7.3 Hz, CH_3), 3.75 (d, 1 H, J = 4.4 Hz, CH), 3.93 (q, 2 H, J = 7.3 Hz, CH_2), 4.19 (d, 1 H, J = 4.4 Hz, CH), 7.19–7.35 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 14.2, 56.8, 57.4, 61.2, 125.8, 128.0, 129.0, 135.0, 166.2; HRMS calcd for $C_{11}H_{12}O_3$ 192.0786, found 192.0801.

***trans*-6a.** This compound was isolated by TLC as a mixture with *cis*-**6a** (cis:trans = 3:2): wax; IR (neat) 1205, 1742 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (t, 3 H, J = 7.3 Hz, CH_3), 3.43 (d, 2 H, J = 1.5 Hz, CH), 4.02 (d, 1 H, J = 1.5 Hz, CH), 4.18–4.24 (m, 2 H, CH_2), 7.19–7.35 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 13.9, 55.8, 57.9, 61.8, 126.7, 128.4, 128.7, 132.9, 166.6; HRMS calcd for $C_{11}H_{12}O_3$ 192.0786, found 192.0766.

***cis*-Benzyl 1,2-Epoxy-2-phenylpropanoate (*cis*-6b).** This compound was isolated by TLC as a mixture with *trans*-**6b** (cis:trans = 2:1) wax; IR (neat) 1190, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.78 (d, 1 H, J = 4.9 Hz, CH), 4.18 (d, 1 H, J = 4.9 Hz, CHPh), 4.86 (d, 1 H, J = 12.2 Hz, one of CH_2Ph), 4.92 (d, 1 H, 12.2 Hz, one of CH_2Ph), 7.16–7.32 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$) δ 55.8, 57.5, 66.8, 126.6, 128.0, 128.3, 128.4, 128.6, 128.7, 132.7, 134.9, 166.4; HRMS calcd for $C_{16}H_{14}O_3$ 254.0943, found 254.0902.

***trans*-Benzyl 1,2-Epoxy-2-phenylpropanoate (*trans*-6b).** This compound was isolated by TLC as a mixture with *cis*-**6b** (cis:trans = 2:1): wax; IR (neat) 1190, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.46 (d, 1 H, J = 1.5 Hz, CH), 4.03 (d, 1 H, J = 1.5 Hz, CH), 5.13 (d, 1 H, J = 12.2 Hz, one of CH_2Ph), 5.20 (d, 1 H, J 12.2 Hz, one of CH_2Ph), 7.16–7.32 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$) δ 56.7, 58.0, 67.4, 125.8, 128.2, 128.3, 128.4, 128.6, 129.0, 134.8, 134.9, 168.1; HRMS calcd for $C_{16}H_{14}O_3$ 254.0943, found 254.0930.

***cis*-*tert*-Butyl 1,2-Epoxy-2-phenylpropanoate (*cis*-6c).** This compound was isolated by TLC as a mixture with *trans*-**6c** (cis:trans = 3:2): wax; IR (neat) 1240, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.11 (s, 9 H, CH_3), 3.64 (d, 1 H, J = 4.9 Hz, CH), 4.15 (d, 1 H, J = 4.9 Hz, CH), 7.19–7.34 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 27.6, 57.0, 57.4, 82.3, 126.6, 127.8, 128.2, 133.2, 165.8. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.87; H, 7.33. Found: C, 70.53; H, 7.32.

***trans*-*tert*-Butyl 1,2-Epoxy-2-phenylpropanoate (*trans*-6c).** This compound was isolated by TLC as a mixture with *cis*-**6c** (cis:trans = 3:2): wax; IR (neat) 1240, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.44 (s, 9 H, CH_3), 3.33 (d, 1 H, J = 1.5 Hz, CH), 3.95 (d, 1 H, J = 1.5 Hz, CH), 7.19–7.34 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 28.0, 55.9, 57.6, 125.8, 128.5, 128.8, 135.3, 167.2. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.87; H, 7.33. Found: C, 70.53; H, 7.32.

