occasional swirling at room temperature. After 4 h, the solution was poured into H_2O (100 mL), and the resulting mixture was extracted with cyclohexane (3 × 50 mL). The aqueous phase was passed through a Dowex column (pyr^+ form) using 4:1 H_2O–pyridine as the eluting solvent, and the eluant was evaporated and coevaporated with MeOH (2 × 100 mL). The residue was dissolved in 0.01 M HCl (300 mL) and the reaction was allowed to stand at room temperature for 6 h, after which the solution was neutralized with 1 M TEAB buffer, evaporated to dryness, coevaporated with MeOH (2 × 200 mL), and dissolved in cold H_2O (500 mL). Purification by anion-exchange chromatography on a column (21 × 6 cm) of DEAE-Sephadex using a linear gradient of 3 L of 0.005 TEAB → 3 L of 0.5 M TEAB followed by 2 L of 1 M TEAB as the eluting solvents gave three major UV-absorbing peaks of approximately equal size, which eluted at ca. 0.3, 0.5, and 0.7 M buffer concentration. The peak that eluted at ca. 0.7 M was determined to be the P–O–P-linked *lin*-benzo-AMP dimer, P^1,P^2-di-*lin*-benzoadenosine 5′-pyrophosphate, based on its characteristic UV absorption spectrum.[11] The peak that had eluted first, i.e., that at ca. 0.3 M TEAB, was evaporated to dryness and coevaporated with MeOH (4 × 100 mL) to provide the desired dinucleoside monophosphate **18b** (35 μmol as estimated by UV using ϵ 10.4 mM^{-1} cm^{-1} at 331 nm; 22%), which was both chromatographically and electrophoretically homogeneous without additional purification: λ_{max}^{pH7} 318, 331, 346 nm; R_f 0.38 (cellulose, solvent I), 0.56 (silica, solvent C); relative migration on thin-layer electrophoresis (pH 7.5), 0.48 (5′-*lin*-benzo-AMP = 1.0).

A 23 mM solution of Fp(*lin*-benzo-A) in 50 mM Tris–acetate buffer (pH 8.6) containing 13 mM $MgCl_2$ was treated with phosphodiesterase I from *C. adamanteus*[53] (ca. 0.05 unit in 15-μL total reaction volume). After 19 h at 25 °C, an additional 0.1 unit of enzyme was added, and after a total of 40 h, 5′-*lin*-benzo-AMP was the only UV-absorbing species present as confirmed by electrophoresis and TLC (R_f 0.06, cellulose, solvent I). Furthermore, TLC using a glass-backed silica plate, elution with solvent A, and visualization by the H_2SO_4/heat treatment indicated the presence of **3a**. A control reaction without added enzyme did not show any notable change in its electrophoresis or TLC characteristics within the time limits of this experiment, nor was the presence of **3a** detected using the same procedure as described above.

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Registry No. 3a, 54193-15-6; **3b**, 80963-86-6; **5a**, 58-96-8; **5b**, 32456-54-5; **7**, 80963-87-7; **8**, 80963-89-9; **9**, 80963-91-3; **11**, 80963-92-4; **12**, 80963-93-5; **13**, 80963-94-6; **14a**, 61-19-8; **14b**, 67126-65-2; **15a**, 80963-95-7; **15b**, 80975-53-7; **16a**, 80963-97-9; **16b**, 80963-99-1; **18a**, 80964-01-8; **18b**, 80964-00-7; *N*-[(2,3,5-tri-*O*-(*p*-nitrobenzoyl))-β-D-ribofuranosyl]formamide, 80964-02-9.

