COR. All these equations give a good fit. The exception can be made to fit, if appropriate σ values corrected for solvation effects are taken into account. The best fit is the Yukawa-Tsuno equation (eq 7), but the difference of R values between these values is small (Table III).

Experimental Section

Materials. Inorganic and organic reagents used were all of the highest commercial grade and used without further purification. A solution of HCl in ethanol–water (90:10 v/v) was prepared by mixing 35% aqueous HCl or gaseous HCl with appropriate amount of 99% ethanol and water. The concentration was confirmed by alkalimetry.

Kinetics. A 90% (v/v) ethanolic solution (25 mL) containing an appropriate amount of HCl and nitro compound (2.5 mmol) and another 90% (v/v) ethanolic solution (25 mL) containing HCl (same amount) and $SnCl_2$ (7.5 mmol) were held at constant temperature (30 ± 0.1 °C). The two solutions were mixed to start the reaction, and aliquots were pipetted out at appropriate intervals of time. The concentration of $SnCl_2$ was measured by introduction of the aliquots into a 0.1 N I_2 solution containing KI followed by titration with 0.1 N $Na_2S_2O_3$. The reduction was quenched by introduction of aliquots into the iodine solution. For the estimation of HCl concentration, an aliquot sample at the beginning of experiment was introduced into aqueous sodium citrate[7] to subtract the amount of HCl produced by the hydrolysis of $SnCl_2$, and then the solution was titrated with 0.5 N NaOH with phenolphthalein as an indicator.

The HCl-catalyzed $SnCl_2$ reduction of nitro compounds ($ArNO_2$) obeys the stoichiometric equation 9:[5]

$$ArNO_2 + 3SnCl_2 + 7HCl \rightarrow ArNH_2{\cdot}HCl + 3SnCl_4 + 2H_2O \quad (9)$$

Assuming that the initial concentration of $SnCl_2$ is a, that of $ArNO_2$ b, that of HCl c, and consumed concentration of $SnCl_2$ at time t x, $[ArNO_2]$ at time t is expressed at $[b - x/3]$ on the basis of eq 9. Hence

$$v = -d[SnCl_2]/dt = dx/dt = k'[a - x][b - x/3] \quad (10)$$

$$k' = \frac{6.909}{t[3b - a]} \log \frac{a[3b - x]}{3b[a - x]} \quad (11)$$

A typical calculation of rate data for nitrobenzene is shown in Table IV as an example.

If [HCl] at time t is expressed as $(c - 7x/3)^{0.5}$ on the basis of eq 9, then

$$dx/dt = k[a - x][b - x/3][c - 7x/3]^{0.5} \quad (12)$$

Microcomputer-calculated k values for the integration of eq 12 are shown in Table IV (right column). The average k value calculated by eq 5 (10^2k = 0.1378 in Table II) is ca. 2% smaller than that by eq 12 (10^2k = 0.1406 in Table IV) for nitrobenzene.

The conversion of the reaction was ca. 30–50% under the duration of the kinetic experiments. A conversion over 50% would substantially decrease the acidity due to the formation of anilines, even if a large excess of HCl were used. As is well-known,[34] the reaction is a clean reaction, producing anilines alone; hence the kinetics were studied at these lower conversions.

Acknowledgment. We thank Professors Jian-Hou Zhang, Zhao-Lien Zhang, and Ren-Zhi Wang of Tianjin University for their generous aid in performing this study and Morio Inaishi for his helpful assistance in typewriting the manuscript.

Registry No. p-$HOC_6H_4NO_2$, 100-02-7; p-$CH_3OC_6H_4NO_2$, 100-17-4; p-$C_2H_5OC_6H_4NO_2$, 100-29-8; p-$CH_3C_6H_4NO_2$, 99-99-0; m-$HOC_6H_4NO_2$, 554-84-7; m-$CH_3C_6H_4NO_2$, 99-08-1; $PhNO_2$, 98-95-3; p-$C_6H_5C_6H_4NO_2$, 92-93-3; p-$FC_6H_4NO_2$, 350-46-9; m-$C_2H_5OC_6H_4NO_2$, 621-52-3; m-$CH_3OC_6H_4NO_2$, 555-03-3; p-$ClCH_2C_6H_4NO_2$, 100-14-1; p-$ClC_6H_4NO_2$, 100-00-5; p-$BrC_6H_4NO_2$, 586-78-7; m-$HOOCC_6H_4NO_2$, 121-92-6; m-$CH_3COC_6H_4NO_2$, 121-89-1; m-$FC_6H_4NO_2$, 402-67-5; m-$IC_6H_4NO_2$, 645-00-1; m-$ClC_6H_4NO_2$, 121-73-3; p-$HOOCC_6H_4NO_2$, 62-23-7; p-$CH_3COC_6H_4NO_2$, 100-19-6; m-$NCC_6H_4NO_2$, 619-24-9; p-$NCC_6H_4NO_2$, 619-72-7; m-$NO_2C_6H_4NO_2$, 99-65-0; $SnCl_2$, 7772-99-8.

Supplementary Material Available: The Hammett and Taft plots of the reduction of meta- and para-substituted nitrobenzenes with $SnCl_2$ (3 pages). Order information is given on any current masthead page.

(34) (a) Gattermann, L.; Wieland, H. "Die Praxis des Organischen Chemikers", 25th ed.; Walter de Gruyter: Berlin, Germany, 1925; p 170. (b) Ogata, Y. "Theories of Organic Reactions", 3rd ed.; Maruzen: Tokyo, 1975, p 461.

Improved Chiral Derivatizing Agents for the Chromatographic Resolution of Racemic Primary Amines

William H. Pirkle* and Kirk A. Simmons

Roger Adams Laboratory, School of Chemical Sciences, University of Illinois, Urbana, Illinois 61801

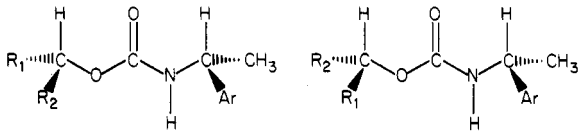
Received August 4, 1981

Several 4- and/or 5-aryl-substituted 2-oxazolidones have been prepared and studied as chiral derivatizing agents (CDA) for the chromatographic resolution of chiral primary amines via diastereomeric allophanates. The diastereomeric allophanates derived from either racemic primary amines and *cis*-4,5-diphenyl-2-oxazolidone-3-carbamyl chloride or racemic isocyanates and *cis*-4,5-diphenyl-2-oxazolidone show sufficient NMR chemical shift differences and chromatographic separability that this heterocyclic system should prove to be a very useful CDA for the chromatographic resolution and determination of the absolute configuration of a variety of chiral primary amines. The diastereomeric allophanates are readily hydrolyzed to return both chiral components of the allophanates in excellent yield. Both solution and adsorbed conformations of these allophanates are discussed in reference to the determination of the absolute configuration of the allophanates (and hence of the chiral primary amine) from the senses of NMR nonequivalence between and chromatographic elution order of the diastereomers.

As part of an ongoing effort to develop improved chiral derivatizing agents (CDAs) for use in determinations of enantiomeric purity, absolute configuration, and preparative resolutions of racemates, we have been concerned with the origins of the chromatographic separability noted for the diastereomers of numerous acyclic type 1 carba-

0022-3263/83/1948-2520$01.50/0

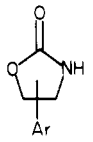
mates. To review briefly,[1] this separability appears to stem from the preferential population of conformations that serve as semirigid "backbones" from which protrude the remaining four substituents (R_1, R_2, Ar, and CH_3 in **1a,b**).



1a **1b**

The relative abilities of the substituents on either side of the backbone to "fend off" or to "anchor" that diastereomer to the adsorbent determine its chromatographic mobility. A rudimentary understanding of the relative "fending off" or "anchoring" capacities of the various substituents can be used to predict the elution order of the diastereomers.

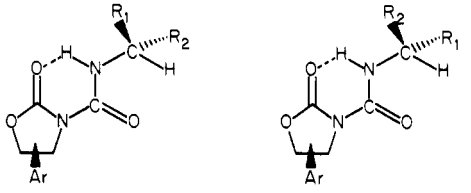
From the foregoing premise, it seemed likely that enhanced chromatographic separability of diastereomers might be engineered through (a) increased backbone rigidity and (b) more effective combinations of "fending off" and "anchoring" substituents. We now report that 4- and/or 5-aryl-substituted 2-oxazolidones (**2**) can be utilized



2

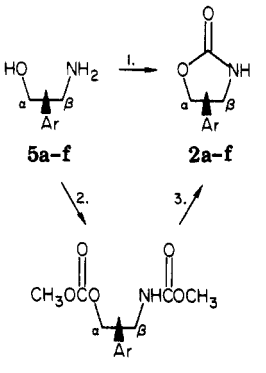
as CDAs and, as such, constitute a powerful addition to the CDAs available to the organic chemist.[2]

Since conformational rigidity appears to play a large role in the chromatographic separability of type 1 carbamates, we anticipated that the enhanced rigidity expected of diastereomeric allophanates **3a,b** (derived from chiral **2** and racemic isocyanates) would confer a high degree of chromatographic separability upon these diastereomers. This rigidity was expected to stem from (a) the 2-oxazolidone ring, (b) dipole–dipole repulsion of the two carbonyls,[3] (c) hydrogen bonding of the NH to the oxazolidone carbonyl oxygen[3] and (d) carbinyl hydrogen bonding of the aminyl hydrogen with the oxygen of the adjacent carbonyl.[9] Aryl groups possess considerable "fending off" ability toward silica or alumina and are, from a synthetic standpoint, relatively easy to incorporate into 2-oxazolidones. Since aryl groups are also efficient chemical shift perturbers, we anticipated that the diastereotopic R_1 and R_2 groups in allophanates **3a,b** would show significant chemical shift nonequivalence, thus enabling NMR determination of diastereomeric ratios and relative/absolution configurations.

