Inert-Molecule-Separated Ion Pairs. Stereochemical, ^{18}O, and Product Studies[1]

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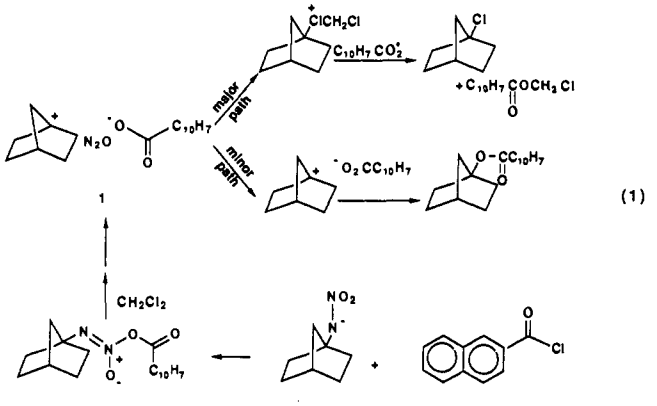
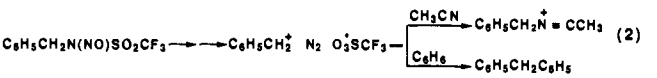
Abstract: Nitrogen- and nitrous oxide-separated carbocation–carboxylate ion pairs have been prepared by five different reactions: the rearrangement of *N*-nitroso amides, the reaction of acid chlorides with *anti*-diazoates, the reaction of acid chlorides with *syn*-diazoates, the reaction of acid chlorides with anions of *N*-nitroamines, and the decomposition of *N*-nitroso-*O*-acylhydroxylamines. Comparative stereochemical, ^{18}O scrambling, and product analyses have been made where common alkyl groups (1-phenylethyl), acyl groups (2-naphthoyl), solvent, and temperature are employed. The five reactions yield the same organic products, and they proceed with the same degree of retention of configuration; the reactions that were examined show the same extent of ^{18}O scrambling. Interestingly, differences in product ratios were detected in a comparison of the nitroso amide and nitrosohydroxylamine reactions, with the latter reaction providing the larger proportion of ester. The results indicate that the structural differences built into the precursor molecules are averaged out with respect to two of the product characteristics, but not to all three. These reactions are proposed to proceed via nitrogen- or nitrous oxide-separated ion pairs. The reactions are little influenced by variables such as temperature and solvent, and the carbocations prepared in this manner exhibit a remarkably high reactivity. The relevance of these results to other methods of deamination is examined.

Solvolytic (S_N1)[2] and deamination[3,4] reactions proceed formally through carbocation intermediates, but the kind and distribution of products in the two cases can differ.[5] For example, the nitrous acid deamination of propylamine in acetic acid yields propyl acetate (60%) and isopropyl acetate (40%), whereas the solvolysis of propyl 4-toluenesulfonate in the same solvent yields only 2.8% of the secondary isomer.[5a] Deamination reactions can be adapted to nonpolar solvents, and under these conditions the carbocations formed can be trapped by the solvent (if certain conditions are met); they also exhibit remarkable reactivity (eqs 1 and 2).[6a,7,8]



(1)



(2)

We now report on reactions designed to reveal the properties of intermediates in deamination reactions. We have examined a set of reactions utilizing chiral and ^{18}O-labeled reactants in which different but related intermediates are formed (Chart I); we examined the *N*-nitroso amide decomposition, a modification of the nitrous acid approach, and four variants in the same solvent and at the same temperature. The reactions produce carbocations and carboxylate ions in common, but they differ in the inert molecule produced (N_2 vs N_2O) and in the spatial arrangements of the key elements in the precursors (reaction 1 (2) vs 3 and reaction 4 vs 5 in Chart I).

Reaction 1, the *N*-nitroso amide decomposition (Chart I), has previously been examined in some depth.[4a,11,12] A rearrangement leads to the *anti*-diazoate ester (**3**); subsequent reactions lead to substitution (ester **4**) and to elimination (styrene and 2-naphthoic

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(1) Part 48 in a series of alkane diazonium ion pairs and deamination (a listing is available from the senior author). Part 47: White, E. H.; Li, M.; Lu, S. *J. Org. Chem.* **1992**, *57*, 1252-1258.

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(3) For deamination involving S_N2-type displacements on amine derivatives, see: Baumgarten, R. J.; Curtis, V. A. In *The Chemistry of Amino, Nitroso, and Nitro Compounds and Their Derivatives*; Patai, S., Ed.; Wiley: New York, 1982; Supplement F, Part 2, Chapter 22.

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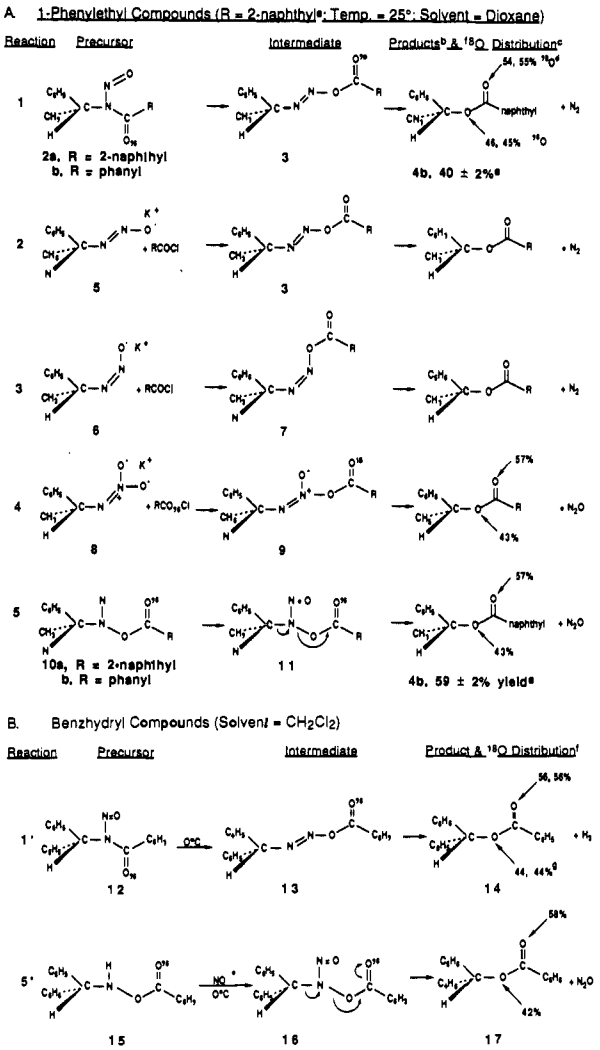
Chart I. Products and ^{18}O Scrambling Observed in Deamination Reactions



[a] Except in "b" series, reactions 1 and 5, where R = phenyl. [b] Styrene and 2-naphthoic acid (or benzoic acid) also formed. [c] Stereochemistry in Table I. [d] ^{18}O distribution from ref 9. [e] Solvent = $CDCl_3$. [f] Related results were reported in ref 10. [g] In the presence of 7 molar equiv of diazomethane the ^{18}O ratio was 54/46 (CO/ether); for a run in toluene at 0 °C the ratio was 54/46.

acid or benzoic acid). The decompositions of compound **2a** in dioxane, methylene chloride, and ethanol at 25 °C are strictly first order, with rate constants of 3.2, 4.3, and 6.4 ($\times 10^{-4}$) s^{-1}, respectively.[13]

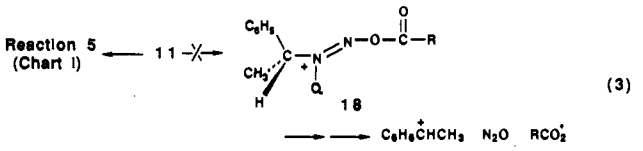
Reaction 2 (Chart I) is an alternative route to the *anti*-diazoate ester **3**. Reaction 3, an analogous reaction utilizing an isomeric diazoate (**6**), produces the syn isomer (**7**) of the diazoate ester.[14,15] The diazoate ion is an ambident ion, and a competitive acylation on nitrogen would yield an *N*-nitroso amide (i.e., **2a**); this compound is relatively stable under our reaction conditions, and spectral analysis suggested that no more than 15% could have been formed in the acylation. Reaction 4 is an analogous acylation in which an *N*-nitroamine salt is used. The nitroamine anion is an ambident ion, but acylation occurs largely on oxygen when the

Table I. Stereochemical Changes Occurring in Different Deamination Reactions Involving the Chiral 1-Phenylethyl Group

reactions (from Chart IA, a series)[a]	% overall retention of configuration in ester[a,b] dioxane	methylene chloride	acetic acid
1[d,e]	73, 74, 76,[c] 76[c]	67,[c] 68,[c] 68	81–82[f]
2	69		
3	72, 74	69	
4	71, 75		
5	68, 69	68 (70)[g]	

[a] Temp = 25 °C except where noted. [b] (100 − net % retention of configuration)/2 = % overall inversion; 100 − % overall inversion = % overall retention of configuration. Polarimetry used except for runs identified with a "c" superscript. [c] Stereochemistry determined by HPLC on a column packed with a chiral substrate. [d] A run in 100% ethanol yielded ester with 85% (84%)[c] overall retention of configuration. [e] Values of 63–81% were reported for a range of compounds in a range of solvents.[11] [f] Range of four runs. 1-Phenylethyl acetate was also formed (55–57% overall retention of configuration). Unpublished work of Dr. T. Huang (The Johns Hopkins University). [g] Temp = −50 °C.

alkyl group is secondary.[9,14] It seems reasonable to assume that the diazenyl 1-oxide ester formed (**9**) is the anti isomer because of the steric effect of the 1-phenylethyl group, but regardless of the geometry, the intermediate formed is different from those of the other four reactions. Reaction 5 involves a nitrosation step and the subsequent decomposition of a very unstable nitrosoacylhydroxylamine.[16a,b] When ^{18}O labeling in the NO group was examined, all of the label was found in the N_2O produced;[16a,b] thus, the reaction mechanism is the one illustrated (Chart I) rather than an alternative mechanism involving a prior rearrangement (to **18**, eq 3) analogous to the rearrangement occurring in the case of the *N*-nitroso amides (**2**).



(3)

All five reactions formally produce the same carbocation and carboxylate ion and, subsequently, the same ester. In the five reactions, the precursors **3**, **7**, **9**, and **11** antecedent to the diazonium ion or its *N*-oxides are very unstable. It has not been possible with reactions 4 and 5 to detect intermediates at −50 °C by IR or NMR spectroscopy, even in a strained bridgehead case (R = 1-*nor*bornyl).[6a] Similar negative results were obtained (NMR) at −80 °C in the case of reaction 5 (R = benzyl). The five reactions produce four analogous intermediates: isomers **3** and **7**, which differ by the disposition of the two attached groups about dinitrogen, and isomers **9** and **11**, which differ by the disposition of the two groups about nitrous oxide. The two sets differ from one another, allowing a comparison of the effects of nitrogen and nitrous oxide on the reaction course. The present study was designed to check whether those variables would influence the extent of ^{18}O scrambling, the loss of chirality, and/or the yields of products. Two analogous reactions yielding benzhydryl carbocation ion pairs (Chart I, part B) were also examined to gain further information about the variables cited above.

