($LiAlH_4$ and alumina steps). Compound **18** was obtained in 18% overall yield: bp 120–123 °C (0.6 mm); ^1H NMR (CCl_4) δ 0.7–1.9 (m), 1.92 (s, 3 H), 2.4–2.8 (m, 2 H), 3.57 (s, 2 H), 6.6–7.3 (m, 5 H); high-resolution mass spectrum, *m/e* (relative intensity) 229.1458 (100, M^+) ($C_{15}H_{19}NO$ requires 229.1467).

4,5-Dihydronapth[2,1-*c*]isoxazole (20). Crude **20** was made by standard formation[2] of a THF solution of the dilithio salt of β-tetralone oxime and then reaction with a solution of $Me_2NCHOMe^+FSO_3^-$, which we made by stirring FSO_3Me with DMF (2 equiv) and then diluting with 0.5 volume of DME. Hydrolysis, cyclization, dehydration, and workup (no $LiAlH_4$ or alumina) yielded a distillation fraction that analyzed (NMR) as 80% pure. An ether solution of this was titrated with CF_3SO_3H, yielding a solid which was triturated with more ether. The solid was partitioned between water and ether, the layers were separated, and the aqueous solution was extracted with more ether. The combined ether extracts were washed with water, dried (Na_2SO_4), and evaporated to give pure **20** in 62% yield (clear oil): bp 112–117 °C (0.3 mm); ^1H NMR (CCl_4) δ 2.79 (s, 4 H), 6.9–7.6 (m, 4 H), 8.38 (s, 1 H); high-resolution mass spectrum, *m/e* (relative intensity) 171.0683 (100, M^+) ($C_{11}H_9NO$ requires 171.0684). When $Me_2NCHOEt^+BF_4^-$ was used as the acylating agent, the crude **20** was obtained in 41% estimated yield (61% pure).

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Registry No. 1, 6944-54-3; 11·2Li$^+$, 83665-90-1; **12a**, 83665-93-4; **12b**, 83665-94-5; **12c**, 83665-96-7; **12d**, 83665-98-9; **12e**, 83666-00-6; **12f**, 83681-31-6; **13**, 83666-01-7; **15a**, 83666-02-8; **15b**, 83666-03-9; **16a**, 83666-04-0; **17**, 83666-05-1; **18**, 83666-06-2; **19**·2Li$^+$, 83681-29-2; **20**, 83666-07-3; $EtCH(Me)C(OEt)NBu_2^+CF_3SO_3^-$, 83666-09-5; $Et_2CHC(OEt)NBu_2^+CF_3SO_3^-$, 83666-11-9; $EtC(OEt)NBu_2^+BF_4^-$, 83666-13-1; $BuC(OEt)NPr_2^+BF_4^-$, 83666-15-3; $Me_2NCHOMe^+FSO_3^-$, 83666-16-4; dilithio-2-methylcyclohexanone oxime, 83666-17-5; dilithioacetophenone oxime, 79043-01-9; dilithioacetone oxime, 83665-91-2.

Following the Course of Resolution of Carboxylic Acids by ^{13}C NMR Spectrometry of Amine Salts

Francis X. Webster, Xiao-nong Zeng, and
Robert M. Silverstein*

Department of Chemistry, College of Environmental Science & Forestry, Syracuse, New York 13210

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Resolution of a racemic carboxylic acid by recrystallization of its salt with an amine enantiomer, such as (−)-quinine, is frequently the method of choice, especially on a large scale.[1] Resolution is followed by decomposition of the salt and determination of the optical rotation on a weighed sample of the regenerated carboxylic acid; the steps are repeated to constant optical rotation. The procedure is tedious, and assignment of enantiomeric purity by optical rotation requires confirmation, usually by HPLC or GC separation of diastereomeric derivatives or by means of NMR spectrometry with chiral shift reagents.[2]

Although ^{13}C NMR spectrometry has been used to measure diastereomeric ratios of covalent compounds,[3,4] we now report that ^{13}C NMR spectrometry of solutions of amine salts affords a direct, facile procedure for determining enantiomeric composition throughout the resolution procedure. Obviously, this procedure is also applicable to the resolution of racemic amines and of racemic alcohols through the half-ester with phthalic anhydride. However, the procedure is not necessarily applicable to all combinations of carboxylic acids and amines; our studies were limited to quinine salts, but the procedure was successful in every case.

Table I. Chemical Shifts for a Pair of Peaks Representing Corresponding Carbon Atoms in Diastereomeric Quinine Salts

compound	no.	chem shifts, Hz
2-ethylhexanoic acid	1	2448.7, 2431.9[a]
2-methylbutanoic acid	2	353.3, 350.4[b]
2-phenylpropanoic acid	3	1807.1, 1767.8[a,d]
trans-phenylcyclopropanecarboxylic acid	4	1582.7, 1525.4[a,d]
2-phenylbutanoic acid	5	366.5, 361.0[b]
3-phenylbutanoic acid	6	754.9, 752.5[b]
2-cyclopenteneacetic acid	7	867.4, 859.0[b]
3-methyl-5-oxo-3- cyclohexene-1-carboxylic acid	8	4071.1, 4065.3[c,d]
tetrahydro-5-oxo-2-furancarboxylic acid	9	2448.7, 2431.9[a]

[a] Bruker widebore WM-360. [b] Varian CFT-20. [c] Varian XL-100. [d] We confirmed that this pair of peaks represented corresponding carbon atoms of the diastereomeric salts by following the change in ratio of peak intensities during the course of resolution.