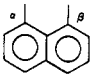


3a **3b**

Scheme I[a,b]



5a–f **2a–f** **6a–f**

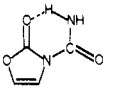
[a] a, Ar = α-Ph; b, Ar = β-Ph; c, Ar = α-1-Naph; d, Ar = β-1-Naph; e, Ar =  ; f, Ar = cis (or erythro) α,β-Ph_2. [b] (1) Dimethyl carbonate, $NaOCH_3$; (2) methyl chloroformate, pyridine; (3) $NaOCH_3$.

The ability to functionalize 2-oxazolidones upon nitrogen by using electrophiles such as phosgene, acid chlorides, acid anhydrides,[10-12] chloroformates,[11] and isocyanates[13] is well established, this chemistry being essential to the proposed usage of 2-oxazolidones as CDAs. Equally important, N-acylated 2-oxazolidones are reported to hydrolyze under mild conditions,[14] useful behavior if both the CDA and the resolved substrate are to be retrieved once the diastereomeric separation has been accomplished.

(1) Prior papers dealing with chromatographic and conformational behavior of diastereomeric type 1 carbamates are: (a) Pirkle, W. H.; Hauske, J. R. *J. Org. Chem.* **1977**, *42*, 1839. (b) Pirkle, W. H.; Hauske, J. R. *Ibid.* **1977**, *42*, 2436. (c) Pirkle, W. H.; Boeder, C. W. *Ibid.* **1978**, *43*, 2091. (d) Pirkle, W. H.; Simmons, K. A.; Boeder, C. W. *Ibid.* **1979**, *44*, 4891. (e) Pirkle, W. H.; Adams, P. E. *Ibid.* **1978**, *43*, 378.

(2) (a) Since submission of this paper, the chromatographic separability (capillary gas chromatography and liquid chromatography on silica) of diastereomeric 2-oxazolidone derivatives has been utilized by Evans in assaying the extent of asymmetric induction in reactions employing 2-oxazolidones as chiral auxiliaries. See: Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127. Evans, D. A.; Ennis, M. D.; Mathre, D. J. *Ibid.* **1982**, *104*, 1737. (b) One of the referees has invited comparison of the general method for resolution of enantiomers via chromatographic separation of diastereomers with methods involving the direct chromatographic separation of enantiomers upon chiral columns. He also suggested the referencing of such techniques. Pertinent reviews are: Blaschke, G. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 13. Davanakov, V. *Adv. Chromatogr.* **1980**, *18*, 139. Krull, I. *Ibid.* **1977**, *16*, 176. Lochmüller, C.; Souter, R. *J. Chromatogr.* **1975**, *113*, 283. Pirkle, W.; Finn, J. "Asymmetric Synthesis"; Morrison, J. D., Ed.; Academic Press: New York; Vol. 1, in press. In principle, direct chromatographic resolutions are preferable to indirect resolutions that employ chiral derivatizing agents. However, perusal of the aforementioned reviews will convince the reader that, for primary amines, direct methods have not yet evolved to the point where they are competitive in scope or scale with indirect methods. Relatively few primary amines have ever been directly resolved on chiral columns of any type. Moreover, chiral *preparative* columns are comparatively rare whereas large silica-packed columns are routinely used in many laboratories.

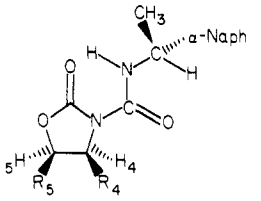
(3) Krieg[4,5] has shown by IR and NMR studies that achiral allophanates like **4** preferentially populate the conformation having the two carbonyls antiperiplanar and the amide proton hydrogen bonded to the ring carbonyl. Additionally, dipole moment studies of 2-oxazolidones and 3-acetyl-2-oxazolidones have shown that *N*-acyl derivatives generally assume conformations placing the carbonyls anti-periplanar.[6-8]



4

(4) Krieg, B.; Lautenschlager, H. *Justus Liebigs Ann. Chem.* **1976**, 208.
(5) Krieg, B.; Lautenschlager, H. *Justus Liebigs Ann. Chem.* **1976**, 788.
(6) Fischer, E. *J. Chem. Soc.* **1952**, 4525.
(7) Fischer, E. *J. Chem. Soc.* **1953**, 2836.
(8) Lee, C.; Kimler, W. *J. Am. Chem. Soc.* **1961**, *83*, 4596.
(9) Pirkle, W. H.; Hauske, J. R. *J. Org. Chem.* **1976**, *41*, 801.
(10) Homeyer, A. *Chem. Abstr.* **1948**, *42*, 4613.
(11) Close, W. *J. Am. Chem. Soc.* **1951**, *73*, 95.
(12) Gross, H.; Brendel, K.; Zimmerman, H. *Justus Liebigs Ann. Chem.* **1964**, *680*, 159.
(13) Sovish, R. *Chem. Abstr.* **1964**, *60*, 10686.
(14) Gompper, R. *Chem. Ber.* **1956**, *89*, 1748.

Table I. Chromatographic Separation Factors, Elution Orders, and Senses and Magnitudes of NMR Nonequivalence between and Absolute Configuration of Diastereomeric Allophanates

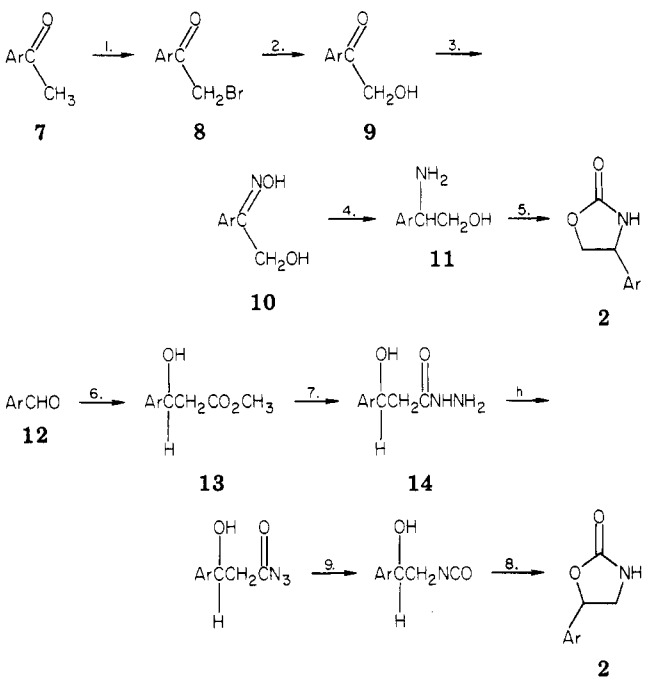


15

15	R_4	R_5	α value[a]	magnitude (sense) of nonequivalence,[b] ppm H_4	R_4	H_5	R_5	CH_3	configuration[c] C_4	C_5	amine
a	H	phenyl	2.05	0.07 (H)	0.03 (L)	0.07 (H)		0.0		*R*	*R*
b	phenyl	H	2.32	0.07 (H)		0.07 (H)	0.03 (L)	0.10 (H)	*S*		*R*
c	H	1-naphthyl	2.37	0.08 (H)	0.02 (L)	0.07 (H)		0.03 (H)		*R*	*R*
d	1-naphthyl	H	2.61	0.10 (H)		0.05 (H)	0.03 (L)	0.05 (H)	*S*		*R*
e	1,8-naphthyl		2.52	0.10 (H)		0.10 (H)		0.10 (H)	*S*	*R*	*R*
f	phenyl	phenyl	3.00	0.12 (H)		0.12 (H)		0.08 (H)	*S*	*R*	*R*

[a] These nonoptimized separations were achieved on an analytical HPLC system by using a 5-μm Spherisorb silica gel stationary phase and eluting with 0.25% isopropyl alcohol in hexane. [b] H means that the high-R_f diastereomer's NMR resonance is to higher field than that of its low-R_f isomer, while L means that the high-R_f diastereomer's NMR resonance is to lower field. [c] Configuration is that of the high-R_f diastereomer.

Scheme II[a]



[a] (1) Br_2, acetic acid; (2) sodium formate, EtOH, Δ; (3) $NH_2OH \cdot HCl$, base; (4) H^- or H_2, Pd/C; (5) dimethyl carbonate, $NaOCH_3$ or methyl chloroformate, Et_3N followed by $NaOCH_3$; (6) methyl bromoacetate, Zn; (7) NH_2NH_2, EtOH; (8) $NaNO_2$, HCl; (9) Δ.

Results and Discussion

The chemistry of the 2-oxazolidone ring system has been reviewed,[15] a variety of methods being known for the synthesis of either the parent system or suitably substituted homologues. Homeyer[16] developed a general route to 2-oxazolidones involving the condensation of a β-amino alcohol, **5**, with dimethyl carbonate under basic conditions (Scheme I). Homeyer's route is satisfactory provided the requisite β-amino alcohols are available. While a number of β-amino alcohols are available through reduction of α-amino acids or ammonolysis of expoxides, our a priori requirement of chemical shift and chromatographic perturbing substituents (in this case aryl groups) as well as regiochemical and stereochemical control (a cis relationship is needed if two aryl groups are present in the oxazolidone) dictated slightly different approaches (Schemes II and III).