Results

The extent of ^{18}O scrambling is indicated directly on the product ester molecules in Chart I; 54–57% of the ^{18}O originally in the carbonyl groups of a precursor amide or nitroso amide (1-phenylethyl series) is retained in the carbonyl group of the product

(11) Huisgen, R.; Rüchardt, C. *Justus Liebigs Ann. Chem.* **1956**, *601*, 21–39.
(12) Southam, R. M.; Whiting, M. C. *J. Chem. Soc., Perkin Trans. 2* **1982**, 597–603.
(13) By comparison, $k_1 = 1.55 \times 10^{-1}$ s^{-1} at 70 °C in 1,2,4-trimethylbenzene for *N*-cyclohexyl-*N*-nitrosobenzamide (Huisgen, R.; Reimlinger, H. *Justus Liebigs Ann. Chem.* **1956**, *599*, 161–182).
(14) Preliminary results were reported in White, E. H.; Ryan, T.; Field, K. W. *J. Am. Chem. Soc.* **1972**, *94*, 1360–1361.
(15) The diazoates used in refs 6b–d were presumably the syn isomers.
(16) (a) White, E. H.; Todd, M. J.; Ribi, M. A.; Ryan, T. J.; Sieber, A. A. F.; Dickerson, R. E.; Bordner, J. *Tetrahedron Lett.* **1970**, *51*, 4467–4472. (b) White, E. H.; Ribi, M. A., Cho, L. K.; Egger, N.; Dzadzic, P. M.; Todd, M. D. *J. Org. Chem.* **1984**, *49*, 4866–4871. (c) White, E. H.; Lewis, C. P.; Ribi, M. A.; Ryan, T. J. *J. Am. Chem. Soc.* **1981**, *46*, 552–558. (d) White, E. H.; Lim, H. M. *J. Org. Chem.* **1987**, *52*, 2162–2166.

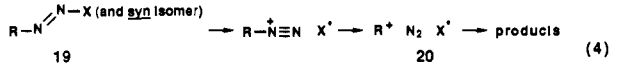
ester. In the benzhydryl series the values are 56–58%. The stereochemical results are listed in Table I; the deaminations in the 1-phenylethyl case proceed with 68–75% overall retention of configuration in dioxane, 68–71% in methylene chloride, and 81–82% in acetic acid. It is probable that the ^{18}O scrambling and the stereochemical results are the same for all of the reactions in the 1-phenylethyl series in dioxane.[17] Interestingly, the product ratios were different for two of the reaction types: the decomposition of *N*-(1-phenylethyl)-*N*-nitrosobenzamide (**2b**) yielded the corresponding ester (**4b**, 40 ± 2%) and styrene (54%), whereas the decomposition of *N*-(1-phenylethyl)-*N*-nitroso-*O*-benzoylhydroxylamine (**10b**) yielded the same products in yields of 59 ± 2 and 33%, respectively. Product distributions for reactions 2–4 were less useful because of side reactions that occur in those cases.

Discussion

Two mechanistic extremes would appear to set reasonable boundary conditions for deamination reactions: (1) differences of geometry with respect to the alkyl and carboxylate moieties among the four initial reaction intermediates (**3** vs **7** and **9** vs **11**) in the 1-phenylethyl series could have been carried through to the product-determining steps, and differences in the shape (and nature) of the inert molecule ejected (**7** vs **9**) could have influenced those steps (also, **13** vs **16** in the benzhydryl series) or (2) the differences cited above in entry 1 could have been averaged out before the final transition state for ester formation had been reached.

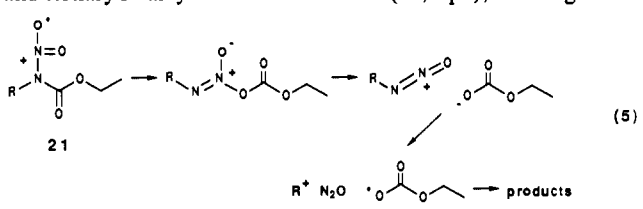
Since it was observed that the five deamination reactions carried out in the 1-phenylethyl series in dioxane proceeded with the same stereochemical results (within experimental error) (Table I), that three of the reactions gave essentially the same amount of ^{18}O scrambling, that reactions 1, 3, and 5, carried out in methylene chloride as the solvent, proceeded with the same stereochemical results (Table I), and that in the benzlhydryl series reactions 1′ and 5′ carried out in methylene chloride gave the same ^{18}O scrambling results (Chart I), it is clear that our results are better accounted for by option 2 than by option 1 insofar as the stereochemical and ^{18}O retention results are concerned. That is, although some order persists in the reactions (retention of configuration and carbonyl-^{18}O retention), there exists sufficient disorder to wipe out certain initially imposed structural differences (cis–trans isomerism, for example) with respect to two of the variables (vide infra for the product ratio differences).

A stepwise decomposition of intermediates **3** and **7**, for example, to give a common diazonium ion pair as a reaction intermediate (eq 4) provides a rational basis for the observation that structural differences in the precursors have a negligible effect on the stereochemical and ^{18}O results. Southam and Whiting[12] have



(4)

proposed that the formation of **20** is a two-step process where R = primary alkyl, but a one-step process where R = secondary alkyl; however, the majority of the evidence does not support that proposal. The two-step nature of deamination reactions was apparent in the decomposition of a series of primary, secondary, and tertiary *N*-alkyl-*N*-nitrocarbamates (**21**, eq 5), since a gradual



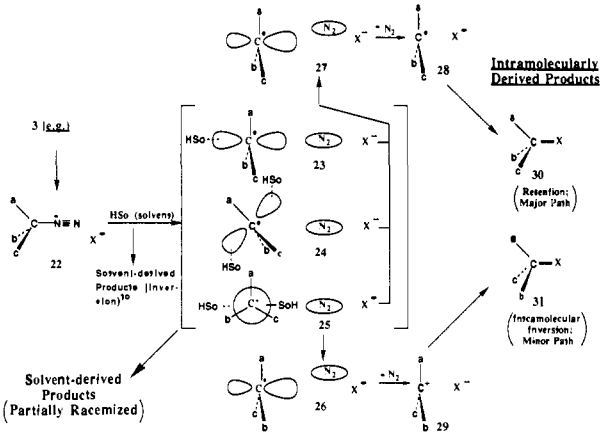
(5)

trend in the distribution of products was noted;[18,19] no evidence

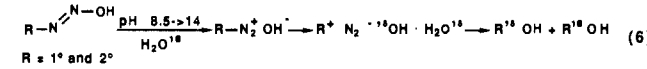
(17) The alkylations of *syn*- and *anti*-1-phenylethanediazoates have different stereochemical outcomes (Moss, R. A.; Powell, C. E. *J. Am. Chem. Soc.* **1976**, *98*, 283–285).

(18) White, E. H.; Field, K. W. *J. Am. Chem. Soc.* **1975**, *97*, 2148–2153.

Scheme I. Reaction Pathways for Alkane Diazonium Ion Pairs



was found for a discontinuity of the type proposed by Whiting et al. The nitrosation of amines under basic conditions (eq 6) also provides support for the stepwise reaction path since the ^{16}O content of the alcohols formed in both the primary and secondary cases was appreciable[6d]; no large change as predicted by the Whiting hypothesis was observed.[20]



(6)

The Inert-Molecule-Separated Ion Pair Hypothesis. The concept of inert-molecule-separated ion pair reaction intermediates for deamination in nonpolar solvents has been developed to account for the following major observations: retention of configuration (in most cases), intramolecular inversion, inefficient capture of the counterion, high reactivity of the carbocations, and carboxylate oxygen equilibration. That is, nitrogen-separated ion pairs are introduced into the reaction scheme involving the intimate (and in some cases, solvent-separated) ion pairs of the solvolytic route. It should be noted that a direct comparison of the two routes in nonpolar solvents is generally not possible because of the difficulty of achieving solvolysis under those conditions. In deamination reactions in nonpolar solvents, it seems likely that intimate ion pairs—other than those with the counterion oriented toward the node of the p-orbital or the back side of bridgehead carbocations—would react largely by internal return. It has been observed, however, that solvent-derived products can be the major products in the reaction (eq 3),[6a] thus indicating a secondary role for the intimate ion pair. The nitrogen molecule, by virtue of its physical separation of the ions for a finite period of time, has an important role to play with respect to competing reaction modes—allowing a carbocation–solvent interaction to not only compete, but to dominate the reaction (eq 1). Our working hypothesis for the mechanism of deamination reactions in nonpolar solvents, outlined in Scheme I, has as its key aspect—following the breaking of the C–N bond of the diazonium pair **22**—the formation of a set of short-lived, nitrogen-separated ion pairs **23–25** (and possibly also **26** and **27**) differing in the orientation of the carbocation with respect to the counterion and in the position of the nitrogen molecule. In structures **23–25**, the nitrogen molecule has been placed directly between the carbocation and the counterion to reflect, approximately, its relative position in the precursors (**3**, **7**, **9**, and **11**). However, it may be that even initially the nitrogen molecule is located in a range of different positions, such as an off-center position (as in structure **27**, for example). The experimental evidence does not narrowly define the location

(19) Southam and Whiting have criticized our comparison of *N*-nitroso amide and *N*-nitro amide decompositions by comparing isocyanides with isocyanates and cyclic azo compounds with their azoxy counterparts.[12] The relevant issue here is the inertness of both nitrogen and nitrous oxide, not the reactivity of analogs. In comparison studies in which the two gases are formed, no differences in the products have been found (this paper and White, E. H.; Grisley, D. W., Jr., *J. Am. Chem. Soc.* **1961**, *83* 1191).

(20) See ref 4 for results at low pH.

of the nitrogen molecule, and in any case, the interpretation of the present experimental results does not depend on a knowledge of its precise location.

Illustrated in Scheme I are nitrogen-separated ion pairs (**23**) in which the orientation of the front face of the chiral carbon atom in the diazonium ion pair with respect to the counterion is carried over unchanged and ion pairs in which there has been rotation of the carbocation relative to the counterion (**24** and **25**); species **23–27** are probably exceedingly short-lived intermediates which together illustrate the options for the positions of the carbocations locked in by solvent molecules as the nitrogen molecule diffuses into the solvent. Together they will be referred to as nitrogen-separated ion pairs. Most of the experimental data can be accounted for if one assumes that a rotation (twist) of the carbocation can occur in the generation of the nitrogen-separated ion pairs, probably as the result of collisions with the solvent and recoil from the formation of the nitrogen molecule (or nitrous oxide). The fastest rotation will presumably occur about the axis with the lowest moment of inertia, crudely approximated here by the *y*-axis of the carbocation illustrated (structures **23** → **25** → **26**, where a C_6H_5, b = CH_3, and c = H). Rotation about the *z*-axis (approximately) would lead to ion pair **24**, while rotation about the *x*-axis would not be detected by our experiments.