Table II. Comparison of Enantiomeric Ratios of 2-Phenylpropanoic Acid (3) to Diastereomeric Ratios of Its Quinine Salt

recrystn no.	$[\alpha]^{22}{}_D$, deg, for acid[a]	ratio of acid enantiomers	ratio of diastereomeric salts
1	−15.5 (*c* 1.188, EtOH)	59.8/40.2	59.0/41.0
2	−44.3 (*c* 1.394, EtOH)	78.0/22.0	79.0/21.0
3	−58.7 (*c* 1.002, EtOH)	87.0/13.0	88.1/11.9
4	−70.8 (*c* 1.340, EtOH)	94.8/5.2	96.5/3.5

[a] The pure (−) acid has a specific rotation of −79.1° (*c* 1.567, EtOH).

Results and Discussion

We obtained NMR spectra of the quinine salts of nine carboxylic acids (Table I) on a Varian CFT-20, a Varian XL-100, and a Bruker Widebore WM-360. Compounds **1–7** were chosen because they were commercially available and had previously been resolved.[5-11] Compounds **8** and **9** were chosen because we were interested in obtaining the enantiomers for another study. In each case, at least one pair of peaks was found for the corresponding carbon atoms in each diastereomer. We followed the course of resolution of compounds **3** and **4** by determining the ratio of the diastereomeric salts, after each recrystallization,

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Table III. Comparison of Enantiomeric Ratios of *trans*-2-Phenylcyclopropanecarboxylic Acid (4) to Diastereomeric Ratios of Its Quinine Salt

recrystn no.	$[\alpha]^{22}{}_D$, deg, for acid[a]	ratio of acid enantiomers	ratio of diastereomeric salts
1	+113.9 (*c* 1.758, EtOH)	68.3/31.7	68.2/31.8
2	+156.8 (*c* 1.660, EtOH)	75.1/24.9	74.5/25.5
3	+168.8 (*c* 1.700, EtOH)	77.1/22.9	75.6/24.4

[a] The pure (+) acid has a specific rotation of +311.7° (*c* 1.776, EtOH).

from the peak heights of a pair of peaks representing the corresponding carbon atoms in each diastereomer. Since the specific rotations of the enantioners of these two compounds were known, we could calculate the enantiomeric ratio from the specific rotation of the regenerated acid after each recrystallization. These diastereomeric and enantiomeric ratios were in good agreement (Tables II and III).

Weighing errors or the presence of impurities (water, solvents, other compounds, or particularly the amine enantiomer) affect the accuracy of the enantiomeric ratio determination but do not affect the diastereomeric ratio determination except for the unlikely superposition of a contaminent peak with one of the pair of peaks selected. Of course, as the peak height of one of the paired peaks approaches base line, the accuracy of the measurement of the peak height decreases. Approach to base line of one of the paired peaks provides direct indication of completion of the resolution.

Experimental Section

General. Optical rotations were obtained on a Perkin-Elmer 531 polarimeter. All spectra were run in CDCl$_3$ solution (80 mg/mL) with Me$_4$Si as internal standard. Spectra recorded on the Varian XL-100 (25.2 MHz) were run in 5- and 12-mm tubes. The spectra were recorded with a 6000-Hz window and full 8K memory. Spectra recorded on Varian CFT-20 (20 MHz) were run in 10-mm tubes with 4000-Hz window and 8K memory. Spectra recorded on the Bruker Widebore WM-360 (90.56 MHz) were run in 10-mm tubes with a 20000-Hz window and 16K memory. All quantitative spectra were obtained on the Bruker WM-360.

Partial Resolution of Compounds 3 and 4. The quinine salts of 2-phenylpropanoic acid (3) and *trans*-2-phenycyclopropanecarboxylic acid (4) were each recrystallized from a saturated solution of refluxing acetone. The salts were vacuum dried at room temperature. The partially resolved acids were regenerated from the salts by acidification with dilute sulfuric acid and extraction with ether. The ether solutions were washed and dried; the ether was evaporated, and the acids were vacuum dried at room temperature.

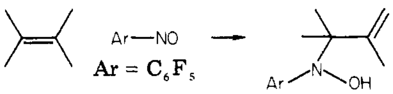
Acknowledgment. The Varian CFT-20 and Bruker Widebore WM-360 NMR spectra were obtained at the NIH Resource for Multi-Nuclei NMR and Data Processing, Department of Chemistry, Syracuse University. We express our thanks to Dr. G. N. Levy and his staff for the courtesies extended during the period of establishing this new facility. We thank Alan Harvey of this college for the spectra obtained on the Varian XL-100. This study was supported by grants from the National Institute of Health and from the National Science Foundation.

Communications

On the Reaction of the Nitroso Group with Olefins. Mechanisms of Ene Reactions[1]

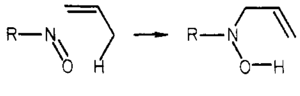
Summary: Intra- and intermolecular isotope effects point to a two-step process for the reaction of pentafluoronitrosobenzene with tetramethylethylene to afford the ene product, 4—rate-determining formation of an intermediate (for which the aziridine *N*-oxide 5 is suggested) followed by C–H (or C–D) cleavage to the ene product.

Sir: Reaction of nitroso compounds with monoolefins has afforded a variety of results including the formation of paramagnetic species[2] and the formation of products of a simple ene reaction (eq 1).[3]



(1)

Recent studies have called attention to the importance of inadvertent photolysis of nitroso compounds as a source of some of the paramagnetic products;[4] and a study of the reaction of CF$_3$NO with a series of olefins[3c] has provided strong evidence for the (overall) ene reaction in this system. In these and some earlier studies the reasonable six-center mechanism (eq 2) was suggested. Some examples of olefin–carbonylnitroso[5a] reactions affording ene products of synthetic value also have been described.[5b]



(2)

Recently the ene reactions of singlet oxygen[6] and of triazolinediones[7] with some olefins have been shown to

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