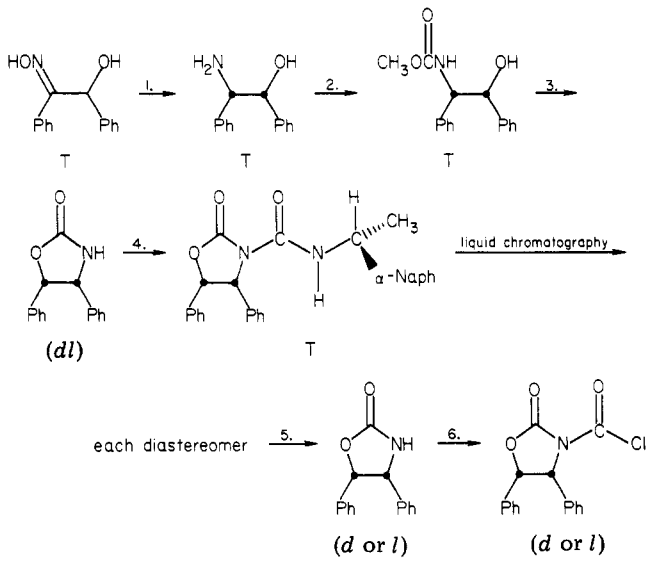
Aryl-substituted 2-oxazolidones **2a–f** were prepared and found to react smoothly with (*R*)-1-(1-naphthyl)ethyl isocyanate in refluxing benzene with 1.0 equiv of triethylamine present to afford the diastereomeric allophanates **15a–f**. These diastereomers proved to separate readily upon silica; values are indicated in Table I for α, the chromatographic separation factor.[17] From the α values, one can see that a phenyl substituent is less effective than is an α-naphthyl in engendering chromatographic separability. Moreover, aryl substituents are more effective in the 4-position than in the 5-position. Note also that two phenyls in a cis-4,5 relationship generate a larger α value than does a single α-naphthyl group. Thus, the most effective of the presently described 2-oxazolidones is also the most readily and inexpensively synthesized (Scheme III).

As expected, the diastereomeric allophanates **15a–f** do show NMR nonequivalence between diastereotopic groups

(15) Dyen, M.; Swern, D. *Chem. Rev.* **1967**, *67*, 197.
(16) Homeyer, A. U.S. Patent 2399118 **1946**; *Chem. Abstr.* **1946**, *40*, 4084.

(17) One of the referees has inquired as to why separability factors (i.e., α values) are reported rather than resolution values. The separability factor (i.e., the ratio of retention times of the diastereomers measured from the time of elution of a nonretained solute) is the ratio of the partition coefficients of the diastereomers between stationary and mobile phases. The ratio of partition coefficients is determined by chemical behavior and is independent of the particle size of adsorbent, column size, sample size (to a point), or how well the column is packed. Resolution, a measure of completeness of separation, depends not only upon the magnitude of α but also upon the aforementioned parameters. The second referee has inquired into the relationship between α and the quantity of material which may be separated. The answer to this question depends not only upon α but also the size and performance level of the column used. For example, the described chromatographic separation of 30 g of crude epimeric **17c** into its components is straightforward owing to the magnitude of α and the performance level of the moderately large column employed. Using the same column, one might be able to separate perhaps only 5 g of **17h** into its epimers owing to the smaller α value (1.24). However, larger columns of comparable performance would be capable of resolving larger samples of **17h**. We will point out that the magnitudes of α observed on the preparative column may differ a bit from those observed on the 5-μm Spherisorb analytical column owing to differences in the chemical nature of the adsorbent surface. A large home-built liquid chromatography system was used for preparative separations.

Scheme III[a]

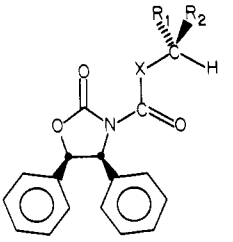


[a] (1) H_2, Pd/C; (2) CH_3OCOCl, TEA; (3) $NaOCH_3$; (4) (*R*)-(α-naphthylethyl)isocyanate; (5) $NaOCH_3$, THF; (6) Na/benzene then $COCl_2$.

(Table I). Senses of nonequivalence were determined by recombining unequal portions of the diastereomers after chromatographic separation. Note that the senses of nonequivalence and elution orders are those expected from these diastereomers provided that conformations **3a,b** determine these properties. These expectations are as follows. (a) Nonequivalence senses for diastereotopic groups on the oxazolidone ring are determined by whether these groups are syn (high field) or anti (low field) to the shielding α-naphthyl group (from the amine moiety) in **15**.[18] Similarly, the diastereotopic methyl resonances are influenced by being syn (high field) or anti (low field) to the aryl substituent(s) of the oxazolidone ring. (b) The diastereomer having the two least effective "fending off" groups (methyl and the oxazolidone ring protons) syn will be adsorbed more tightly (low R_f) than when these groups are anti (high R_f). The absolute/relative configurations of the diastereomers of allophanates **15b** and **15f** were established rigorously; the configurations, nonequivalence senses, and the elution orders are consistent with the aforementioned model. The presumption is that the remaining allophanates in Table I behave accordingly. The configurations of allophanates **15b** and **15f** were determined as follows. Oxazolidone **2b** was prepared (Scheme I) from (*R*)-phenylglycinol and allowed to react with the (*R*)-isocyanate to afford **15b**, the high-R_f diastereomer. Preparative separation of the diastereomers of **15f** followed by retrieval of the 2-oxazolidone from the low-R_f diastereomer afforded (+)-**2f**, known to be of the 4*R*,5*S* configuration.[20]

A quantity of *cis*-4,5-diphenyl-2-oxazolidone (**2f**) was prepared and converted by the action of phosgene to the corresponding carbamyl chloride **16f**, a stable, crystalline compound, which was then used to derivatize various racemic primary amines.[21] The resultant diastereomeric allophanates, **17a–h**, proved readily separable (Table II).

Table II. Epimeric Derivatives Synthesized from *cis*-4,5-Diphenyl-2-oxazolidone-3-carbamyl Chloride 121



17a–h

17	R_1	R_2	X	α value[a]
a	CH_3	CH_2CH_3	NH	1.32
b	CH_3	$(CH_2)_5CH_3$	NH	2.50
c	CH_3	phenyl	NH	2.69
d	phenyl	benzyl	NH	1.66
e	CH_3	4-biphenyl	NH	4.14
f	$(CH_2)_4CH_3$	$(CH_2)_3CH_3$	NH	1.17
g	CH_3	$C(CH_3)_3$	NH	1.68
h	CH_3	phenyl	NCH_3	1.24

[a] These nonoptimized separations were achieved on an analytical HPLC system by using a 5-μm Spherisorb silica gel stationary phase and eluting with 0.50% isopropyl alcohol-hexane.

Particularly noteworthy are the separations of the diastereomers derived from 2-butylamine and 5-decylamine. In the former case, the "fending off" difference between a methyl and an ethyl gives rise to an α value of 1.32. In the latter instance, the difference between *n*-butyl and *n*-pentyl gives rise to an α value of 1.17. In instances where the groups are more disparate (e.g., methyl vs. *n*-hexyl, methyl vs. biphenyl), the chromatographic separability of the diastereomers is such as to facilitate rather large-scale chromatographic resolutions.[22] We in fact chose to resolve 20 g of oxazolidone **2f** through chromatographic separation of the diastereomeric allophanates derived from (*S*)-1-phenylethyl isocyanate. The high-R_f diastereomer from this complete separation was treated with sodium methoxide in dry THF to retrieve (4*R*,5*S*)-(+)-**2f**. The overall yield of resolved **2f** was 77% from the corresponding β-amino alcohol. The resolved **2f** was converted to the corresponding carbamyl chloride **16f**. The carbamyl chloride reacts readily with primary and secondary amines in refluxing benzene (1 equiv of triethylamine present), allophanate derivatives **17a–h** being so prepared. The absolute configuration(s) of **17c** has been rigorously established and is in accord with the foregoing model which relates relative configuration to either elution order from silica or to NMR spectral differences.[23] To apply the chromatographic model, it is necessary to rank groups in order of chromatographic "fending off" or "anchoring" ability in order to relate elution order to relative/absolute configuration. These rankings may change with the nature of the adsorbent, particularly for some of the functionalized bonded phases now being used in HPLC. For each entry in Table II, it appears that R_2 is of a greater "fending off" ability than R_1 when silica is used as an adsorbent. Hence, the low-R_f diastereomer (most tightly adsorbed) in each case is expected to be that diastereomer having R_2 syn to

(18) The NMR assignment of the ring protons is not always straightforward; the methods used in reaching the assignments reported in the Experimental Section are discussed elsewhere.[19]

(19) Simmons, Kirk A. Ph.D. Dissertation, University of Illinois, 1980.

(20) Stefanovsky, J.; Spassov, S.; Kurtev, B.; Balla, M.; Otvos, L. *Chem. Ber.* **1969**, *102*, 717.

(21) Aliphatic isocyanates (e.g., 2-butyl or 2-octyl isocyanate) self-condense in preference to reaction with 2-oxazolidones.

(22) These diastereomeric allophanates are generally crystalline, offering as a bonus the opportunity for possible separation by recrystallization.

(23) Since submission of the manuscript, the allophanates derived from **2f** and either 1-(α-thienyl)ethylamine or 1-(*p*-anisyl)ethylamine have been found to show the expected chromatographic and NMR spectral behavior.

the oxazolidone phenyls in **17**.