The major experimental evidence in favor of the rapid formation of a population of intimate ion pairs (**27** → **28**) is the following: (a) intramolecular products (RX) are always formed in nitroso amide decompositions—even in reactive solvents such as methanol or acetic acid; about one-fourth of the carbocation–X ion pairs (**23** → **27** → **28** → **30**) cannot be intercepted by reactive solvents;[4a,7,9] (b) the intramolecularly generated products of those reactions (RX) are formed with a high degree of retention of configuration (~80% for secondary cation, ~100% for tertiary cation).[4a] In reactions where X = a carboxylate ion, the carbonyl and ether oxygens do not become fully equivalent (Chart I);[4a,9] thus, the steps leading to ester from **23** must proceed at an exceedingly high rate since the motions that lead to an equivalency of the oxygens of the carboxylate ion are expected to be rapid.

The evidence for orientations **25** and **26** is the fact that an intramolecular inversion process occurs in reactive, scavenging solvents (acetic acid, methanol, etc.) to yield product **31** (about 20% of the ester, in the case of the 1-phenylethyl cation; the ^{18}O distribution in the *R* and *S* products is the same).[4a,9]

The major evidence for nitrogen-separated ion pairs such as **24** and **25** (solvated on one or both faces, depending on the structure) in which interaction with the solvent is maximized is the fact that for highly reactive carbocations, such as 1-norbornyl, solvent-derived products are the principal compounds formed even in relatively nonreactive solvents such as methylene chloride (1-chloronorbornane is formed in that case; eq 1).[6a] For less reactive carbocations such as 1-adamantyl, solvolysis products can also dominate the product distribution, but only if the solvent reactivity is high (as in the case of ethanol, for example).[6a]

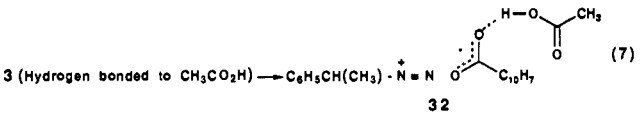
It appears that the initial ratio of aligned and nonaligned inert-molecule-separated ion pairs formed is fairly independent of the structure and reactivity of the carbocations. Following are some maximum yields of "solvolysis" product: 1-norbornyl in CH_2Cl_2, 56% RCl, and in ether, 34% ROC_2H_5 (isolated yield);[6a] 1-adamantyl in CH_2Cl_2, 2% RCl, and in ether, 31% ROC_2H_5;[6a] benzyl in CH_2Cl_2, 0% RCl, and 4-nitrobenzyl in benzene, 55% RC_6H_5.[7] These values suggest that for most carbocations about two-thirds of the nitrogen-separated ion pairs are of the **24,25** type where sufficient rotation has occurred to favor solvent interaction. The formation of solvent-derived products will occur only if the carbocation and solvent reactivities are high enough. It seems reasonable that, in cases where the solvolysis product is not observed because of the relative unreactiveness of the participants (benzyl in CH_2Cl_2, for example), the quantitative formation of the intramolecular product of the reaction (ester) stems in part from the realignment of the initially formed rotated ion pairs (**24**, **25**) to the aligned forms (**23**, **27**).

A strong interactive role for the counterion has surfaced in experiments on the benzylation of benzene (eq 2). If the counterion is the triflate ion (as shown), the yield of diphenylmethane is ~60%,[7] whereas if the counterion is the 4-toluenesulfonate ion, the yield of diphenylmethane is only ~7%. Thus, despite the fact that both of the counterions being compared are weak bases, they differ in their ability to influence the ratio of the competitive reactions that occur. These results suggest that the initial solvent interaction where it is relatively weak does not necessarily commit the carbocation to form the solvolysis product; species **24** and **25** can apparently be converted by the more basic counterions to ion pair **28**, which leads to the intramolecular part of the reaction.

The three processes observed, intramolecular inversion, ^{18}O scrambling, and the formation of solvent-derived products, appear to have rates that are similar to within an order of magnitude, since each, in general, accounts for an appreciable fraction of the overall reaction. This observation is a reasonable one since all three processes are at least partially dependent on, or influenced by, diffusion of the nitrogen molecule into the solvent.

Interpretation of the Results. In the non-hydrogen-bonding solvents dioxane and methylene chloride, ^{18}O scrambling in the carboxylate ion is almost total; the values range from 84% scrambling and 16% excess retention in the carbonyl group to 92% and 8%, respectively (Chart I). The listed values for ^{18}O in a specified position (54–58% ^{18}O in the CO group) are probably the same, within experimental error (av = ~56%), unaffected at the present level of precision by the solvent (non-hydrogen-bonding type), the type of reaction, the alkyl group, the carboxylate group, and in one case the temperature of the reaction (−75 vs 25 °C).[9] The oxygens of the carboxylate ion clearly approach equivalency with respect to the carbocation; ion pair collapse is only slightly faster than symmetrization of the carboxylate group.

In hydrogen-bonding solvents, the extent of ^{18}O retention is significantly greater. The carbonyl/ether ^{18}O distribution for ester obtained from the decomposition of nitroso amide **2a** in methanol was 64/36 and in acetic acid 69/31;[9] for nitroso amide **12**, corresponding values were 60/40 in ethanol and 67/33 in acetic acid. Hydrogen bonding by these reactive solvents would render the carboxylate ions unsymmetrical, which could lead to a greater fraction of subsequent alkylation at the "free" oxygen position. "Bicarboxylate" anions such as that illustrate in **32** are well-known.[21] Another role of the reactive solvents is their scavenging



(7)

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of reaction intermediates with less direct trajectories for ester formation (Scheme I, **24** and **25**) that otherwise would form ester with more ^{18}O scrambling. This hypothesis is consistent with the fact that, in reactive solvents such as ether and ethanol, solvent-derived products (ethers) often exceed in yield those of the intramolecularly derived products (naphthoate and benzoate esters).

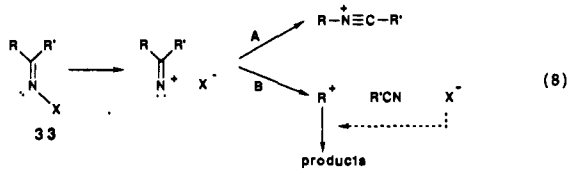
This latter factor also can account for the fact that the extent of retention of configuration is higher in the more reactive solvents than in less reactive ones, such as methylene chloride. For example, the decomposition of nitroso amide **2a** in ethanol yielded naphthoate ester with 85% retention of configuration, and in acetic acid the same ester was formed with 81% retention of configuration. In the less reactive solvents, the values are 68–75% (Table I). A similar effect of reactive solvents was observed in the decomposition of nitroso amide **12**. A reasonable interpretation of these observations is that nonaligned ion pairs such as **24** and **25** (which are on the pathway to "intramolecular inversion") can be scavenged by reactive solvents (the solvent-derived products are usually highly racemized).

In contrast to the ^{18}O and stereochemical results, which were independent of reaction type, the distribution of products for reactions 1b and 5b were substantially different (Chart I) (40 ± 2% ester from the nitroso amide route and 59 ± 2% from the

(21) Whaley, T. P. In *Comprehensive Inorganic Chemistry*; Bailar, J. C., Jr., Ed.: Pergamon Press: New York, 1973; Chapter 8, pp 463–465.

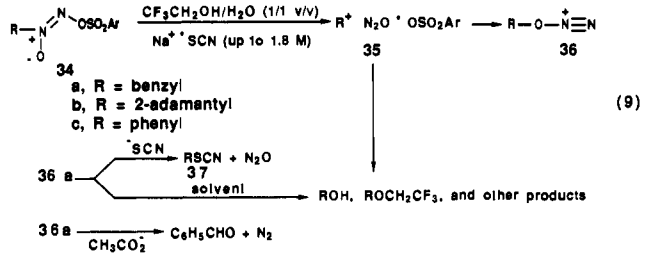
nitrosohydroxylamine route; similar but less quantitative results were obtained for reactions 1a and 5a). The difference between the stereochemical and yield findings can be accounted for by the relatively minor differences of the trajectories for the interaction of the counterion with the sp^2 center and with a β-hydrogen atom (as in structures **23** and **24**, for example); thus, small differences in the relative positions of the counterion and the carbocation will be expressed in the relative proportions of the reactions. In contrast, the difference between retention and inversion of configuration involves a rotation of the carbocation which is not influenced in any direct way by the position of the counterion with respect to it. The interpretation of the ^{18}O scrambling results is not as apparent; the nonequivalency of the carboxylate oxygen is most apparent in polar, hydrogen-bonding solvents, and perhaps the lifetime of the ion pair is lengthened sufficiently in those solvents so that the birth-engendered differences are eliminated before ester formation occurs.

The Central Molecule in Inert-Molecule-Separated Ion Pairs. The nitrogen-separated ion pairs, e.g., **23**, are formally related to a solvolysis intermediate, the solvent-separated ion pair;[2] however, the interposed molecule in the latter case is a better nucleophile than nitrogen or nitrous oxide, and it thus interacts more strongly with the carbocation. Other inert molecules can apparently serve the same role as nitrogen and nitrous oxide. The reactions of chloro carbonate esters with silver salts (such as the tetrafluoroborate) yield highly reactive carbocations, suggesting that carbon dioxide in those reactions has a role parallel to that of nitrogen and nitrous oxide in the deamination reactions.[22] The deoxygenation of alcoholate ions by dichlorocarbene suggests that carbon monoxide under certain conditions can serve as the inert molecule.[23] Finally, the similarity of deamination to the chloro sulfite and chloro carbonate S_Ni reactions (under conditions where retention of configuration occurs) suggests that sulfur dioxide[24,25] and, again, carbon dioxide[26] are candidate molecules. When the central molecule is chemically more reactive than in the examples cited above, a rearrangement, rather than a dissociation, can result as for example in the Beckmann rearrangement of oxime derivatives (**33**) (eq 8, path A). Interestingly, when the migrating group is a relatively stable one, e.g., *tert*-butyl a fragmentation reaction occurs[27] (eq 8, path B) that bears a formal resemblance to the deamination reactions.