2,5-Dioxa-3-phenylspiro[4.2]bicycloheptan-4-one (6d). This compound was obtained as two stereoisomeric diastereomers whose stereochemistry was unknown (major:minor = 3:2). Major isomer: wax; IR (neat) 1235, 1775 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.07 (ddd, 1 H, J = 3.9, 8.3, and 14.2 Hz, one of CH_2), 2.44–2.53 (m, 1 H, one of CH_2), 4.36–4.43 (m, 2 H, PhCH and one of CH_2O), 4.51 (td, 1 H, J = 9.8 and 3.0 Hz, one of CH_2O), 7.26–7.53 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 22.5, 61.6, 62.3, 64.7, 126.3, 128.6, 128.9, 132.9, 173.1; HRMS calcd for $C_{11}H_{10}O_3$ 190.1986, found 190.0614. Minor isomer: wax; IR (neat) 1235, 1775 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.44–2.53 (m, 1 H, one of CH_2), 2.72 (ddd, 1 H, J = 9.3, 10.3, and 13.7 Hz, one of CH_2), 4.27 (td, 1 H, J = 8.3 and 9.3 Hz, one of CH_2O), 4.36–4.43 (m, 2 H, PhCH and one of CH_2O), 7.26–7.53 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 27.8, 58.4, 63.9, 65.5, 127.0, 127.8, 128.7, 129.1, 170.4; HRMS calcd for $C_{11}H_{10}O_3$ 190.1986, found 190.0618.

3-Benzoyl-2-phenyloxolane (9b) (General Procedure for the Preparation of Oxolanes). A representative procedure for the preparation of **9b** is as follows (Table III, entry 2): To a solution of Bu_3SnOMe (0.96 g, 3 mmol) in dry THF (3 mL) under N_2 atmosphere was added PhN=C=NPh (0.58 g, 3 mmol) at 0 °C. After 10 min, the IR band at 2200 cm^{-1} due to the carbodiimide disappeared and a new band at 1660 cm^{-1} was detected, which indicated the formation of **7**.[17] Chloro ketone **8b** (0.36 g, 3 mmol), **3a** (0.32 g, 3 mmol), and HMPA (0.54 g, 3 mmol) were added to the mixture. After being heated at 60 °C for 3 h, the solvent was evaporated, and the mixture was chromatographed on a silica gel column. Bu_3SnCl and phenyl cyclopropyl ketone were eluted by hexane (200 mL). Subsequent eluting with hexane/EtOAc (1:1 v/v, 200 mL) gave a pure mixture (0.26 g, 35% cis:trans = 23:77). Further purification was performed by preparative TLC with 4:1 hexane/ethyl ether and gave a pure mixture of *cis*-**9b** and *trans*-**9b** (cis:trans = 3:2). The relative stereochemistry of diastereomers was assigned by ^1H NMR chemical shifts of ring methine protons (δ 3.9–5.3): wax; IR (neat) 1065, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.13–2.19 (m, 1 H, one of CH_2), 2.63–2.72 (m, 1 H, one of CH_2), 3.99 (td, 1 H, J = 8.3 and 7.3 Hz, one of CH_2O), 4.38 (td, 1 H, J = 7.8 and 7.3 Hz, one of CH_2O), 4.45 (td, 1 H, J = 8.3 and 3.9 Hz, CHC=O), 5.29 (d, 1 H, J = 8.3 Hz, CHPh); ^{13}C NMR ($CDCl_3$) δ 28.6, 51.2, 68.4, 83.0, 126.6, 127.4, 127.9, 128.1, 128.4, 132.5, 137.6, 138.5, 198.3; HRMS calcd for $C_{17}H_{16}O_2$ 252.1150, found 252.1136.

***trans*-3-Benzoyl-2-phenyltetrahydrofuran (*trans*-9b).** This compound was isolated as a single diastereomer by TLC: wax; IR (neat) 1065, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.27 (m, 1 H, one of CH_2), 2.44–2.54 (m, 1 H, one of CH_2), 3.92 (ddd, 1 H, J = 6.8, 7.3, and 9.3 Hz, CHC=O), 4.08 (ddd, 1 H, J = 7.3, 7.8, and 8.3 Hz, one of CH_2O), 4.24 (ddd, 1 H, J = 5.4, 7.3, and 8.3 Hz, one of CH_2O), 5.26 (d, 1 H, J = 7.3 Hz, CHPh), 7.21–7.82 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$) δ 32.2, 54.8, 68.5, 83.2, 125.9, 127.7, 128.50, 128.52, 128.6, 133.3, 136.6, 141.6, 199.9; HRMS calcd for $C_{17}H_{16}O_2$ 252.1150, found 252.1136.

***cis*-3-Acetyl-2-phenyltetrahydrofuran (*cis*-9a).** This compound was isolated as a mixture with *trans*-**9a** by TLC (cis:trans = 2:3): wax; IR (neat) 1060, 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.05 (s, 3 H, CH_3), 2.05–2.15 (m, 1 H, one of CH_2), 2.37–2.48 (m, 1 H, one of CH_2), 3.42 (ddd, 1 H, J = 4.9, 7.3, and 8.3 Hz, one of CHC=O), 3.85 (td, 1 H, J = 7.3 and 8.3 Hz, one of CH_2O), 4.27 (td, 1 H, J = 8.3 and 4.9 Hz, one of CH_2O), 5.10 (d, 1 H, J = 7.3 Hz, CHPh), 7.25–7.36 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 30.3, 30.5, 57.0, 68.1, 82.6, 126.3, 127.9, 128.3, 138.3, 208.0; HRMS calcd for $C_{12}H_{14}O_2$ 190.0994, found 190.0983.