Table II contains one entry, **17h**, derived from a secondary amine. The reduced separability of these diastereomers (α 1.24 vs. 2.69 for the analogous primary amine-derived **17c**) stems from two features. First, there is no longer an amide hydrogen to assist in backbone rigidity through hydrogen bonding to the oxazolidone carbonyl. Second, the rotational bias about the amine nitrogen–carbonyl bond no longer favors the *Z* rotamer as heavily as in **17c**. Since inverted elution orders and nonequivalence senses would be expected to accompany *Z* to *E* rotation, population of the *E* rotamer will diminish the time-averaged summations represented by α and the nonequivalence magnitudes. In the extreme case, extensive population of what we here term the *E* rotamer (the priorities of the two nitrogen substituents will determine nomenclature) might invert elution orders and nonequivalence senses. Hence, we make no claims at present with regard to NMR and chromatographic properties of the allophanates derived from secondary amines.[24]

Conclusion

Diastereomeric type **17** allophanates show appreciable degrees of chromatographic separability and NMR equivalence. Elution orders and nonequivalence senses appear to correlate with the absolute/relative configuration of the diastereomeric allophanates. Hence, the carbamyl chloride derived from enantiomerically pure *cis*-4,5-diphenyl-2-oxazolidone is a valuable chiral derivatizing agent for primary amines. It should also be evident that many amino alcohols (e.g., **5**) can be similarly resolved (via the oxazolidones), absolute configurations being assigned from elution orders of the allophanates. Application of this type of CDA to both chromatographic and NMR determinations of enantiomeric purity and absolute configuration is being investigated for other substrates.

Experimental Section

Melting points were taken on a Büchi apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 237B or Beckman IR-12 spectrophotometer. NMR spectra were obtained with a Varian Associates EM-390 or HR-220 spectrometer. Mass spectra were determined by using a Varian MAT CH-5 spectrometer, and microanalyses were performed by J. Nemeth and associates at the University of Illinois.

Preparation of 4-(Bromoacetyl)biphenyl. 4-Acetylbiphenyl (9.10 g, 46.0 mmol) and 100 mg of $AlCl_3$ were slurried in anhydrous Et_2O and cooled to 0 °C. Bromine (7.40 g, 46.0 mmol) was slowly added, and the reaction mixture was allowed to warm to room temperature and stirred for 1 h. The white solid was isolated by filtration to give 9.70 g (76%) of pure 4-(bromoacetyl)biphenyl. Concentration of the mother liquors and recrystallization of the solid from 95% ethanol gives an additional 2.20 g of product: total yield 11.90 g (94%); mp 124–125 °C (lit.[25] mp 125 °C); NMR ($CDCl_3$) δ 4.45 (s, 2 H), 7.3–7.7 (m, 5 H), 7.6–8.0 (AB pattern, 4 H).

Conversion of α-Bromo Ketones to α-Hydroxy Ketones. A solution of 35 mmol of α-bromo ketone and 15.0 g (220 mmol) of sodium formate in 90 mL 85% ethanol was heated to reflux for 12 h. After distillation of the ethanol, dilution with water dissolved the excess sodium formate and caused the product to precipitate. The ketols were isolated by filtration and recrystallized from 95% ethanol.

α-Hydroxyacetophenone: pale yellow solid; mp 84–85 °C (lit.[25] mp 86 °C); 90% yield; NMR ($CDCl_3$) δ 3.50 (t, 1 H, exchanges D_2O), 4.90 (d, 2 H), 7.3–7.7 (m, 3 H), 7.8–8.0 (m, 2 H).

α-Hydroxy-4-phenylacetophenone: pale yellow solid: mp 127–128 °C; NMR ($CDCl_3$) δ 3.50 (t, 1 H, exchanges D_2O), 4.90 (d, 2 H), 7.2–7.7 (m, 5 H), 7.7–8.0 (AB pattern, 4 H). Anal. Calcd for $C_{14}H_{12}O_2$: C, 79.23; H, 5.70. Found: C, 79.09; H, 5.58.

Preparation of Oximes from α-Hydroxy Ketones. α-Ketol (20 mmol), 2.60 g (38 mmol) of hydroxylamine hydrochloride, and 4.0 g of sodium carbonate were heated to reflux in 45 mL 70% ethanol for 24 h. Dilution with water caused the α-hydroxy oximes to precipitate.

2-Phenyl-2-isonitrosoethanol: pale yellow solid: mp 68–70 °C (CH_3OH–water) (lit.[25] mp 70 °C); 92% yield; NMR ($CDCl_3$) δ 4.4 (br s, 2 H, exchanges D_2O), 4.67 (s, 2 H), 7.2–7.8 (m, 5 H).

2-(4-Biphenylyl)-2-isonitrosoethanol: pale yellow solid: mp 160–161 °C (ethanol–water); 85% yield; NMR (acetone-d_6) δ 4.80 (s, 2 H), 7.2–7.8 (m, 9 H); IR (KBr) 3500–3200, 1620, 1490, 1400, 1310, 1205, 1080, 1030, 850 and 765 cm^{-1}. Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.20; H, 5.51; N, 6.25.

β-Amino Alcohols. 2-Amino-2-(1-naphthyl)ethanol (5d). Sodium cyanide (2.55 g, 52 mmol) in 10 mL of H_2O was added to a mixture of 7.80 g (50 mmol) of 1-naphthaldehyde, 10 mL of ether, 3.05 g (57 mmol) of ammonium chloride, and 9 mL of H_2O, all at 0 °C. After the mixture was stirred rapidly for 20 h, the intermediate amino nitrile was isolated by ether extraction and precipitated with anhydrous HCl; yield 5.90 g (54%). This solid was dissolved in anhydrous CH_3OH (125 mL), cooled to 0 °C, and saturated with anhydrous HCl for 4 h. H_2O was added (1.5 mL) and the reaction mixture purged with nitrogen. The solvents were removed under vacuum to afford methyl 1-(1-naphthyl)aminoacetate hydrochloride as a pale yellow solid: yield 4.50 g (67%); NMR (D_2O) δ 3.60 (s, CH_3), 5.90 (s, 1 H), 7.25–7.7 (m, 4 H), 7.7–8.0 (m, 3 H). This product was reduced with sodium borohydride (3.0 g, 79 mmol) in 50 mL 80% ethanol–H_2O at reflux for 8 h. The ethanol was removed under vacuum and the aqueous portion extracted with ethyl acetate. Concentration of the dried organic extracts gave 1.71 g (52%) of **5d** as a viscous oil: NMR ($CDCl_3$) δ 2.40 (br s, 3 H, exchanges D_2O), 3.5–4.0 (overlapping patterns, 2 H), 5.9 (d of d, 1 H), 7.2–8.2 (m, 7 H).

***erythro*-1,2-Diphenyl-2-aminoethanol (5f).** Benzoin oxime (25.0 g, 110 mmol) in 250 mL of absolute ethanol containing 7.0 g of anhydrous HCl and 1.0 g 5% Pd/C were shaken under an atmosphere of hydrogen at 60 psi. After 2.5 h, 185 mL of H_2O was added to dissolve the amine hydrochloride, and the catalyst was removed by filtration. After dilution to 750 mL with H_2O and basification with concentrated NH_4OH (100 mL), the amino alcohol was isolated by filtration: yield 23.0 g (98%) of pure **5f**; mp 161–163 °C (lit.[26] mp 163 °C); NMR ($CDCl_3$) δ 1.93 (br s, 3 H, exchanges D_2O), 4.16 (d, 1 H), 4.73 (d, 1 H), 7.23 (s, 10 H).

2-Amino-2-phenylethanol (5b). This compound was obtained by hydrogenation of the oxime by a procedure identical with that used in preparing **5f**. For **5b**: white solid; mp 76–77 °C (EtOAc–hexane) (lit.[25] mp 75–77 °C); 90% yield; NMR ($CDCl_3$) δ 2.6 (br s, 3 H, exchanges D_2O), 3.5–3.9 (m, 2 H), 4.0–4.2 (d of d, 1 H), 7.5 (s, 5 H).

Reaction of β-Amino Alcohol 5 with Methyl Chloroformate. Methyl chloroformate (3.5 g, 37 mmol) in 25 mL of dry THF was added to a solution of 15.0 mmol of β-amino alcohol and 3.0 g (38 mmol) of pyridine in 30 mL dry THF at −15 °C. After the mixture was stirred for 3 h, 25 mL of 3 N HCl was added, and the products were isolated by ether extraction. Evaporation of the dried extracts affords carbamate carbonate **6** which was used without further purification.

Methyl [2-[(methoxycarbonyl)oxy]-2-phenylethyl]carbamate (6b): clear, colorless oil; 89% yield; NMR ($CDCl_3$) δ 3.60 (s, 3 H), 3.70 (s, 3 H), 4.1–4.4 (m, 2 H), 4.8–5.2 (m, 1 H), 5.80 (d, 1 H), 7.3 (s, 5 H).

Methyl [2-[(methoxycarbonyl)oxy]-2-(1-naphthyl)-ethyl]carbamate (6d): clear, colorless oil; 87% yield; NMR ($CDCl_3$) δ 3.60 (s, 3 H), 3.75 (s, 3 H), 4.2–4.6 (2 m, 2 H), 5.6 (br m, 1 H), 5.8 (m, 1 H), 7.2–7.5 (m, 4 H), 7.6–7.9 (m, 3 H).

***erythro*-Methyl [2-[(Methoxycarbonyl)oxy]-1,2-diphenylethyl]carbamate (6f).** When **5f** was treated with 2.5

(24) We do know, however, that for type 1 carbamates derived from *N*-methyl-α-methylbenzylamine, the *Z* rotamer is still preferentially populated and does determine both the NMR senses of nonequivalence (in the fast-exchange limit) and the chromatographic elution orders.

(25) Rappoport, Z. "Handbook of Tables for Organic Compound Identification"; 3rd ed.; Chemical Rubber Co.; Cleveland, OH, 1967.