(8)

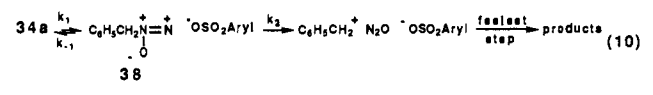
A Related Deamination Reaction. A detailed and thorough study of a newer type of deamination reaction involving the decomposition of 2-alkyldiazenyl 2-oxide tosylates (**34a,b**)[16a,c,d] has been reported in a series of papers by Maskill and co-workers (eq 9).[28] The authors proposed (eq 9) a synchronous concerted bond heterolysis to produce an "N_2O-separated ion pair" **35** (termed



(9)

a "very short-lived species") and a rebonding of the nitrous oxide to 47%[29] of the carbocations to give **36** (termed a "long-lived intermediate"). The long-lived intermediate was invoked to account for the formation of benzyl thiocyanate **37**[30] and benzaldehyde under appropriate reaction conditions[33] (an analog of **36**, R = CH_3, has been reported).[34]

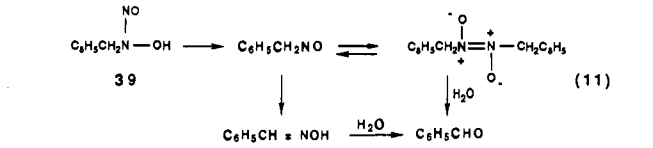
The proposed intermediates are related to those outlined in this paper (eqs 3 and 5, Scheme I). However, with respect to species **36** it seems unusual that the benzyl cation would react so efficiently with the relatively unreactive nitrous oxide molecule in such preference to the water and trifluoroethanol in which it is embedded. If the reaction occurred in a stepwise fashion (eq 10), species **36** could arise by a competetive 1,2 rearrangement from intermediate **38**.[34] If k_{-1} were approximately equal to or



(10)

somewhat larger than k_2, the overall rate would be affected by substituents on the aromatic ring of the arenesulfonate group (as observed)[35a] and also by substituents on the benzyl group (as observed).[35b] The stepwise dissociation, further, could account for the low values of the α-kinetic isotope effect.[35c]

On the other hand, if the alkoxydiazonium ion **16a** has a lifetime long enough to permit reaction with 0.25 M acetate ion to produce benzaldehyde, it would be expected to react with solvent molecules to form, for example, benzyl trifluoroethyl hyponitrite, which would be detectable either directly or via its decomposition products (little information is available, however, concerning the basic chemistry of ions such as **36**). Finally, the benzaldehyde yields are low (<1%), and it would appear that they parallel the amounts of *N*-benzyl-*N*-nitrosohydroxylamine (**38**) formed in the reaction when acetate ion is present in the medium. Compound **38** was isolated from such reactions. The small amounts of benzaldehyde could well stem from that nitrosohydroxylamine by a sequence of known reactions (eq 11).[36]



(11)

(22) Beak, P.; Trancik, R. J.; Simpson, D. A. *J. Am. Chem. Soc.* **1969**, *91*, 5073–5080.
(23) Skell, P. S.; Starer, I. H. *J. Am. Chem. Soc.* **1959**, *81*, 4117–4118.
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(26) Lewis, E. S.; Herndon, W. C. *J. Am. Chem. Soc.* **1961**, *83*, 1955. Wiberg, K. B.; Shryne, T. M. *J. Am. Chem. Soc.* **1955**, *77*, 2774.
(27) Brown, R. F.; van Gulick, N. M.; Schmidt, G. H. *J. Am. Chem. Soc.* **1955**, *77*, 1094. Smith, P. A. S. In *Molecular Rearrangement*; de Mayo, P., Ed.; Interscience Publishers: New York, 1963; pp 503–504.
(28) (a) Maskill, H.; Jencks, W. P. *J. Am. Chem. Soc.* **1987**, *109*, 2062–2070. (b) Maskill, H.; Thompson, J. T.; Wilson, A. A. *J. Chem. Soc., Perkins Trans. 2* **1984**, 1693–1703. (c) Maskill, H.; Jencks, W. P. *J. Chem. Soc., Chem. Commun.* **1984**, 944–946. (d) Gordon, I. M.; Maskill, H. *J. Chem. Soc., Chem. Commun.* **1989**, 1358–1360. (d) Maskill, H. *J. Chem. Soc., Chem. Commun.* **1986**, 1433–1435. (e) Maskill, H. *J. Chem. Soc., Chem. Commun.* **1980**, 788–789. (f) Maskill, H.; Thompson, J. T.; Wilson, A. A. *J. Chem. Soc., Chem. Commun.* **1981**, 1239–1240. (g) Conner, J. K.; Maskill, H. *Bull. Soc. Chim. Fr.* **1988**, 342–348.

(29) From a double reciprocal plot of NaSCN concentration and mole fraction of benzyl thiocyanate (benzyl isothiocyanate was not reported as a product).[30]
(30) Both thiocyanate and isothiocyanate isomers are produced in analogous trapping experiments with alkanediazonium ions (or ion pairs), where the alkyl group = isobutyl,[31] benzhydryl,[31] and benzyl.[32]
(31) Connell, L. G.; Taft, R. W., Jr. *Abstracts of Papers*, 129th National Meeting of the American Chemical Society, Dallas, TX, April 1956; American Chemical Society: Washington, DC, 1956; Abstract 74, p 46N.
(32) Part 47 cited in ref 1.
(33) The observations were that, in the absence of acetate ion, the yields of benzyl alcohol were high (76%) and no benzaldehyde was detected. In the presence of 1 M acetate ion (unbuffered), the alcohol yield was low (7%) and ~1% of benzaldehyde was detected. Clearly, the alcohol and benzaldehyde need not stem from a common precursor.
(34) Olah, G. A.; Herges, R.; Laali, K.; Segal, G. A. *J. Am. Chem. Soc.* **1986**, *108*, 2054–2057.
(35) (a) $\rho(\sigma_y) = 1.07$.[28d] (b) $\rho(\sigma_x^+) = -3.27$.[28d] (c) 1.090–1.133 measured for **34b**.[28b]
(36) Mueller, E.; Metzger, H. *Chem. Ber.* **1956**, *89*, 396. Ribi, M. A.; White, E. H. *Helv. Chim. Acta* **1975**, *58*, 120–130 (action of electrophiles on nitrosoalkane dimers). Exner, O. *Collect. Czech. Chem. Commun.* **1951**, *16*, 258 (rapid hydrolysis of nitrones).

As an alternative hypothesis,[37] therefore, perhaps thiocyanate **37** arises from the reaction of thiocyanate ion with intermediate **38**. If the rate of decomposition of **38** were high (governed by k_2) relative to the rate of reaction with thiocyanate ion, a limit would be imposed on the yield of the trapped product (**37**), as observed. By way of analogy, the decomposition of *N*-(1-phenylethyl)-*N*-nitroso-2-naphthamide (**2a**; Chart I) in acetic acid as the solvent does yield the "trapped" product, 1-phenylethyl acetate, but about one-fourth of the ester formed is 1-phenylethyl 2-naphthoate,[9] which is believed to arise from very short-lived noninterceptible intermediates (Scheme I and text).

Experimental Section

General Methods and Material. Spectra were recorded on the following spectrometers: Perkin-Elmer Model 457A, Varian HA-100 and XL-400, Bruker AMX-300, and Beckman DK-2A. The optical rotation data were obtained with a Perkin-Elmer No. 141 polarimeter using a 1-dm jacketed cell; the stereochemical results were verified by HPLC of the 1-phenylethyl naphthoate samples on a chiral (Pirkle) column. All reaction solvents, except ethanol, were dried and distilled prior to use. Dioxane was distilled from lithium aluminum hydride and stored under nitrogen in the dark. Steady-state UV/vis spectra and time-dependent absorption studies were recorded on a Hewlett-Packard Model 8452 diode array spectrophotometer. Analytical high-performance liquid chromatography (HPLC) was performed with a Gilson Medical Electronics instrument equipped with a Model 112 UV/vis detector. For the determination of 1-phenylethyl 2-naphthoate enantiomeric purity, the instrument was equipped with a Regis 5 μm, 4.6 × 250 mm Pirkle covalent D-phenylglycine column with 2% 2-propanol in heptane as eluant at 0.4 mL/min; the enantiomeric purity of (*R*)-*N*-(1-phenylethyl)-2-naphthalenecarboxamide was determined with 35% 2-propanol in heptane as eluant at 0.8 mL/min. The decomposition product mixtures were quantified with this instrument equipped with an Alltech 5 μm, 4.6 × 250 mm Econosphere C_{18} column with 35% water in acetonitrile as eluant at 1.0 mL/min. Spinning-disk chromatographic separations were performed on a Harrison Research Model 7924 T chromatotron. Mass spectra were obtained with a Hewlett-Packard Model 5890 gas chromatograph equipped with a Model 5970 mass selective detector. Analyses for ^{18}O content were carried out using the procedure of Dahn, Moll, and Menasse.[38]

Benzoic acid-^{18}O, benzoyl-^{18}O chloride, and dibenzoyl-*carbonyl*-^{18}O peroxide were prepared by known procedures.[39] 2-Naphthoic acid-*^{18}O* was prepared by the hydrolysis of 2-naphthoyl chloride with $H_2{}^{18}O$, and 2-naphthoyl-*^{18}O* chloride was prepared from that acid by treatment with refluxing thionyl chloride containing a catalytic amount of pyridine.

2-Naphthoyl-^{18}O Peroxide. 2-Naphthoyl-*^{18}O* chloride (15.7 g, 82.2 mmol; 2.8 atom % excess ^{18}O) in 40 mL of toluene was added with vigorous stirring over 30 min to a solution of 4.55 g (53.4 mmol) of sodium peroxide in 40 mL of water kept at 0–5 °C. The mixture was allowed to reach 20 °C and then stirred at that temperature for 4 h. The mixture was filtered, and the solid was washed with water and then dried to give 11.6 g of the crude peroxide. Recrystallization from a dioxane–water mixture yielded 10.1 g (72%) of the pure peroxide: dec temp 138.5 °C dec (lit.[40] mp 142–144 °C); IR ($CHCl_3$) 1785, 1760 cm^{-1}.

(−)-(*R*)-*N*-(1-Phenylethyl)-2-naphthalenecarboxamide was prepared by the procedure of White and Aufdermarsh[9] using a 2-fold excess of optically active 1-phenylethylamine ($[\alpha]^{24}_D$ +37.9° (*c* 0.95, neat), 94% optically pure):[41] mp 168.5–169 °C (lit.[9] mp 171.7–172.2 °C); $[\alpha]^{24}_D$ −45.7° (*c* 0.877, $CHCl_3$) [based on the value of 48.6° for optically pure material,[9,42] the amide was 94% optically pure]. Anal. ($C_{19}H_{17}NO$): C, H, N.

(*R*)-*N*-(1-Phenylethyl)-*N*-nitroso-2-naphthalenecarboxamide (2a) and the ^{18}O-labeled analog were prepared from the optically active amides prior to each decomposition run by the N_2O_4 method of White and Aufdermarsh (N_2O_4, CH_2Cl_2, sodium acetate, 0 °C, 1 h);[9] at no time during its preparation and subsequent purification was the nitroso amide allowed to reach a temperature above 0 °C. A sample of the nitroso amide (ca. 3 g) was dissolved in dichloromethane (25 mL) and precipitated by the addition of cold hexane (200 mL). The yellow solid was collected by Buchner filtration, washed with 3 × 25 mL portions of cold hexane, and dried in vacuo: mp 71.5 °C dec; IR (CH_2Cl_2) 1710 (C=O); 1500 (NNO) cm^{-1}; ^1H NMR ($CDCl_3$, −21 °C) δ 1.77 (d, 3 H, *J* = 7 Hz), 6.15 (q, 1 H, *J* = 7 Hz), 7.2–8.4 (m, 12.6 H); UV (dioxane) λ_{max} 408 nm (ε = 95), 425 (ε = 98).

Control Experiment. (*R*)-*N*-(1-Phenylethyl)-*N*-nitroso-2-naphthalenecarboxamide was denitrosated in chloroform with gaseous hydrogen chloride by the method of White and Aufdermarsh.[9] The recovered (−)-(*R*)-*N*-(1-phenylethyl)-2-naphthalenecarboxamide was shown not to have lost optical integrity, within experimental error, during the nitrosation and denitrosation cycle.