***cis*-3-Acetyl-2-phenyltetrahydrofuran (*trans*-9a).** This compound was isolated by TLC as a mixture with *cis*-**9a** (cis:trans = 1:4): wax; IR (neat) 1060, 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.05 (s, 3 H, CH_3), 2.12–2.28 (m, 2 H, CH_2), 3.07 (td, 1 H, J = 7.3 and

8.8 Hz, CHC=O), 3.94 (ddd, 1 H, J = 6.8, 7.8, and 8.3 Hz, one of CH_2O), 4.08 (ddd, 1 H, J = 6.4, 7.3, and 8.3 Hz, one of CH_2O), 4.99 (d, 1 H, J = 7.3 Hz, CHPh), 7.25–7.36 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 28.5, 30.3, 60.2, 68.3, 82.5, 125.8, 127.8, 128.5, 141.5, 207.7; HRMS calcd for $C_{12}H_{14}O_2$ 190.0983, found 190.0983.

***cis*-3-Benzoyl-2-(*p*-chlorophenyl)tetrahydrofuran (*cis*-9c).** This compound was obtained by TLC as a mixture with *trans*-**9c** (cis:trans = 1:1): mp 38–40 °C; IR (KBr) 1065, 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.15–2.23 (m, 1 H, one of CH_2), 2.63–2.73 (m, 1 H, one of CH_2), 4.00 (ddd, 1 H, J = 6.8, 8.3, and 8.8 Hz, one of CH_2O), 4.40 (td, 1 H, J = 7.8 and 6.8 Hz, one of CH_2O), 4.46 (ddd, 1 H, J = 3.9, 7.8, and 8.3 Hz, CHC=O); 5.28 (d, 1 H, J = 7.8 Hz, CHAr), 6.92–7.83 (m, 9 H, Ar); HRMS calcd for $C_{17}H_{15}ClO_2$ 286.0761, found 286.0777.

***trans*-3-Benzoyl-2-(*p*-chlorophenyl)tetrahydrofuran (*trans*-9c).** This compound was obtained by TLC as a mixture with *cis*-**9c** (cis:trans = 1:1): mp 38–40 °C; IR 1065, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.24–2.34 (m, 1 H, one of CH_2), 2.43–2.53 (m, 1 H, one of CH_2), 3.85 (td, 1 H, J = 7.3 and 9.3 Hz, CHC=O), 4.07 (td, 1 H, J = 7.8 and 6.8 Hz, one of CH_2O), 4.25 (ddd, 1 H, J = 5.4, 7.8, and 8.3 Hz, one of CH_2O), 5.25 (d, 1 H, J = 7.3 Hz, CHAr), 6.92–7.83 (m, 9 H, Ar); HRMS calcd for $C_{17}H_{15}ClO_2$ 286.0761, found 286.0717.

***cis*-2-(*p*-Nitrophenyl)-3-benzoyltetrahydrofuran (*cis*-9d).** This compound was isolated by TLC as a mixture with *trans*-**9d** (cis:trans = 2:1): mp 86–88 °C; IR (KBr) 1060, 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.23–2.32 (m, 1 H, one of CH_2), 2.60–2.70 (m, 1 H, one of CH_2), 4.08 (td, 1 H, J = 14.7 and 7.3 Hz, one of CH_2O), 4.47–4.56 (m, 2 H, one of CH_2O and CHC=O), 5.38 (d, 1 H, J = 7.8 Hz, CHAr), 7.20–8.16 (m, 9 H, Ar); HRMS calcd for $C_{17}H_{15}NO_4$ 297.1501, found 297.0972.

***trans*-2-(*p*-Nitrophenyl)-3-benzoyltetrahydrofuran (*trans*-9d).** This compound was obtained by TLC as a mixture with *cis*-**9d** (cis:trans = 2:1): mp 86–88 °C; IR (KBr) 1060, 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.23–2.32 (m, 1 H, one of CH_2), 2.49–2.58 (m, 1 H, one of CH_2), 3.85 (td, 1 H, J = 7.3 and 9.8 Hz, CHC=O), 4.25–4.36 (m, 2 H, CH_2O), 5.45 (d, 1 H, J = 7.3 Hz, CHAr), 7.20–7.86 (m, 10 H, Ar); HRMS calcd for $C_{17}H_{15}NO_4$ 297.1001, found 297.0995.