(26) Weijlard, J.; Pfister, K., III; Swanezy, E.; Robinson, C.; Tishler, M. *J. Am. Chem. Soc.* **1951**, *73*, 1216.

equiv of methyl chloroformate, only the N-acyloxylated product was formed: white needles; mp 193–193.5 °C (EtOAc–CCl_4); 95% yield; NMR ($CDCl_3$) δ 2.37 (br s, 1 H, exchanges D_2O), 3.65 (s, 3 H), 4.9–5.1 (d and br s, 2 H), 5.50 (d, 1 H), 6.9–7.4 (m, 10 H); IR ($CHCl_3$) 3600, 1730 cm^{-1}.

Cyclization of the Carbamates to 2-Oxazolidones. The carbamate (15.0 mmol), 50 mL of dry THF and ca. 200 mg of $NaOCH_3$ were stirred at room temperature for 12 h and diluted with H_2O (5 mL), and the product was extracted into CH_2Cl_2. Concentration under vacuum of the dried extracts afforded the 2-oxazolidones as solids which were recrystallized from the appropriate solvents.

4-Phenyl-2-oxazolidone (2b): white needles; mp 137–138 °C (EtOAc–hexane); 90% yield; NMR ($CDCl_3$) δ 4.0–4.3 (m, OCH), 4.5–4.7 (m, OCH), 4.7–5.0 (m, NCH), 6.5 (br s, 1 H), 7.3 (br s, 5 H); IR ($CHCl_3$) 3430, 1765 cm^{-1}. Anal. Calcd for $C_9H_9NO_2$: C, 66.25; H, 5.56; N, 8.58. Found: C, 66.12; H, 5.68; N, 8.63.

4-(1-Naphthyl)-2-oxazolidone (2d): white solid; mp 112–113 °C ($CHCl_3$–hexane); 85% yield; NMR ($CDCl_3$) δ 4.13 (d of d, OCH), 4.92 (t, OCH), 5.67 (d of d, NCH), 6.60 (br s, 1 H), 7.2–8.0 (m, 7 H). Anal. Calcd for $C_{13}H_{11}NO_2$: C. 73.23; H, 5.20; N, 6.57. Found: C, 72.83; H, 4.96; N, 6.56.

***cis*-4,5-Diphenyl-2-oxazolidone (2f)**: lustrous white needles; mp 224–225 °C (EtOAc–hexane); 95% yield; NMR ($CDCl_3$) δ 5.16 (d, NCH), 5.5 (br s, 1 H), 5.95 (d, OCH), 6.8–7.3 (m, 10 H); IR ($CHCl_3$) 3460, 1770, 1460, 1395, 1350, 1070, 1040, 730 cm^{-1}. Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.30; H, 5.52; N, 5.82.

Modified Reformatsky Reaction. Granulated zinc (6.54 g, 100 mmol), 30 mL of anhydrous THF, 100 mmol of aromatic aldehyde, and 25 mL of trimethyl borate were mixed and 11.1 mL ethyl bromoacetate added all at once. The reaction mixture was stirred at 25 °C until the zinc was consumed, 25 mL concentrated NH_4OH and 25 mL glycerin were added, and the product was extracted with Et_2O. Concentration of the dried extracts followed by distillation gave the β-hydroxy esters.

Ethyl 3-hydroxy-3-phenylpropionate (13a): clear, colorless liquid; bp 105–106 °C (0.10 torr); 93% yield; NMR ($CDCl_3$) δ 1.25 (t, 3 H), 2.5–2.7 (m, 2 H), 3.4 (br s, 1 H, exchanges D_2O), 4.10 (qt, 2 H), 5.10 (d of d, 1 H), 7.2–7.4 (m, 5 H).

Ethyl 3-hydroxy-3-(1-naphthyl)propionate (13b): pale yellow liquid which tended to dehydrate during distillation; 84% yield; NMR ($CDCl_3$) δ 1.23 (t, 3 H), 2.84 (m, 2 H), 3.6 (br s, 1 H, exchanges D_2O), 4.18 (qt, 2 H), 5.86 (d of d, 1 H), 7.27–8.06 (m, 7 H).

Conversion of Type 13 Esters to Acylhydrazides 14. Ethyl ester (ca. 60 mmol) in 50 mL of absolute ethanol was added dropwise to a solution of 6.0 mL of 85% hydrazine hydrate (100 mmol) in 10 mL of absolute ethanol at 50 °C. The reaction mixture was heated to reflux for 30 min and cooled, and the solvents were removed under vacuum. The products were recrystallized from 95% ethanol.

3-Hydroxy-3-phenylpropionhydrazide (14a): white solid; mp 154–155 °C; 92% yield; NMR (acetone-d_6) δ 2.70 (m, 2 H), 2.8–3.2 (br s, 3 H, exchanges D_2O), 5.14 (m, 1 H), 7.1–7.5 (m, 5 H), 9.1 (br s, 1 H). Anal. Calcd for $C_9H_{12}N_2O_2$: C, 59.99; H, 6.71; N, 15.54. Found: C, 59.95; H, 6.60; N, 15.41.

3-Hydroxy-3-(1-naphthyl)propionhydrazide (14b): white solid; mp 200–202 °C; 77% yield; NMR, too insoluble in common NMR solvents. Anal. Calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.93; H, 6.18; N, 12.34.

Conversion of Acylhydrazides to 2-Oxazolidones. To a cold (−10 °C) slurry of 100 mmol of acylhydrazide in 75 mL of 3 N HCl was added a solution of 100 mmol of sodium nitrite in 75 mL of H_2O at a rate so the reaction temperature was kept below −3 °C. After the addition, the reaction mixture was warmed to 50 °C, whereby the acyl azide decomposed with the evolution of N_2 into the isocyanate. After N_2 evolution ceased, it was heated at 80 °C for 12 h and filtered to isolate the 2-oxazolidone, which was purified by recrystallization.

5-Phenyl-2-oxazolidone (2a): clear, colorless needles; mp 120–121 °C (EtOAc–hexane); 94% yield; NMR ($CDCl_3$) δ 3.60 (t, NCH), 4.00 (t, NCH), 5.63 (t, OCH), 6.7 (br s, 1 H), 7.4 (br s, 5 H). Anal. Calcd for $C_9H_9NO_2$: C, 66.25; H, 5.56, N, 8.58. Found: C, 66.28; H, 5.52; N, 8.72.

5-(1-Naphthyl)-2-oxazolidone (2c): while solid; mp 152–153 °C (EtOAc–hexane), 85% yield; NMR (acetone-d_6) δ 3.48 (d of d, NCH), 4.28 (t, NCH), 6.37 (d of d, OCH), 6.6 (br s, 1 H), 7.3–7.8 (m, 4 H), 7.8–8.1 (m, 3 H); IR (KBr) 1765 cm^{-1}. Anal. Calcd for $C_{13}H_{11}NO_2$: C, 73.23; H, 5.20; N, 6.57. Found: C, 73.35; H, 5.18; N, 6.45.

Preparation of Ethyl (1-Hydroxyacenaphthen-2-yl)carbamate. Ethyl sodiochlorocarbamate[27] (1.10 g, 7.5 mmol), 2.55 g (15 mmol) of $AgNO_3$, and 50 mL of reagent grade acetonitrile were stirred 10 min at room temperature, and then 0.40 mL (22 mmol) of H_2O, 0.76 g (5 mmol) of acenaphthylene, and 0.005 mmol of OsO_4 in *tert*-butyl alcohol were added. The reaction mixture was stirred until the olefin was consumed (TLC, silica gel), saturated NaCl (1.25 mL) was added, and the filtrate was stirred with 7 mL of 8% $NaHSO_3$ for 15 min. The product, isolated by CH_2Cl_2 extraction, was chromatographed on silica gel (eluted with EtOAc–hexane, 1:1). There was obtained 400 mg (31%) of product as a moist solid: NMR ($CDCl_3$) δ 1.18 (t, 3 H), 4.18 (qt, 2 H), 5.43 (br s, 1 H), 5.57 (br s, 2 H), 7.4–7.6 (m, 3 H), 7.7–7.8 (m, 1 H), 7.85 (t, 1 H), 8.2 (d of d, 1 H); IR ($CHCl_3$) 3550, 1720 cm^{-1}.

Preparation of 4,5-(1,8-Naphthylene)-2-oxazolidone (2e). The preceding crude product (400 mg), 5.0 mL of dry THF, and 20 mg of $NaOCH_3$ were stirred under N_2 for 8 h and diluted with H_2O (5.0 mL), and the crude oxazolidone was extracted into ethyl acetate. Concentration of the dried extracts and recrystallization of the residue gave **2e**: mp 210–211.5 °C (EtOAc–hexane); NMR ($CDCl_3$) δ 5.53 (d, NCH), 6.1–6.3 (br s, 1 H), 6.33 (d, OCH), 7.3–7.9 (m, 6 H); IR (KBr) 1785 cm^{-1}.

Reaction of Aryl-2-oxazolidone with (*R*)-(−)-1-(1-Naphthyl)ethyl Isocyanate. 2-Oxazolidone (1.0 mmol), 1.05 mmol of (*R*)-(−)-1-(1-naphthyl)ethyl isocyanate, 1.0 mmol of triethylamine, and ca. 3 mL of dry benzene were heated to reflux for 24 h and then allowed to stir at room temperature for 24 h, by which time the isocyanate band (2260 cm^{-1}) had mostly disappeared. The reaction mixture was concentrated under vacuum and chromatographed on silica gel (eluted with CH_2Cl_2–hexane (1:1)) to separate the diastereomers from other materials. In all cases reported, the diastereomeric allophanates were isolated in >95% yield.