1-Phenylethyl Ethyl Ether. 1-Phenylethyl ether was prepared from the reaction of 1-phenylethyl alcohol, ethyl iodide, and freshly prepared silver oxide using the method of Mislow.[43] The crude ether (61%) was purified by distillation: bp 72–74 °C (15 Torr) [lit.[43] bp 89 °C (31 Torr)]; IR (CCl_4) 1100 cm^{-1}; ^{1}NMR ($CDCl_3$) δ 1.16 (t, 2.9 H, *J* = 7.0 Hz), 1.43 (d, 3.1 H, *J* = 6.5 Hz), 3.35 (q, 1.9 H, *J* = 7.0 Hz), 4.40 (q, 1.0 H, *J* = 6.5 Hz), 7.34 (s, 4.8 H).

(+)-(*R*)-(1-Phenylethyl)hydrazine. The procedure of Baumgarten et al. was followed.[44] (+)-(*R*)-1-Phenylethylamine (94% optically pure) was converted into (1-phenylethyl)urea (87%); the crude product, mp 121–122 °C, gave $[\alpha]^{25}_D$ + 46.5° (*c* 1.025, EtOH). A Hofmann rearrangement led to (+)-(*R*)-*N*-(1-phenylethyl)-*N'*-(*tert*-butoxycarbonyl)-hydrazine (59%). Deblocking with hydrogen chloride in ethanol yielded (+)-(*R*)-(1-phenylethyl)hydrazine hydrochloride (79%). Neutralization and distillation yielded the free hydrazine: $[\alpha]^{25}_D$ +32.6° (*c* 0.55, benzene) [lit. $[\alpha]^{25}_D$ 32.49° (*c* 1.010, benzene)].[44]

(±)-(1-Phenylethyl)hydrazine oxalate was prepared from acetaldehyde azine and phenylmagnesium bromide by the method of Overberger and DiGiulio[45] (Procedure B); the product was recrystallized from ethanol (43% yield): mp 167–167.5 °C dec (lit.[43] mp 170–171 °C); ^1H NMR (DMSO-d_6) δ 1.43 (d, 3 H, *J* = 7 Hz), 4.23 (q, 1 H, *J* = 7 Hz), 7.42 (s, 5 H), 8.20 (s, 6 H; exchangeable with D_2O).

(−)-(*R*)-*N*-(1-Phenylethyl)-*N*-nitrosohydrazine. The method of Bamberger and Hauser[46] for the preparation of phenylnitrosohydrazine was followed. Sodium acetate (4.36 g, 53.2 mmol) in 10 mL of water was added to (+)-(*R*)-(1-phenylethyl)hydrazine hydrochloride (4.60 g, 26.6 mmol) (94% optically pure). The solution was stirred at 0 °C and sodium nitrite (4.59 g, 66.5 mmol) in 10 mL of water was added. After 30 min the precipitate that formed was collected and dried in vacuo to yield 2.86 g (65%) of the title compound. Recrystallization from benzene–petroleum ether (1:1) gave off-white crystals: mp 85.0–85.7 °C; ^1H NMR ($CDCl_3$) δ 1.85 (d, 3 H, *J* = 7.0 Hz), 5.54 (br s, 2 H), 5.77 (q, 1 H, *J* = 7.0 Hz), 7.38 (s, 5 H); $[\alpha]^{23}_D$ −18.9° (*c* 3.23, CH_2Cl_2); IR (CH_2Cl_2) 3300, 3200, 1550, 1500, 1360 cm^{-1}. Anal. ($C_8H_{11}N_3O$) C, H, N.

(±)-*N*-(1-Phenylethyl)-*N*-nitrosohydrazine. This compound was prepared by the method described for the optically active sample: mp 61.5–62.5 °C; UV (diethyl ether) λ_{max} 340 nm (ε 88). Anal. ($C_8H_{11}N_3O$) C, H, N.

Potassium *anti*-(*R*)-1-Phenylethanediazoate (5). Following the method of Thiele,[47] (−)-(*R*)-*N*-(1-phenylethyl)-*N*-nitrosohydrazine (1.84 g, 11.1 mmol) in methanol (2.2 mL) was added to a stirred mixture of 3 mL of 3.69 M potassium methoxide, methanol (11.1 mmol), and ether (45 mL) at 0 °C under nitrogen. Isoamyl nitrite (3.0 mL, 2.61 g, 22.3 mmol) in ether (2 mL) was added dropwise to the stirred solution. After 1.5 h, ether (50 mL) was added, and the resulting white precipitate was filtered off under a nitrogen atmosphere and washed with ether. The white solid was dried in vacuo to give 1.24 g of potassium *anti*-(*R*)-1-phenylethanediazoate (6.6 mmol, 59%): mp 242 °C dec; IR (Nujol) 1600, 1490, 1415, 1300, 1075, 1012, 760, 700 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.35 (d, 3 H, *J* = 6.8 Hz), 4.73 (q, 1 H, *J* = 6.8 Hz), 7.1–7.4 (br s, 5 H). The optical purity of the diazoate was assumed to be 94%, which was the optical purity of the starting 1-phenylethylamine.[48] Anal. ($C_8H_9N_2OK \cdot 0.5H_2O$) C, H, N.

(37) As a further complication, a prior rearrangement of the toluenesulfonyl group to the second oxygen atom has been reported for the decomposition of analog **34c**. (Neiman, L. A.; Smolyakov, V. S.; Nekrasov, Y. S.; Shemyakin, M. V. Tetrahedron **1970**, *26*, 4963.)

(38) Dahn, H.; Moll, H.; Menasse, R. *Helv. Chim. Acta* **1959**, *42*, 1225. See also: White, E. H.; McGirk, R. H.; Aufdermarsh, C. A., Jr.; Tiwari, H. P.; Todd, M. J. *J. Am. Chem. Soc.* **1973**, *95*, 8107.

(39) Denney, D. B.; Denney, D. Z. *J. Am. Chem. Soc.* **1957**, *79*, 4809. Denney, D. B.; Denney, D. Z. *J. Am. Chem. Soc.* **1960**, *82*, 1392.

(40) Medvedev, S.; Blokh, O. *Zh. Fiz. Khim.* **1933**, *4*, 721–30.

(41) For optically pure amine, $[\alpha]^{22}_D$ = 40.3° (neat) (Theilaker, W.; Winkler, H. G. *Chem. Ber.* **1954**, *87*, 690).

(42) For optically pure (*S*)-(+)-*N*-(1-phenylethyl)-2-naphthamide-^{18}O, $[\alpha]^{23}_D$ = +48.6° (*c* 3.28, $CHCl_3$).[9]

(43) Mislow, K. *J. Am. Chem. Soc.* **1951**, *73*, 4043.

(44) Baumgarten, H. E.; Chen, P. Y.-N.; Taylor, H. W.; Hwang, D.-R. *J. Org. Chem.* **1976**, *41*, 3805.

(45) Overberger, C. G.; DiGiulio, A. V. *J. Am. Chem. Soc.* **1958**, *80*, 6562.

(46) Bamberger, E.; Hauser, H. *Justus Liebigs Ann. Chem.* **1910**, *375*, 316.

(47) Thiele, J. *Justus Liebigs Ann. Chem.* **1910**, *376*, 239.

(48) The *syn*- and *anti*-diazoates were assumed to have retained the optical integrity of the amine.

The *anti*-diazoate dissolved in water without nitrogen evolution which, however, occurred vigorously upon acidification. Addition of aqueous cupric acetate yielded a violet precipitate (a violet color had been reported for the methyl *anti*-diazoate ion).[47]

Potassium *anti*-(±)-1-Phenylethanediazoate (5). Using the method described for the optically active sample, the title compound was obtained in a yield of 68%: mp 208 °C dec (sealed tube); IR (Nujol) 1600, 1490, 1410, 1300, 1166, 1079, 1015 cm^{-1}. Anal. ($C_8H_9N_2OK \cdot {}^1/_2H_2O$) C, H, N. A less pure sample was prepared by the direct nitrosation of (1-phenylethyl)hydrazine using isoamyl nitrite and potassium methoxide.

(+)-(*R*)-Ethyl *N*-(1-phenylethyl)carbamate was prepared in 89% yield by the method of Hartman and Brethen[49] using (+)-(*R*)-1-phenylethylamine ($[\alpha]^{25}_D$ 38.2° (neat), 95% optically pure): bp 87–93 °C (10^{-2} Torr) [lit.[50] bp 110–113 °C (10^{-1} Torr)]; mp 33–34.5 °C; IR (CCl_4) 3430, 1725, 1495, 695 cm^{-1}; $[\alpha]^{23}_D$ + 69.9° (*c* 0.86, $CHCl_3$).

(+)-(*R*)-Ethyl *N*-Nitroso-*N*-(1-phenylethyl)carbamate. A solution of N_2O_4 (7.0 mL, 10.2 g, 0.111 mol) in CH_2Cl_2 (40 mL) was added dropwise to a stirred mixture of the carbamate (7.09 g, 0.037 mol) and sodium acetate (15.2 g, 0.185 mol) in CH_2Cl_2 (75 mL) at −50 °C.[9,51] Workup afforded a yellow oil (8.3 g, 0.037 mol, 100%): IR (CH_2Cl_2) 1755, 1515 cm^{-1}; ^1H NMR (CCl_4, racemic material) δ 1.3 (t, 3.1 H, *J* = 7 Hz), 1.6 (d, 3.1 H, *J* = 7 Hz), 4.35 (q, 2.0 H, *J* = 7 Hz), 5.97 (q, 0.9 H, *J* = 7 Hz), 7.2 (s, 5 H).

Potassium *syn*-(*R*)-1-Phenylethanediazoate (6).[52] To a stirred mixture of potassium *tert*-butoxide (0.68 g, 6.0 mmol) in diethyl ether (20 mL) under nitrogen at 0 °C was injected through a rubber septum a solution of (+)-(*R*)-ethyl-*N*-nitroso-*N*-(1-phenylethyl)carbamate (1.4 g, 6.1 mmol) in diethyl ether (10 mL). A light tan solid formed immediately; the mixture was stirred for an additional 20 min and then warmed to room temperature. The diazoate was collected by vacuum filtration on a fritted disk Büchner funnel and then washed with several portions of ether under a nitrogen atmosphere. The salt was dried in vacuo at room temperature, giving the desired material (0.95 g, 5.1 mmol, 83%): dec temp 153–154 °C (sealed tube); IR (Nujol mull) 1600, 1490, 1375, 1160, 1150, 1087, 758, 697 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.19 (d, 3.0 H, *J* = 6.8 Hz), 5.58 (q, 1.0 H, *J* = 6.8 Hz), 7.05–7.43 (m, 5.2 H).