***cis*-3-Benzoyl-2-phenyltetrahydropyran (*cis*-11).** To a solution of Bu_3SnOMe (0.96 g, 3 mmol) in dry THF (3 mL) under N_2 atmosphere was added PhN=C=NPh (0.58 g, 3 mmol) at 0 °C. After 10 min, **10** (0.86 g, 3 mmol), **3a** (0.32 g, 3 mmol), and HMPA (0.54 g, 3 mmol) were added to the mixture. After being heated at 60 °C for 3 h, the solvent was evaporated, and the mixture was chromatographed on a silica gel column. Bu_3SnI was eluted by hexane (200 mL). Subsequent elution with hexane/EtOAc (1:1 v/v, 200 mL) gave a almost pure mixtures of *cis*- and *trans*-**11** (0.43 g, 54% cis:trans = 21:79). Further purification was performed by preparative TLC with 4:1 hexane/ethyl ether, and a mixture (cis:trans = 1:5) was obtained. The relative stereochemistry of diastereomers was assigned by ^1H NMR spectra: wax; IR (neat) 1095, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.83–2.14 (m, 4 H, CH_2), 3.68–3.78 (m, 2 H, CHC=O and one of CH_2O), 4.20 (ddd, 1 H, J = 2.0, 2.4, and 11.7 Hz, one of CH_2O), 4.71 (d, 1 H, J = 9.8 Hz, CHPh), 7.11–7.67 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$) δ 25.2, 28.7, 50.9, 68.6, 81.8, 127.0, 127.9, 128.0, 128.3, 128.4, 132.9, 136.7, 140.7, 202.2; HRMS calcd for $C_{18}H_{18}O_2$ 266.1308, found 266.1305.

***trans*-3-Benzoyl-2-phenyltetrahydropyran (*trans*-11).** This compound was obtained by TLC as a mixture with *cis*-**11** (cis:trans = 1:5): wax; IR (neat) 1095, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.84–2.44 (m, 4 H, CH_2), 3.70 (td, 1 H, J = 2.4 and 11.2 Hz, one of CH_2O), 3.97 (td, 1 H, J = 3.0 and 5.4 Hz, one of CHC=O), 4.33 (ddd, 1 H, J = 4.4, 4.9, and 6.8 Hz, one of CH_2O), 4.78 (d, 2 H, J = 3.0 Hz, CHPh), 7.16–7.60 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$) 21.6, 26.6, 4.9, 68.9, 80.1, 125.8, 127.1, 127.8, 128.0, 128.2, 132.2, 137.9, 140.6, 200.9; HRMS calcd for $C_{18}H_{18}O_2$ 266.1307, found 266.1317.

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Supplementary Material Available: ^1H NMR spectra and HRMS data for **4a–f**, **6a–d**, **9a–d**, and **11** (34 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Synthesis of Optically Active Arylglycines by Photolysis of Optically Active (β-Hydroxyamino) Carbene–Chromium(0) Complexes

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Photolysis of [(amino)(aryl)carbene]chromium complexes having the optically active amino alcohol (1*R*,2*S*)-(−)- or (1*S*,2*R*)-(+)-2-amino-1,2-diphenylethanol as the amino group produced aryl-substituted oxazinones in good yield with reasonable diastereoselectivity. Facile separation of diastereoisomers followed by mild reductive cleavage produced several arylglycines, having either electron-donating or withdrawing groups on the aromatic ring, in good overall yield and with excellent enantiomeric excess.

Introduction

Although arylglycines are nonproteinogenic amino acids, they are found in a number of important biologically active compounds, including the vancomycins,[1] amoxicillins,[2] nocardicins,[3] and cephalecins.[4] The asymmetric synthesis of this class of compounds[5] is complicated by the lability of the α-proton, and syntheses involving basic conditions are compromised by attendant racemization. Because of

(1) Williams, D. H. *Acc. Chem. Res.* **1984**, *17*, 364 and references cited therein.

(2) Meyer, E. M.; Boesten, W. H. J.; Schoemaker, H. E.; vanBalken, J. A. M. In *Biocatalysts in Organic Synthesis*; Tramper, J., van der Plas, H. C., Linko, P., Eds.; Elsevier: Amsterdam 1985; p 135.

(3) Townsend, C. A.; Brown, A. M. *J. Am. Chem. Soc.* **1983**, *105*, 913.

(4) Spencer, J. L.; Flynn, E. H.; Roeske, R. W.; Sriv, F. Y.; Chaivette, R. R. *J. Med. Chem.* **1966**, *9*, 746.

(5) For an extensive survey of amino acid synthesis see: Williams, R. M. The Synthesis of Optically Active α-Amino Acids. In *Organic Chemistry Series*; Baldwin, J. E., Ed.; Pergamon Press: Oxford, 1989.

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