***N*-[(*R*)-1-(1-Naphthyl)ethyl]-5-phenyl-2-oxazolidone-3-carboxamides (15a).** High-R_f diastereomer: clear, colorless oil; NMR ($CDCl_3$) δ 1.67 (d, CH_3), 3.85 (d of d, NCH), 4.27 (d of d, NCH), 5.37 (t, OCH), 5.87 (quintet, NCH), 6.7 (br d, NH), 7.1–8.4 (m, 12 H); IR (film) 3250, 3050, 2900, 1750, 1690, 1570, 1480, 1390, 1370, 1240, 1110, 1020 cm^{-1}; mass spectrum (70 eV), *m/e* (relative intensity) 360 (M^+, 23), 345 (32), 202 (11), 197 (13), 182 (59), 171 (16), 170 (100), 169 (26), 168 (25), 167 (14), 156 (25), 155 (40), 154 (30), 153 (28), 152 (13), 149 (24), 129 (32), 128 (34), 127 (30), 119 (40), 113 (10), 111 (17), 109 (12), 107 (21), 105 (22), 104 (27), 97 (26), 91 (26), 86 (31), 85 (29), 83 (80), 81 (20), 77 (27), 71 (51), 69 (38), 57 (84), 55 (48). Low-R_f diastereomer: clear, colorless oil; NMR ($CDCl_3$) δ 1.68 (d, CH_3), 3.83 (d of d, NCH), 4.35 (d of d, NCH), 5.45 (t, OCH), 5.87 (quintet, NCH), 6.7 (br d, NH), 7.1–8.4 (m, 12 H); IR (film) 3240, 3050, 2900, 1745, 1690, 1570, 1480, 1385, 1370, 1240, 1110, 1020 cm^{-1}.

***N*-[(*R*)-1-(1-Naphthyl)ethyl]-4-phenyl-2-oxazolidone-3-carboxamides (15b).** High-R_f diastereomer: mp 166–167 °C (benzene–hexane); NMR ($CDCl_3$) δ 1.57 (d, CH_3), 4.06 (d of d, OCH), 4.40 (t, OCH), 5.20 (d of d, NCH), 5.77 (quintet, NCH), 6.8 (br d, NH), 7.1–8.5 (m, 12 H); IR ($CHCl_3$) 3360, 3050, 1760, 1710, 1540, 1400, 1335, 1270, 1110 cm^{-1}. Anal. Calcd for $C_{22}H_{20}N_2O_3$: C, 73.32; H, 5.59; N, 7.77. Found: C, 73.17; H, 5.52; N, 7.54. Low-R_f diastereomer: mp 172–173 °C (CH_2Cl_2–petroleum ether); NMR ($CDCl_3$) δ 1.67 (d, CH_3), 4.03 (d of d, OCH), 4.50 (t, OCH), 5.37 (d of d, NCH), 5.75 (quintet, NCH), 6.60 (br d, NH), 7.0–8.3 (m, 12 H); IR ($CHCl_3$) 3355, 3050, 1760, 1710, 1540, 1395, 1335, 1270, 1110 cm^{-1}.

***N*-[(*R*)-1-(1-Naphthyl)ethyl]-5-(1-naphthyl)-2-oxazolidone-3-carboxamides (15c).** High-R_f diastereomer: mp 83–85 °C (CH_2Cl_2–petroleum ether); NMR ($CDCl_3$) δ 1.67 (d, CH_3), 3.90 (d of d, NCH), 4.48 (d of d, NCH), 5.83 (quintet, NCH), 6.07 (t, OCH), 6.90 (br d, NH), 7.3–8.4 (m, 14 H); IR ($CHCl_3$) 3360, 3020,

(27) The synthesis and use of ethyl sodiochlorocarbamate was described by Sharpless and co-workers: Herranz, E.; Biller, S. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1978**, *100*, 3596; see also footnote 6 therein.

1760, 1695, 1540, 1485, 1400, 1250, 1190, 1120 cm^{-1}. Low-R_f diastereomer: mp 120–122 °C (EtOAc–hexane); NMR ($CDCl_3$) δ 1.70 (d, CH_3), 3.90 (d of d, NCH), 4.57 (t, NCH), 5.87 (quintet, NCH), 6.17 (t, OCH), 6.80 (br d, NH), 7.3–8.4 (m, 14 H); IR ($CHCl_3$) 3360, 3020, 1760, 1690, 1540, 1485, 1395, 1250, 1195, 1120 cm^{-1}. Anal. Calcd for $C_{26}H_{22}N_2O_3$: C, 76.08; H, 5.40; N, 6.82. Found: C, 76.04; H, 5.46; N, 6.59.

***N*-[(*R*)-1-(1-Naphthyl)ethyl]-4-(1-naphthyl)-2-oxazolidone-3-carboxamides (15d).** High-R_f diastereomer: mp 163–165 °C (EtOAc–hexane); NMR ($CDCl_3$) δ 1.67 (d, CH_3), 4.17 (d of d, OCH), 4.78 (t, OCH), 5.80 (quintet, NCH), 6.17 (d of d, NCH), 6.90 (br d, NH), 7.3–8.6 (m, 14 H); IR ($CHCl_3$) 3350, 3060, 1760, 1700, 1535, 1400, 1335, 1315, 1270, 1110, 1080 cm^{-1}. Low R_f diastereomer: mp 187–188 °C (EtOAc–hexane); NMR ($CDCl_3$) δ 1.73 (d, CH_3), 4.13 (d of d, OCH), 4.83 (t, OCH), 5.87 (quintet, NCH), 6.27 (d of d, NCH), 6.90 (br d, NH), 7.1–8.4 (m, 14 H); IR ($CHCl_3$) 3350, 3060, 1760, 1700, 1535, 1405, 1330, 1310, 1270, 1110 cm^{-1}. Anal. Calcd for $C_{26}H_{22}N_2O_3$: C, 76.08, H, 5.40; N, 6.82. Found: C, 76.26; H, 5.29; N, 6.96.

***N*-[(*R*)-1-(1-Naphthyl)ethyl]-4,5-(1,8-naphthylene)-2-oxazolidone-3-carboxamides (15e).** High-R_f diastereomer: mp 157–159 °C ($CHCl_3$–hexane); NMR ($CDCl_3$) δ 1.63 (d, CH_3), 5.93 (quintet, NCH), 6.10 (s, NCH and OCH), 6.8 (br d, NH), 7.3–8.5 (m, 13 H); IR ($CHCl_3$) 3360, 3060, 1760, 1700, 1545, 1380, 1275, 1200, 1120, 1105, 1030 cm^{-1}. Anal. Calcd for $C_{26}H_{20}N_2O_3$: C, 76.46; H, 4.94; N, 6.86. Found: C, 76.47; H, 4.90; N, 6.66. Low-R_f diastereomer: mp 133–135 °C (CH_2Cl_2–petroleum ether); NMR ($CDCl_3$) δ 1.72 (d, CH_3), 5.93 (quintet, NCH), 6.18 (s, NCH and OCH), 6.80 (br d, NH), 7.3–8.4 (m, 13 H); IR ($CHCl_3$) 3360, 3055, 1760, 1705, 1545, 1380, 1270, 1200, 1120, 1100, 1030 cm^{-1}.

***N*-[(*R*)-1-(1-Naphthyl)ethyl]-*cis*-4,5-diphenyl-2-oxazolidone-3-carboxamides (15f).** High-R_f diastereomer: mp 146–147 °C (benzene–hexane); NMR ($CDCl_3$) δ 1.65 (d, CH_3), 5.57 (AB d, NCH, J = 9 Hz), 5.80 (quintet, NCH), 5.80 (AB d, OCH, J = 9 Hz), 6.7 (br d, NH), 6.8–7.3 (m, 10 H), 7.4–8.5 (m, 7 H); IR ($CHCl_3$) 3360, 3060, 1765, 1705, 1540, 1365, 1270, 1195, 1130, 1040 cm^{-1}. Low-R_f diastereomer: mp 152–153 °C (CH_2Cl_2–petroleum ether); NMR ($CDCl_3$) δ 1.75 (d, CH_3), 5.70 (AB d, NCH, J = 9 Hz), 5.82 (quintet, NCH), 5.93 (AB d, OCH, J = 9 Hz), 6.7 (br d, NH), 6.8–7.3 (m, 10 H), 7.4–8.5 (m, 7 H); IR ($CHCl_3$) 3360, 3060, 1760, 1705, 1540, 1365, 1270, 1195, 1135, 1045 cm^{-1}. Anal. Calcd for $C_{28}H_{24}N_2O_3$: C, 77.04; H, 5.54; N, 6.42. Found: C, 77.00; H, 5.36; N, 6.88.

Attempted Reaction of 2f with Chiral Alkyl Isocyanates. In separate experiments, 1.0 mmol of **2f**, 3 mL of dry benzene, 1.0 mmol of Et_3N, and 1.0 mmol of 2-butyl isocyanate (or 2-heptyl isocyanate or 4-methyl-2-pentyl isocyanate) were heated to reflux for 48 h, by which time the isocyanate band (ca. 2260 cm^{-1}) had minimized.[21] When the mixture cooled, a white solid crystallized which proved to be unreacted **2f** recovered in essentially quantitative yield.