The syn salt reacts vigorously with water, resulting in gas evolution and the production of an orange-red color (probably the corresponding diazoalkane). Treatment of the *syn*-diazoate with an aqueous cupric acetate solution did not afford a violet precipitate (which is produced from the anti isomer). **CAUTION**: While manipulating the dry diazoate in a glove bag under nitrogen, the material on one occasion exothermally decomposed, producing white fumes with the odor of styrene and scorching a cloth on which a portion of the diazoate had fallen.[53]

Attempted Isomerization of the *syn*-Diazoate to the *anti*-Diazoate. A freshly prepared sample of potassium *syn*-1-phenylethanediazoate (**6**) was dissolved in dimethyl sulfoxide-d_6, and an NMR spectrum was obtained. After heating this solution to 50 °C for 51 h in a sealed tube, reanalysis of the solution by ^1H NMR (100 MHz) revealed that no isomerization or decomposition of the diazoate had occurred.

(+)-(*R*)-(1-Phenylethyl)nitroamine was prepared by the method of Winters et al.[54] using (+)-(*R*)-1-phenylethylamine (8.0 g, 66 mmol, $[\alpha]^{22}_D$ +38.4° (neat), 95% optically pully), butyllithium (83 mL, 132 mmol), and methyl nitrate (5.1 g, 66 mmol) in diethyl ether. The crude product was recrystallized from methanol–water to yield 5.19 g (31.2 mmol, 47%) of optically pure (+)-(*R*)-(1-phenylethyl)nitroamine: mp 121.5–122.5 °C; IR (KBr) 3205, 1585, 1425, 1372, 1340, 1328, 1305, 1279, 703 cm^{-1}; ^1H NMR (CCl_4) δ 1.43 (d, 3.3 H, *J* = 7 Hz), 2.52 (s, 1 H), 5.12 (q, 1 H, *J* = 7 Hz), 7.28 (s, 5 H); $[\alpha]^{22}_D$ +26.7° (*c* 2.40, 95% EtOH). In a control experiment, (+)-(*R*)-1-phenylethylamine showed no detectable racemization when treated with *n*-butyllithium and then recovered.

(+)-(*R*)-(1-Phenylethyl)nitroamine, Potassium Salt (8). Pure (+)-(*R*)-(1-phenylethyl)nitroamine (1.50 g, 9.03 mmol) in 20 mL of methanol was titrated with 0.086 M aqueous potassium hydroxide (106.2, 9.13 mmol) to a phenolphthalein end point. The aqueous solution was washed with 2 × 50 mL portions of ether. The water was removed on a rotary evaporator connected to a vacuum pump, and the residue was dried in vacuo to yield the nitroamine salt as a white solid (1.68 g, 91%): mp 214–218 °C; IR (KBr) 1415, 1310, 693 cm^{-1}; $[\alpha]^{22}_D$ +40.9° (*c* 1.83, 95% EtOH). The optical purity was assumed to be the same as that of the neutral nitroamine.

(+)-(*R*)-*N*-(1-Phenylethyl)-*O*-(2-naphthoyl-*carbonyl*-^{18}O)hydroxylamine (10a). The method of Zinner[55] was modified. A solution of (+)-(*R*)-1-phenylethylamine (15.62 g, 127.2 mmol; $[\alpha]^{22}_D$ +38.4° (neat), 95% optically pure) in chlorobenzene (15 mL) was added dropwise over 1 h to a stirred mixture of 2-naphthoyl peroxide [22.1 g, 64.6 mmol; ~2.8 atom % excess ^{18}O (C=O)] in chlorobenzene (65 mL) at 45 °C. A copious precipitate formed. When IR spectra and TLC indicated a disappearance of the peroxide (1–6 h), the mixture was cooled to room temperature. The reaction mixture was filtered, and the precipitate ((1-phenylethyl)ammonium 2-naphthoate, mp 162–164 °C, ~70% yield) was washed with chlorobenzene and ether (15 mL and 2 × 30 mL, respectively). The combined filtrate washings were cooled in an ice bath to precipitate *N*-(1-phenylethyl)-2-naphthalenecarboxamide, which was removed by filtration. The filtrate was washed with 5% aqueous sodium bicarbonate, dried, and placed in a freezer (−10 °C) for 40 h to precipitate more of the amide (total recovery 6.07 g, 34%). Upon removal of the solvents, a brown solid (11.4 g) remained. Fractional crystallization from hexane–ether yielded fairly pure hydroxylamine, but the full removal of the amide could be effected only by either chromatography on silica gel (CH_2Cl_2 elution) or by precipitation of the hydroxylamine hydrochloride. The crude product (11.4 g) was dissolved in 150 mL of ether, and hydrogen chloride was introduced over ~20 min. The solid was filtered, washed with ether, and dried (yield, 21%). The hydrochloride was mixed with 75 mL of CH_2Cl_2, and sufficient 0.1 M Na_2CO_3 solution was added to reach basicity. The organic phase was removed, dried, and evaporated. The product was recrystallized from hexane–ether to yield colorless crystals of (+)-(*R*)-*N*-(1-phenylethyl)-*O*-(2-naphthoyl-*carbonyl*-^{18}O)hydroxylamine: mp 93–94 °C (lit.[16b] mp 95.5 °C for ± material); IR (KBr) 3208, 1723 cm^{-1}; IR (CH_2Cl_2) 3220, 1720, 1270, 1195 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.55 (d, 3 H, *J* = 6.5 Hz), 4.38 (q, 1 H, *J* = 6.5 Hz), 7.2–8.0 (m, 11 H), 8.5 (br s, 1 H), 9.0 (br s, 1 H); 2.8 atom % excess ^{18}O (CO). The spectra were identical to those of the racemic nonlabeled material reported earlier.[16b] The following specific rotations were measured for 98.6% optically pure material in benzene at 22 °C (*c* 1.51): $[\alpha]_D$ +118.7°, $[\alpha]_{578}$ +124.3°, $[\alpha]_{546}$ +143.3°, $[\alpha]_{436}$ +270°, $[\alpha]_{365}$ +490°. The highest rotation obtained for **10** in this study was $[\alpha]^{25}_D$ +120.3° (benzene); this material was assumed to be optically pure.

***N*-Benzhydrylbenzamide-^{18}O** was prepared from benzhydrylamine and benzoyl-^{18}O chloride (1.56, 1.56 atom % excess ^{18}O) by the method of White and Dzadzic.[56] The recrystallized amide melted at 174.5–176 °C (lit.[56] mp 174–175 °C), 1.56, 1.56 atom % excess ^{18}O. Anal. ($C_{20}H_{17}NO$) C, H, N.

***N*-Benzhydryl-*O*-(benzoyl-*carbonyl*-^{18}O)hydroxylamine (15).** To a solution of dibenzoyl-*carbonyl*-^{18}O peroxide (25.0 g, 0.103 mol) in 100 mL of benzene was added a solution of 33.7 g (0.206 mol) of benzhydrylamine in 20 mL of benzene over a period of 15–20 min with stirring at ~5 °C. The reaction mixture was then warmed with a water bath (ca. 90 °C) for 10 min, and subsequently it was cooled to 0 °C for 1 h. The white solid material (benzhydrylammonium benzoate) was filtered off and washed with 100 mL of benzene. The filtrate and washings were washed with water and then dried. The removal of solvent by rotary evaporation afforded 28.2 g of a yellowish solid; the IR spectrum (CH_2Cl_2) indicated a 3/2 mixture of *N*-benzhydryl-*O*-benzoylhydroxylamine and *N*-benzhydrylbenzamide. Compound **15** was obtained pure by chromatography of this mixture on silica gel (benzene elution). Alternatively, the mixture was dissolved in a minimal amount of anhydrous ether (ca. 200 mL), and then dry hydrogen chloride was passed through the solution for 15 min. The gummy precipitate was treated with 0.1 M Na_2CO_3; the mixture was extracted with ether, the organic phase was dried, and the solvent was evaporated. The product was recrystallized from absolute ethanol to yield 6.10 g (20.1 mol, 20%) of *N*-benzhydryl-*O*-(benzoyl-*carbonyl*-^{18}O)hydroxylamine: mp 100–102°C (lit.[55] mp for ^{16}O analog 99–101 °C); IR (CCl_4) 3230, 3060, 1725 (s), 1600, 1265 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.34 (s, 1 H, *CH*), 7.37 and 7.82 (m, 16 H, aromatic H and NH); ^{18}O Anal. 1.70 atom % excess. Anal. ($C_{20}H_{17}O_2N$) C, H, N.

Decomposition of (*R*)-*N*-(1-Phenylethyl)-*N*-nitroso-2-naphthalenecarboxamide (2a). A. In Dioxane. The nitroso amide (1.70 g, 5.6 mmol, prepared from 96% optically pure amide) was dissolved in pure dioxane (150 mL) and stirred for 10 h at 25 °C. The mixture was then poured into 250 mL of water, and the resultant mixture was extracted with 3 × 50 mL portions of ether. The combined ethereal extracts were washed

(49) Hartman, W. W.; Brethen, M. R. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. II, p 278.
(50) Muller, G.; Merten, R. *Chem. Ber.* **1965**, *98*, 1097.
(51) White, E. H. *J. Am. Chem. Soc.* **1955**, *77*, 6008.
(52) The methods employed were similar to those of Hantzsch, A.; Lehmann, M. *Chem. Ber.* **1902**, *35*, 897 and Moss, R. A. *J. Org. Chem.* **1966**, *31*, 1082.
(53) A potassium *syn*-methyl diazoate has been reported to explode on grinding: Müller, E.; Hoppe, W.; Hagenmaier, H.; Haiss, H.; Huber, R.; Rundel, W.; Suhr, H. *Chem. Ber.* **1963**, *96*, 1712.
(54) Winters, J.; Learn, D. B.; Desai, S. C. *J. Org. Chem.* **1965**, *30*, 2471.
(55) Zinner, G. *Arch. Pharm.* **1963**, *296*, 57.
(56) White, E. H.; Dzadzic, P. M. *J. Org. Chem.* **1974**, *39*, 1517–1519.

with 2 × 50 mL portions of 5% sodium bicarbonate solution, dried (Na_2SO_4), and filtered. Analysis of the ethereal solution by GLC [6 ft × 0.13 in. SE-30 (10%) on Chromosorb W] indicated that styrene was present (25%). Crude product was obtained by removal of the volatiles in vacuo; the ester was purified by column chromatography (SiO_2; CCl_4, CH_2Cl_2 mixtures) to yield (0.397 g, 1.44 mmol, 26%) of pure 1-phenylethyl 2-naphthoate: IR (CCl_4) 1720 cm^{-1}; $[\alpha]^{21}_D$ −52.8° (*c* 1.14, 95% EtOH) (44.5% optically pure;[57] 46.3% net retention of configuration). Thus, the decomposition proceeded with 73% overall retention of configuration (and 27% overall inversion).

A repeat of the above reaction at double the scale using 94% optically pure amide yielded styrene (50%), 1-phenylethyl 2-naphthoate (19%), and 2-naphthoic acid (54%). The product ester, $[\alpha]^{24}_D$ −53.7° (*c* 2.48, 95% EtOH), was formed with 74% overall retention of configuration. Anal. ($C_{19}H_{16}O_2$) C, H,

Duplicate decompositions of **2a** in dioxane afforded ester with 76%, 76% net retention of configuration whose configuration was determined by chiral column HPLC. Duplicate decompositions of racemic material yielded ester (38%, 38%) as determined by HPLC.