Preparation of (4*R*,5*S*)-*cis*-4,5-Diphenyl-2-oxazolidone-3-carbamyl Chloride (16f). A slurry of 1.5713 g (6.567 mmol) of vacuum-dried **2f** and pentane-washed NaH (7.2 mmol) in 25 mL of dry toluene was maintained at reflux under dry N_2 overnight, chilled to −17 °C, and then added in portions to 11.2 g (113 mmol) of phosgene in dry toluene also at −17 °C. The mixture was removed from the ice bath after 1 h, filtered, and concentrated under reduced pressure to afford 1.8925 g (95.5%) of carbamyl chloride **16f**. The product can be recrystallized from CCl_4–hexane, although the "crude" product was quite pure by NMR: mp 125–138 °C; NMR ($CDCl_3$) δ 5.65 (AB d, NCH), 5.95 (AB d, OCH), 6.8–7.2 (m, 10 H); IR ($CHCl_3$) 3060, 1840, 1810, 1765, 1460, 1340, 1250, 1170, 1045, 980, 935, 880 cm^{-1}; MS (70 eV) m/e (relative intensity) 303 (M + 2, 3.8), 301 (M$^+$, 11.4), 266 (2), 222 (6), 195 (11), 159 (8), 133 (10), 132 (100), 107 (31), 105 (22), 104 (11), 89 (8), 77 (31), 51 (9), 44 (26). Anal. Calcd for $C_{16}H_{12}NO_3Cl$: C, 63.69; H, 4.01; N, 4.64; Cl, 11.75. Found: C, 63.98; H, 3.93; N, 4.52; Cl, 11.50.

Recrystallization of **16f** is hardly necessary and, unless appropriate precautions are taken, can result in some hydrolysis (atomospheric moisture) and decarboxylation to regenerate **2f**.

Reaction of 16f with Chiral Primary and Secondary Amines. Compound **16f** (1.0 mmol), 1.1 mmol of chiral amine, 1.1 mmol of Et_3N, and 3 mL of dry benzene were heated to reflux for ca. 3 h, cooled, diluted with ether, and washed with 1 N HCl and H_2O. Evaporation of the dried organic extracts affords the product, in yields always greater than 90%. Characterization was done on the epimeric mixture.

***N*-2-Butyl-*cis*-4,5-diphenyl-2-oxazolidone-3-carboxamides (17a):** white solid: mp 88–92 °C (EtOAc–hexane); NMR ($CDCl_3$) δ 0.75–1.05 (2 overlapping t, CH_3), 1.05–1.30 (2 overlapping d, CH_3), 1.3–1.7 (m, CH_2), 3.75 (heptet, NCH), 5.65 (AB d, NCH), 5.95 (AB d, OCH), 6.7–7.2 (m, 10 H), 7.75 (br d, NH); IR ($CHCl_3$) 3330, 3020, 2950, 1750, 1690, 1530, 1445, 1370, 1350, 1180, 1030, 700 cm^{-1}. Anal. Calcd for $C_{20}H_{22}N_2O_3$: C, 70.99; H, 6.55; N, 8.28. Found: C, 70.79; H, 6.34; N, 8.03.

***N*-(2-Octyl)-*cis*-4,5-diphenyl-2-oxazolidone-3-carboxamides (17b):** clear, colorless solid; mp 75–85 °C (CH_2Cl_2–hexane); NMR ($CDCl_3$) δ 0.7–1.0 (2 overlapping t, CH_3), 1.1–1.6 (m, 13 H, $(CH_2)_5CH_3$), 3.85 (heptet, NCH), 5.65 (AB d, NCH), 5.92 (AB d, OCH), 6.77–7.20 (m, 10 H), 7.8 (br d, NH); IR ($CHCl_3$) 3330, 3020, 2950, 1750, 1685, 1530, 1450, 1370, 1350, 1180, 1030 cm^{-1}; mass spectrum (70 eV), m/e (relative intensity) 394 (M$^+$, 7), 310 (15), 309 (100), 265 (15), 222 (37), 220 (15), 196 (21), 149 (15), 129 (30), 121 (29), 107 (72), 105 (29), 104 (19), 91 (34), 84 (29), 79 (16), 77 (34), 57 (18), 44 (47).

***N*-(1-Phenylethyl)-*cis*-4,5-diphenyl-2-oxazolidone-3-carboxamides (17c):** white solid; mp 145–158 °C (EtOAc–hexane); NMR ($CDCl_3$) δ 1.5–1.65 (2 overlapping d, CH_3), 4.8–5.2 (m, NCH), 5.50–5.70 (2 AB d, NCH), 5.75–6.0 (2 AB d, OCH), 6.7–7.2 (m, 10 H), 7.2–7.4 (m, 5 H), 8.3 (br d, NH); IR ($CHCl_3$) 3360, 3040, 1765, 1700, 1535, 1460, 1360, 1270, 1195, 1120, 1040 cm^{-1}. Anal. Calcd for $C_{24}H_{22}N_2O_3$: C, 74.59; H, 5.74; N, 7.25. Found: C, 74.57; H, 5.71; N, 6.89.

***N*-(1,2-Diphenylethyl)-*cis*-4,5-diphenyl-2-oxazolidone-3-carboxamides (17d):** white solid; mp 157–165 °C (EtOAc–hexane); NMR ($CDCl_3$) δ 3.0–3.2 (m, CH_2), 4.9–5.15 (m, NCH), 5.40–5.60 (2 AB d, NCH), 5.70–5.90 (2 AB d, OCH), 6.5–7.3 (m, 20 H), 8.45 (br d, NH); IR ($CHCl_3$) 3340, 3040, 1760, 1705, 1535, 1360, 1270, 1195, 1120, 700 cm^{-1}. Anal. Calcd for $C_{30}H_{26}N_2O_3$: C, 77.90; H, 5.67; N, 6.06. Found: C, 77.81; H, 5.82; N, 5.90.

***N*-[1-(4-Biphenylyl)ethyl]-*cis*-4,5-diphenyl-2-oxazolidone-3-carboxamides (17e):** white solid; mp 150–160 °C (EtOAc–hexane); NMR ($CDCl_3$) δ 1.4–1.6 (2 overlapping d, CH_3), 4.8–5.1 (m, NCH), 5.50–5.70 (2 AB d, NCH), 5.80–5.95 (2 AB d, OCH), 6.7–7.2 (m, 10 H), 7.2–7.6 (m, 9 H), 8.3 (br d, NH); IR ($CHCl_3$) 3330, 3010, 2990, 1750, 1690, 1520, 1350, 1255, 1180, 1110, 700 cm^{-1}. Anal. Calcd for $C_{30}H_{26}N_2O_3$: C, 77.90; H, 5.67; N, 6.06. Found: C, 77.59; H, 5.73; N, 6.02.

***N*-(5-Decyl)-*cis*-4,5-diphenyl-2-oxazolidone-3-carboxamides (17f):** white solid; mp 82–86 °C (CH_2Cl_2–petroleum ether); NMR ($CDCl_3$) δ 0.7–0.95 (m, 6 H, CH_3), 1.0–1.6 (m, 14 H, CH_2), 3.69 (m, NCH), 5.59 (AB d, NCH), 5.77 (AB d, OCH), 6.7–7.0 (m, 10 H), 7.68 (br d, NH); IR ($CHCl_3$) 3350, 2960, 2940, 1760, 1700, 1540, 1360, 1190 cm^{-1}. Anal. Calcd for $C_{26}H_{34}N_2O_3$: C, 73.90; H, 8.11; N, 6.63. Found: C, 73.62; H, 7.91; N, 6.66.

***N*-(3,3-Dimethylbut-2-yl)-*cis*-4,5-diphenyl-2-oxazolidone-3-carboxamides (17g):** clear, colorless solid, mp 125–132 °C (CH_2Cl_2–petroleum ether); NMR ($CDCl_3$) δ 0.95 (s, *t*-Bu), 1.00 (s, *t*-Bu), 1.0–1.2 (2 overlapping d, CH_3), 3.5–3.9 (2 quintets, NCH), 5.57–5.73 (AB d, NCH), 5.80–6.00 (AB d, OCH), 6.7–7.2 (m, 10 H), 7.95 (br d, NH); IR ($CHCl_3$) 3360, 3020, 2980, 1760, 1700, 1535, 1455, 1360, 1270, 1190, 1120, 1035 cm^{-1}. Anal. Calcd for $C_{22}H_{26}N_2O_3$: C, 72.11; H, 7.15; N, 7.64. Found: C, 71.99; H, 7.18; N, 7.53.

***N*-Methyl-*N*-(1-phenylethyl)-*cis*-4,5-diphenyl-2-oxazolidone-3-carboxamides (17h):** white solid; mp 173–184 °C (CH_2Cl_2–petroleum ether); NMR ($CDCl_3$) δ 1.40–1.57 (2 overlapping d, CH_3), 2.82 (s, NCH_3), 2.87 (s, NCH_3), 5.3–5.7 (2 overlapping qt, NCH), 5.7–5.9 (AB pattern, NCH and OCH), 6.7–7.2 (m, 10 H), 7.23 (s, 5 H), 7.30 (s, 5 H); IR ($CHCl_3$) 3060, 3040, 1770, 1685, 1460, 1395, 1350, 1240, 1070, 1030, 985 cm^{-1}; mass spectrum (70 eV), m/e (relative intensity) 400 (M$^+$, 1), 222 (6), 180 (7), 179 (8), 178 (6), 135 (10), 134 (100), 105 (39), 77 (15).