B. In Methylene Chloride. The nitroso amide (3.15 g, 10.3 mmol, prepared from the 94% optically pure amide) in CH_2Cl_2 (250 mL) was stirred for 6.4 h at 25 °C. GLC analysis of the mixture revealed the presence of styrene (51%) and 1-phenylethyl 2-naphthoate (47%). Workup as described in part A above gave pure ester (0.40 g, 1.46 mmol, 14%), $[\alpha]^{24}_D$ −39.1° (*c* 1.142, 95% EtOH). This specific rotation corresponds to an optical purity of 32.9% for the ester.[57] The decomposition proceeded with 35.0% net retention of configuration; this value corresponds to 68% overall retention of configuration accompanied by 32% overall inversion. Anal. ($C_{19}H_{16}O_2$) C, H.

HPLC analysis of duplicate decompositions of **2a** afforded ester with 67%, 68% net retention of configuration (method of part A), while the racemic material produced ester in 37% and 37% yields.

C. In Ethanol. The nitroso amide (0.663 g, 2.17 mmol, prepared from 95% optically pure amide) in absolute ethanol (50 mL) was stirred for 6 h at 25 °C. GLC analysis of the mixture revealed the presence of styrene (55%), 1-phenylethyl ethyl ether (37%), and 1-phenylethyl 2-naphthoate (21%). A repeat of the above reaction afforded styrene (47%), 1-phenylethyl ethyl ether (38%), and 1-phenylethyl 2-naphthoate (21%). The two reaction mixtures were combined; workup as described in part A above gave pure ester (0.23 g, 0.82 mmol, 21%), $[\alpha]^{24}_D$ −77.2° (*c* 0.972, 95% EtOH). This specific rotation corresponds to an optical purity of 65% for the ester;[57] thus the decomposition proceeded with 85% retention of configuration accompanied by 15% inversion.

As outlined in parts A and B, HPLC analysis of duplicate decompositions of **2a** afforded ester in 83%, 84% net retention of configuration, while the racemic material produced ester in 19% and 20% yields.

D. Rate Measurements. The nitroso amide was dissolved in the appropriate solvent (ca. 1 × 10^{-3} M), and a 3.00-mL aliquot was placed in a 1.0-cm quartz fluorescence cell equipped with a stopcock. After the UV/vis absorption spectra were recorded, the decomposition, at 25 °C, was monitored at 410 and 424 nm for 20000 s. The first-order rate constants were determined from that portion of the data in which the absorbance had decreased to 0.75 of the initial value. First-order rate constants for decomposition in dioxane, methylene chloride, and ethanol were 3.2, 4.3, and 6.4 (× 10^{-4}) s^{-1}, respectively.

Decomposition of *N*-Nitroso-*N*-(1-phenylethyl)benzamide (2b). The title compound [NMR ($CDCl_3$) δ 1.76 (d, 3 H, *J* = 7.1 Hz), 6.11 (q, 1 H, *J* = 7.1 Hz), 7.4–7.8 (m, 5 H)], prepared as described for **2a**, was decomposed in $CDCl_3$ at 25 °C to cleanly produce 1-phenylethyl benzoate (40 ± 2%) and styrene (54 ± 2%); the data are an average of eight runs (range: 37–42% ester).[61]

Reaction of Potassium *anti*-(*R*)-1-Phenylethanediazoate (5) with 2-Naphthoyl Chloride. To a stirred suspension of the diazoate (0.47 g, 2.5 mmol, 94% optically pure) in pure dioxane (25 mL) under nitrogen at 25 °C was added a solution of 2-naphthoyl chloride (0.48 g, 2.5 mmol) in dioxane (18.8 mL) dropwise over 10 min. The diazoate dissolved as the acid chloride was added; an IR spectrum of an aliquot (taken after 10 min) showed an absence of the acid chloride (1750 cm^{-1}). Also absent were nitroso amide (from N-acylation) (1500 cm^{-1}) and azoxy compounds (1490 cm^{-1}).[58] After 50 min, the mixture was poured into water (125 mL) and extracted with ether (3 × 30 mL). The combined ethereal extracts were washed with 5% aqueous sodium bicarbonate solution, dried (Na_2SO_4), and filtered. Volatile components were removed on the rotary evaporator and analyzed by GLC; styrene (24% yield) was quantitated in this way. The nonvolatile residue (0.415 g) was analyzed by NMR (toluene as internal standard) to reveal a 17% yield of 1-phenylethyl 2-naphthoate and a 14% yield of 1-phenylethanol mixed with 2-naphthoic anhydride and other products. The crude ester was separated from 2-naphthoic anhydride by pentane trituration, and the solubles were purified by fractional sublimation (25–70 °C, 10^{-2} Torr). The fraction that sublimed at 70 °C was pure 1-phenylethyl 2-naphthoate as shown by ^1H NMR and IR, $[\alpha]^{22}_D$ −41.7° (*c* 1.596, 95% EtOH). The optical purity was 35.1%,[57] and the net retention of configuration was 37.6%; the ester had been formed with 69% overall retention of configuration and 31% overall inversion.

Reaction of Potassium *syn*-(*R*)-1-Phenylethanediazoate (6) with 2-Naphthoyl Chloride. A. In Dioxane. Potassium *syn*-(*R*)-phenylethanediazoate (1.45 g, 7.7 mmol, prepared from 95% optically pure amine) in dioxane (40 mL) was treated with a solution of 2-naphthoyl chloride (1.54 g, 8.1 mmol) in dioxane (30 mL). The mixture was stirred for 3 h and then worked up as described for the anti isomer to give styrene (24%) and crude 1-phenylethyl 2-naphthoate. The ester was purified by column chromatography (silica gel; CCl_4, then mixtures with CH_2Cl_2) to yield 0.426 g (1.54 mmol, 20%) of the ester (IR and NMR spectra identical to those of the pure racemic ester), $[\alpha]^{24}_D$ −54.3° (*c* 0.584, 95% EtOH). Anal. ($C_{19}H_{16}O_2$) C, H. The ester was 45.7% optically pure;[57] thus, the reaction had proceeded with 48.2% net retention—or with 74% overall retention of configuration (accompanied by 26% overall inversion). In a similar experiment, the half-life for the reaction of naphthoyl chloride with the *syn*-diazoate in dioxane at 25 ± 1 °C was determined by IR spectroscopy; $t_{1/2}$ = 15.0 min.

B. In Methylene Chloride. The *syn*-diazoate (0.362 g, 1.92 mmol, prepared from 95% optically pure amine), 2-naphthoyl chloride (0.548 g, 2.87 mmol), and methylene chloride (40 mL) were stirred for 20 h. Workup as in run A above afforded styrene (9% by GLC analysis) and, after column chromatography (as in run A), pure (*R*)-1-phenylethyl 2-naphthoate (14%): $[\alpha]^{23}_D$ −41.7° (*c* 0.729, 95% EtOH). Anal. ($C_{19}H_{16}O_2$) C, H. The ester was 35.1% optically pure;[57] the reaction proceeded with retention of configuration (37% net, or 69% overall + 31% overall inversion). The half-life for the reaction of 2-naphthoyl chloride with the diazoate in dichloromethane at 25 ± 1 °C was determined by IR spectroscopy: $t_{1/2}$ = 10 min.

Controls. The reaction in dioxane at 25 °C was followed by UV and IR spectroscopy at 5-min intervals in a search for N-acylation, which would yield nitroso amide **2a**. No detectible absorption was seen at 408 and 425 nm, indicating that a maximum of ~5% of **2a** could have been been formed. By following the absorption band for naphthoyl chloride at 1750 cm^{-1}, it was determined that the reaction was complete in 20 min; the absorption bands of the nitroso amide at 1500–1510 and 800 cm^{-1} were not observed during the reaction (similar results were obtained in CH_2Cl_2). At the end of the reaction, authentic nitroso amide was added to the reaction mixture, and its decomposition was followed at 425 nm; in this system, the half-life of decomposition was ~37 min. A run in DMSO-d_6 was followed by NMR; the doublet of the nitroso amide (δ 2.05 in this solvent) was not detected, indicating that the maximum possible yield would have been <15%.

Reaction of *syn*-(*R*)-1-Phenylethanediazoate (6) (Prepared in Situ) with 2-Naphthoyl Chloride in Dioxane. A solution of ethyl (+)-(*R*)-*N*-nitroso-*N*-(1-phenylethyl)carbamate (3.53 g, 15.9 mmol, prepared from 95% optically pure amine) in dioxane (25 mL) was added dropwise, over a 13-min period, to a stirred suspension of potassium *tert*-butoxide (1.87 g, 16.7 mmol) in dioxane (40 mL) at 0 °C. The mixture was warmed to 25 °C, and a solution of 2-naphthoyl chloride (3.04 g, 15.9 mmol) in dioxane (40 mL) was added over a 5-min period. Upon workup, as described for the diazoate–acid chloride runs, styrene (6% by GLC analysis) and 1-phenylethyl 2-naphthoate (11% after column chromatography) were obtained. The pure ester had $[\alpha]^{24}_D$ −49.7° (*c* 1.027, 95% EtOH); the optical purity was 41.8% and the net retention of configuration was 44.0%. The latter value corresponds to 72% of overall retention of configuration (accompanied by 28% overall inversion).

Reaction of (+)-(*R*)-(1-Phenylethyl)nitroamine Potassium Salt (8) with 2-Naphthoyl-^{18}O Chloride in Dioxane. A solution of 2-naphthoyl-^{18}O chloride (1.91 g, 10 mmol, 1.00 atom % excess ^{18}O)[9] in pure dioxane (75 mL) was added dropwise over a 10-min period to a stirred suspension of the optically pure nitroamine salt (2.04 g, 9.99 mmol, 95% optically pure) in dioxane (100 mL) at 25 °C. After 4 h, water (500 mL) was added and the mixture was extracted with ether (3 × 175 mL). The ethereal extracts were washed with 5% aqueous sodium bicarbonate (2 × 125 mL) and with water (2 × 125 mL). The aqueous phases upon acidification yielded (1-phenylethyl)nitroamine (8%) and 2-naphthoic acid (8%). The organic solution was dried (Na_2SO_4) and filtered; solvent removal on a rotary evaporator afforded 1.86 g of a white solid. Trituration of this

(57) For optically pure (*S*)-(+)-1-phenylethyl 2-naphthoate, $[\alpha]^{25}_D$ = +118.7° (*c* 3.33, 95% ethanol).[9]

(58) Moss, R. A.; Landon, M. *Tetrahedron Lett.* **1969**, 3897.

(59) Possibly *N*-(1-phenylethyl)-*N*-nitro-2-naphthamide (White, E. H.; Grisley, D. W., Jr. *J. Am. Chem. Soc.* **1961**, *83*, 1191).

(60) Bamberger, E.; Bakmann, O. *Ber. Dtsch. Chem. Ges.* **1887**, *20*, 1118.

(61) Determined by ^1H NMR using toluene as an internal standard.

material with hexane removed 1-phenylethyl 2-naphthoate, leaving 2-naphthoic anhydride (1.24 g, 38%). The hexane solution of the ester was concentrated and subjected to chromatography on silica gel to give ester (0.48 g, 1.73 mmol, 17%) contaminated with a compound with an IR band at 1555 cm^{-1} ($CHCl_3$).[59] Further purification by sublimation and pot-to-pot distillation afforded pure 1-phenylethyl 2-naphthoate (spectra identical with those of analytically pure material): $[\alpha]^{22}_D$ −55.6° (*c* 2.12, 95% EtOH) (47% optically pure).[57] The ester had been formed with 49% net retention of configuration; the overall retention was 75% (accompanied by 25% overall inversion; 0.50 atom % excess ^{18}O (for each oxygen)).

The procedure for determining oxygen-18 distribution in the pure ester was similar to that reported by White and Aufdermarsh.[9] The ester (0.295 g, 1.07 mmol) in ether (10 mL) was slowly added to a mixture of lithium aluminum hydride (0.0262 g, 0.64 mmol) in ether (15 mL) at 0 °C. After 3 h, water (1 mL) was added and the mixture was filtered to remove the white precipitate, which was washed with 20 mL of ether. The combined ether solutions were dried (Na_2SO_4), filtered, and evaporated to yield a white solid (0.27 g). 1-Phenylethanol (50.7 mg, 38%), free of 2-naphthylmethanol (<2% by GLC analysis; 3% SE-30, 180 °C), was obtained by pot-to-pot distillation at 80 °C (0.5 Torr) (0.55 atom % excess ^{18}O). The residue in the distillation, 2-naphthylmethanol, was purified by sublimation (60 °C, 10^{-2} Torr) followed by two recrystallizations from aqueous ethanol, mp 80–80.5 °C (lit.[60] mp 80–81.5 °C, 0.40, 0.42 atom % excess ^{18}O).

A repeat of the above reaction using unlabeled acid chloride afforded styrene (29%), 1-phenylethyl 2-naphthoate (19%), and 2-naphthoic anhydride (33%). The ester was 39.7% optically pure:[57] $[\alpha]^{23}_D$ −47.1° (*c* 1.57, 95% EtOH); this value corresponds to 42.2 net retention, or 71% overall retention of configuration accompanied by 29% overall inversion. Anal. ($C_{19}H_{16}O_2$) C, H.

Nitrosation of (+)-(*R*)-*N*-(1-Phenylethyl)-*O*-(2-naphthoyl)-hydroxylamine. A. In Dioxane. A mixture of the hydroxylamine (1.00 g, 3.44 mmol, $[\alpha]^{25}_D$ + 120.3° (optically pure)) and sodium acetate (766 mg, 9.35 mmol) in dioxane (100 mL) was stirred at 25 °C. Dinitrogen tetraoxide gas (193 mL, 8.6 mmol) was slowly added to the mixture. After 1 h an additional 25 mL (1.1 mmol) of N_2O_4 was added to react with a small amount of remaining hydroxylamine detected by TLC. After 30 min, the mixture was poured into water (300 mL) and extracted with ether (3 × 150 mL). The combined ethereal extracts were washed with saturated aqueous sodium bicarbonate (3 × 150 mL) and dried with Na_2SO_4. Evaporation of the solvent afforded a yellow oil (0.55 g). Pure ester (12%) was obtained by column chromatography (silica gel/CH_2Cl_2) followed by fractional sublimation (50 °C, 10^{-2} Torr) to remove impurities absorbing at 1580 and 1560 cm^{-1}: ^1H NMR ($CDCl_3$) δ 1.75 (d, 3 H, *J* = 6.5 Hz), 6.23 (q, 1 H, *J* = 6.5 Hz), 7.2–8.2 (m, 11 H), 8.7 (s, 1 H); $[\alpha]^{23}_D$ −42.4° (*c* 2.15, 95% EtOH) corresponds to an optical purity of 35.7%.[57] The net retention of configuration was 36%; the ester had been formed with 68% overall retention of configuration accompanied by 32% overall inversion.

B. In Methylene Chloride. The reaction outlined in part A was repeated using methylene chloride as solvent. The ester, 1-phenylethyl 2-naphthoate (39%),[61] was purified by fractional sublimation and was formed with 67% overall retention of configuration. Another run, performed in methylene chloride at −50 °C with nitrosyl chloride as the nitrosating agent, gave pure ester (after pot-to-pot distillation and two sublimations) with 70% overall retention of configuration.

Nitrosation of (+)-(*R*)-*N*-(1-Phenylethyl)-*O*-(2-naphthoyl-*carbonyl*-^{18}O)hydroxylamine (10a). The title compound (1.92 g, 6.59 mmol), with $[\alpha]^{24}_D$ + 117.9° (*c* 2.26, 95% EtOH) (98% optically pure; 2.76 atom % excess ^{18}O (CO)), was deaminated in dioxane as described above for the ^{16}O analog; a 47% yield of ester was obtained.[61] Pure 1-phenylethyl 2-naphthoate was obtained in 24% yield by column chromatography and pot-to-pot distillation: $[\alpha]^{23}_D$ −43.26° (*c* 2.663, 95% EtOH) (0.72 atom % excess ^{18}O (for each oxygen)). The ester (36.4% optically pure)[57] was formed with 37.2% net retention of configuration (or 69% overall retention accompanied by 31% overall inversion). The oxygen-18 distribution of the ester was determined as described for the reaction of (+)-(*R*)-(1-phenylethyl)nitroamine potassium salt with 2-naphthoyl-^{18}O chloride. The results were 1-phenylethanol (1.19, 1.21 atom % excess) and 2-naphthylmethanol (1.57 atom % excess).

Nitrosation of *N*-(1-Phenylethyl)-*O*-benzoylhydroxylamine (10b). Nitrosation of 0.05 M solutions of the title compound[55] in the presence of 0.07 M pyridine at 25 °C as described for **10a** yielded, cleanly, 1-phenylethyl benzoate (59 ± 2%) and styrene (33 ± 2); the data are averaged from 11 runs (range: 55–64% ester).[61]

Preparation and Decomposition of *N*-Nitroso-*N*-benzhydrylbenzamide-^{18}O (12). Dinitrogen tetraoxide (14.3 mL, 21.3 g, 0.23 mol) was added in two portions to a stirred mixture of *N*-benzhydrylbenzamide-^{18}O (2.87 g, 10.0 mmol; 1.56, 1.56 atom % excess ^{18}O), sodium sulfate (5 g), sodium acetate (30.0 g, 0.37 mol), and methylene chloride (150 mL) at −40 °C. The mixture was stirred for 2 h at −15 °C and then 7 h at 0 °C. IR spectra indicated that the decomposition at 20 °C had a half-life of ~10 min. The mixture was then washed with water (300 mL), 5% aqueous sodium carbonate (2 × 200 mL), and again with water (2 × 200 mL). The organic solution was dried (Na_2SO_4) and filtered, and the solvent was removed to leave crude benzhydryl benzoate (2.73 g, 9.47 mmol, 98%). This material was chromatographed (Woelm Neutral Alumina, benzene) and recrystallized (95% ethanol) to give the pure ester (2.11 g, 73%): mp 87–89 °C (lit.[62] mp 88–89 °C); 0.78, 0.77 atom % excess ^{18}O (at each oxygen). Anal. ($C_{20}H_{16}O_2$) C, H.

The ester was cleaved with lithium aluminum hydride as described in the run utilizing (1-phenylethyl)nitroamine. Benzhydryl alcohol was recrystallized to give white needles (0.251 g, 1.36 mmol, 52%): mp 66–68 °C (lit.[63] mp 69 °C); 0.665, 0.685 atom % excess ^{18}O. Anal. ($C_{13}H_{12}O$) C, H. Benzyl alcohol, recovered by distillation, was converted to benzyl *N*-phenylcarbamate, and the derivative was recrystallized from isooctane (0.241 g, 1.3 mmol, 41%): mp 75–76 °C (lit.[64] mp 78 °C); 0.85, 0.85 atom % excess ^{18}O (calculated in the ether position). Anal. ($C_{14}H_{13}O_2N$) C, H, N. Thus, the decomposition occurred with 56% of the ^{18}O being retained in the carbonyl group and 44% in the ether position.

In a second run, 1 g (3.48 mmol) of amide, mp 169–176 °C (1.18, 1.22 atom % excess ^{18}O. Anal. ($C_{20}H_{17}NO$) C, H), was nitrosated and the product decomposed as described for run 1. Pure ester, mp 88.2–90.8 °C, was obtained in 58% yield; 0.60, 0.62 atom % excess ^{18}O (for each oxygen). Anal. ($C_{20}H_{16}O_2$) C, H. The reduction of 500 mg (1.74 mmol) of the ester, separation of the products, and derivatization of the benzyl alcohol formed yielded (1) 210 mg (1.14 mmol) of benzhydrol, mp 65.4–66.4 °C, after one recrystallization from hexane and 80 mg after one more recrystallization; 0.57, 0.56 atom% excess ^{18}O. Anal. ($C_{13}H_{12}O$) C, H; and (2) benzyl *N*-phenylcarbamate (90 mg after recrystallization from octane), mp 76–77 °C; 0.71 atom % excess ^{18}O (calculated at the ether position). Anal. ($C_{14}H_{13}O_2N$) C, H.

Deamination of *N*-Benzhydryl-*O*-(benzoyl-*carbonyl*-^{18}O)-hydroxylamine (15). Nitrosyl chloride gas (150 mL, 6.70 mmol) was added in three portions to a stirred mixture of the hydroxylamine (1.50 g, 4.94 mmol; 1.70 atom % excess ^{18}O (CO)), sodium acetate (5.0 g, 61.0 mmol), and sodium sulfate (2.0 g, 14.1 mmol) in methylene chloride (150 mL) at 0 °C. The mixture was stirred for 1 h at room temperature and then washed with saturated aqueous sodium bicarbonate followed by water. The organic phase was dried (Na_2SO_4) and filtered, and the solvent was removed on a rotary evaporator to give crude benzhydryl benzoate (1.31 g, 4.54 mmol, 92%). The ester was recrystallized from 95% ethanol to yield white needles: mp 88–89 °C (lit.[24] mp 88–89 °C); 0.83, 0.87 atom % excess ^{18}O (for each oxygen). Anal. ($C_{20}H_{16}O_2$) C, H.

A sample of the benzhydryl benzoate-^{18}O (0.500 g, 1.737 mmol) was cleaved by the procedure used for 1-phenylethyl 2-naphthoate. Benzyl alcohol and benzhydryl alcohol were separated by distillation. The benzhydryl alcohol was recrystallized from petroleum ether to yield white needles (0.175 g, 0.95 mmol, 55%): mp 67–68 °C (lit.[63] mp 69 °C); 0.68 and 0.68 atom % excess ^{18}O. Anal. ($C_{13}H_{12}O$) C, H. The benzyl alcohol-^{18}O was purified via its *N*-phenylcarbamate derivative, which was prepared by heating the alcohol with phenyl isocyanate in isooctane. Upon recrystallization from isooctane, benzyl *N*-phenylcarbamate-*ether*-^{18}O was obtained in 38% yield (0.137 g): mp 75–76 °C (lit.[64] mp 78 °C); 0.94, 0.94 atom % excess in the ether position. Anal. ($C_{14}H_{13}O_2N$) C, H, N.

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