Preparative Scale Synthesis, Separation, and Hydrolysis of the Epimeric Allophanates 17c. Following exactly the procedures already described for the synthesis of compounds **6f** and **2f**, 22.0 g (103 mmol) of **5f** was converted to 20.70 g (84%) of **2f** (pure by NMR). Recrystallization from EtOAc–hexane (1:9, 600 mL) afforded 19.8 g (80% from **5f**) of analytically pure **2f**. **2f** (18.3 g, 76.5 mmol), 250 mL of dry benzene, 11.4 g (77.6 mmol)

of (S)-1-phenylethyl isocyanate, and 7.80 g (77.2 mmol) of Et_3N were heated to reflux for ca. 60 h and then allowed to stir at room temperature for 24 h. Removal of the solvents under reduced pressure gave the mixed epimers of **17c** (~30 g) which were chromatographically separated on a 2 in. × 48 in. column of 58-μm silica gel (eluent CH_2Cl_2–hexane, 1:1) by using a previously described preparative chromatography system.[28] There was recovered 2.0 g of unreacted **2f**. Each of the epimeric allophanates was recrystallized from CH_2Cl_2–hexane (1:3, ~400 mL). High-R_f epimer: white needles; mp 145–146 °C; NMR ($CDCl_3$) δ 1.49 (d, CH_3), 4.92 (quintet, 1 H), 5.54 (AB d, NCH), 5.78 (AB d, OCH), 6.7–7.2 (m, 10 H), 7.34 (s, 5 H), 8.3 (br d, 1 H). Anal. Calcd for $C_{24}H_{22}N_2O_3$: C, 74.59; H, 5.74; N, 7.25. Found: C, 74.75; H, 5.67; N, 7.29. Low-R_f epimer: white needles; mp 151–152.5 °C; NMR ($CDCl_3$) δ 1.56 (d, CH_3), 4.98 (quintet, 1 H), 5.64 (AB d, NCH), 5.91 (AB d, OCH), 6.7–7.2 (m, 10 H), 7.32 (s, 5 H), 8.3 (br d, NH). Anal. Calcd for $C_{24}H_{22}N_2O_3$: C, 74.59; H, 5.74; N, 7.25. Found: C, 74.29; H, 5.76; N, 7.32.

The reaction afforded a slight excess of the low-R_f epimer (low R_f, 12.97 g; high R_f, 11.12 g).

Hydrolysis of the low-R_f epimer (12.30 g, 31.9 mmol) by using 2.0 g (36 mmol) of KOH, CH_3OH (175 mL), and H_2O (25 mL) at reflux affords in 4 h 11.0 g (96%) of the corresponding β-hydroxyurea: mp 186–187 °C (CH_3OH–H_2O, 7:1); NMR (acetone-d_6) δ 1.41 (d, CH_3), 3.1 (br s, 3 H), 5.02 (qt, 1 H), 5.22 (AB pattern, OCH and NCH), 7.2–7.6 (m, 15 H). Anal. Calcd for $C_{23}H_{24}N_2O_2$: C, 76.64; H, 6.71; N, 7.77. Found: C, 76.48; H, 6.75; N, 7.83.

Hydrolysis of the high-R_f epimer (9.66 g, 25.0 mmol) by using 1.50 g (28.0 mmol) of $NaOCH_3$ in anhydrous THF (ca. 300 mL) at room temperature for 3 h affords a 1:1 mixture of the parent heterocycle (5.95 g) and the methyl carbamate of 1-phenylethylamine (4.45 g) in quantitative yield. These two components could easily be separated by liquid chromatography (α = 6.0, 2% isopropyl alcohol–hexane, silica gel) or by fractional crystallization from EtOAc–EtOH–hexane (3:1:5). Chiroptic data: **2f** from high-R_f epimer (4R,5S), $[\alpha]^{23}_D$ +57.1 ± 3.0° (c 0.95, $CHCl_3$); **2f** from low-R_f epimer (4S,5R), $[\alpha]^{23}_D$ −58.1 ± 2.5° (c = 0.91, $CHCl_3$). The optical rotation of the recovered (S)-methyl (1-phenylethyl)carbamate was $[\alpha]^{23}_D$ −83.2 ± 0.5° (c = 7.25, $CHCl_3$) compared to $[\alpha]^{23}_D$ −83.7 ± 1.2° (c 4.2, $CHCl_3$) for optically pure carbamate.

(28) Pirkle, W. H.; Anderson, R. W. *J. Org. Chem.* **1974**, *39*, 3901.

Acknowledgment. This work has been supported by a grant from the National Science Foundation. We are indebted to Scott Bergeson for his contributions to the presently described preparation of carbamoyl chloride **16f**.

Registry No. (±)-**2a**, 60426-44-0; (±)-**2b**, 86217-38-1; (±)-**2c**, 86217-39-2; (±)-**2d**, 86217-40-5; (±)-**2e**, 86217-41-6; (±)-**2f**, 86286-49-9; (+)-**2f**, 86286-50-2; (−)-**2f**, 23204-70-8; (±)-**5b**, 71006-16-1; (±)-**5d**, 86217-42-7; (±)-**5f**, 23412-95-5; (±)-**6b**, 86217-43-8; (±)-**6d**, 86217-44-9; (±)-**6f**, 86217-45-0; **12a**, 100-52-7; **12b**, 66-77-3; (±)-**13a**, 86286-51-3; (±)-**13b**, 86217-46-1; (±)-**14a**, 86217-47-2; (±)-**14b**, 86217-48-3; **15a** (isomer 1), 86217-49-4; **15a** (isomer 2), 86238-44-0; **15b** (isomer 1), 86217-50-7; **15b** (isomer 2), 86217-51-8; **15c** (isomer 1), 86217-52-9; **15c** (isomer 2), 86217-53-0; **15d** (isomer 1), 86217-54-1; **15d** (isomer 2), 86217-55-2; **15e** (isomer 1), 86217-56-3; **15e** (isomer 2), 86286-52-4; **15f** (isomer 1), 86217-57-4; **15f** (isomer 2), 86217-58-5; **16f**, 86217-59-6; **17a** (isomer 1), 86217-60-9; **17a** (isomer 2), 86217-61-0; **17b** (isomer 1), 86238-45-1; **17b** (isomer 2), 86217-62-1; **17c** (isomer 1), 86217-63-2; **17c** (isomer 2), 86217-64-3; **17d** (isomer 1), 86217-65-4; **17d** (isomer 2), 86217-66-5; **17e** (isomer 1), 86217-67-6; **17e** (isomer 2), 86217-68-7; **17f** (isomer 1), 86217-69-8; **17f** (isomer 2), 86217-70-1; **17g** (isomer 1), 86217-71-2; **17g** (isomer 2), 86217-72-3; **17h** (isomer 1), 86217-73-4; **17h** (isomer 2), 86217-74-5; 4-acetylbiphenyl, 92-91-1; 4-(bromoacetyl)biphenyl, 135-73-9; α-bromoacetophenone, 70-11-1; α-hydroxyacetophenone, 582-24-1; α-hydroxy-4-phenylacetophenone, 37166-61-3; 2-phenyl-2-isonitrosoethanol, 25070-24-0; 2-(4-biphenylyl)-2-isonitrosoethanol, 86217-75-6; (±)-α-amino-1-naphthaleneacetonitrile, 86217-76-7; methyl (±)-1-(1-naphthyl)aminoacetate hydrochloride, 86217-77-8; benzoin oxime, 441-38-3; methyl chloroformate, 79-22-1; ethyl bromoacetate, 105-36-2; ethyl (1-hydroxyacenaphthen-2-yl)carbamate, 86217-78-9; ethyl sodiochlorocarbamate, 17510-52-0; acenaphthylene, 208-96-8; (R)-(−)-1-(1-naphthyl)ethyl isocyanate, 42340-98-7; (±)-2-butyl isocyanate, 86217-79-0; (±)-2-heptyl isocyanate, 86217-80-3; (±)-4-methyl-2-pentyl isocyanate, 86217-81-4; (±)-2-butanamine, 33966-50-6; (±)-2-octanamine, 44855-57-4; (±)-1-phenylethylamine, 618-36-0; (±)-1,2-diphenylethylamine, 35373-59-2; (±)-1-(4-biphenylyl)ethylamine, 86217-82-5; (±)-5-aminodecane, 86217-83-6; (±)-2-amino-3,3-dimethylbutane, 59367-75-8; (±)-N-methyl-1-phenylethylamine, 42882-26-8; (S)-1-phenylethyl isocyanate, 14649-03-7; methyl (S)-(1-phenylethyl)carbamate, 14185-42-3.

Methyl-Transfer Reactions. 6. Arenesulfonates as Nucleophiles and Leaving Groups. Methyl Trinitrobenzenesulfonate

Edward S. Lewis,* Michael J. Smith, and J. Joseph Christie

Department of Chemistry, Rice University, Houston, Texas 77251

Received February 2, 1983

The methyl-transfer reactions from several substituted methyl arenesulfonates to potassium benzenesulfonate in sulfolane have been studied with respect to both rates and equilibria. Because the reactions were followed by proton NMR of the methoxy group, only cases of methyl arenesulfonates with quite distinct methoxy chemical shifts from the unsubstituted ester could be studied, and this, in fact, required the use of ortho substituents. Hammett plots for these data were thus impossible, but a plot of log k_+ vs. log K, although somewhat scattered, did allow an estimation of the rate of the identity reaction for the unsubstituted compound. These methyl arenesulfonates, as well as methyl iodide, were placed roughly on the scale of equilibrium methylating agents studied earlier in the same solvent. Methyl 2,4,6-trinitrobenzenesulfonate is a very reactive substance not compatible with sulfolane. It is soluble and stable only in thionyl chloride among a large number of solvents attempted and methylates a few weak nucleophiles more extensively than methyl trifluoromethanesulfonate.

Introduction

Methyl-transfer reactions have been recently of interest both experimentally, including studies of rates and equilibria,[1-4] and isotope effects,[5,6] and theoretically[7-9] as an apparently simple model for the S_N2 reaction.

The majority of the theoretical work, as well as a little

(1) Lewis, E. S.; Kukes, S.; Slater, C. D. *J. Am. Chem. Soc.* **1980**, *102*, 1619–1623 and earlier papers in this series.

(2) Arnett, E. M.; Reich, R. *J. Am. Chem. Soc.* **1980**, *102*, 5892–5902.

(3) Pellerite, M. J.; Brauman, J. I. *J. Am. Chem. Soc.* **1980**, *102*, 5993–5999.

(4) Bowie, J. H. *Acc. Chem. Res.* **1980**, *13*, 76–82.

0022-3263/83/1948-2527$01.50/0