Communications to the Editor

On the Migration of a HOOC Group in a Wagner–Meerwein Rearrangement in Superacid Solution: Proof by Double Labeling with Carbon-13

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1,2 Shifts of electron-withdrawing groups (COR, COOR,[1] COSR, $CONR_2$, $PO(OR)_2$, etc.) toward electron-deficient centers have been observed in several carbenium ion rearrangements, including the pinacol,[2] glycidic ester,[3] semipinacol,[4] dienone–phenol,[5] and Wagner–Meerwein rearrangements.[6-8] We have recently shown by double labeling with ^{13}C that the β-hydroxy esters **1** (**b**, R = Me; **c**, R = Et) undergo Wagner–Meerwein

$$\underset{\mathbf{1}}{\mathrm{PhCHOHCMe_2COOR}} \xrightarrow[\sim 0\ ^\circ C]{HSO_3F} \underset{\mathbf{2}}{\mathrm{PhC(COOR){=}CMe_2}}$$

a, R = H; **b**, R = Me; **c**, R = Et

rearrangement to **2b,c** by 1,2 shifts of the alcoxycarbonyl groups exclusively.[9] Whereas migrations of COO^- occur in the benzilic acid[10] and the tertiary ketol[11] rearrangements, no Whitmore-type 1,2 shift of a COOH group seems to be known. *We now report what appears to be the first example of a 1,2 shift of a COOH group (or equivalent) toward an electron-deficient center.*

We dissolved the acid **1a**[9] in HSO_3F and SO_2ClF (1:3) at −100 °C and slowly heated to 0–10 °C, where it was kept until the starting material and its unrearranged derivatives had disappeared from the NMR spectrum; numerous new peaks appeared, among which we observed those belonging to derivatives of **2a**; the same signals were formed from the authentic unsaturated acid **2a** by protonation (in the same medium) [^1H NMR δ 8.0–7.5 (m, 5 H), 2.62 (s, 3 H), 2.07 (s, 3 H); ^{13}C NMR δ 186.9 (C(3)), 180.2 (C(1)), 122.2 (C(2)), 28.9 (Me), 25.5 (Me)] and by subsequent cleavage into the corresponding oxocarbonium ion, Ph-C(CO^+)$=CMe_2$ (3)[9,12] [^1H NMR δ 2.85 (s, 3 H), 2.47 (s, 3 H); ^{13}C NMR δ 94.2 (C(2))].[13,14,16] By quenching and extraction, 40–44% yields

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(13) The signals of protonated **2a** and **3** had also been observed in experiments starting with the esters **1b,c** as well as with the unsaturated esters **2b,c**.[9]

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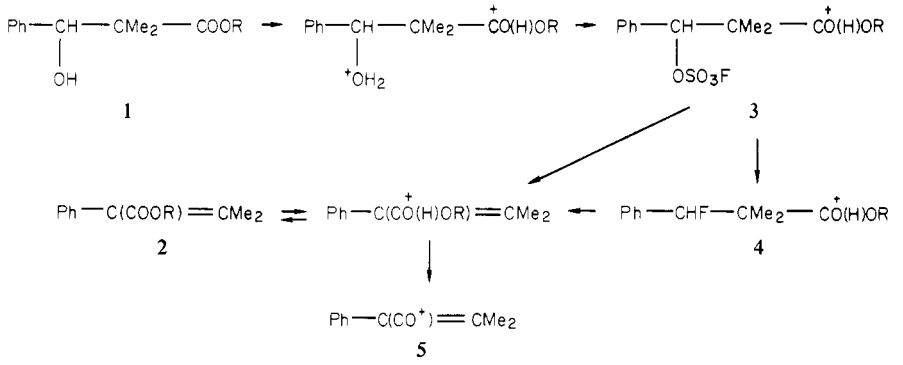
Scheme I[a]



[a] a, R = H; b, R = Me; c, R = Et.

of nearly pure, crystallized rearrangement product **2a** were isolated as the only carboxylic product: mp 149–150 °C (lit.[6] 151 °C); ^{1}H NMR ($CDCl_3$) δ 7.26 (m, 5 H), 2.22 (s, 3 H), 1.70 (s, 3 H); ^{13}C NMR ($CDCl_3$) 173.6 (C(1)), 150.7 (C(3)), 138.2–127.1 (Ph), 129.1 (C(2)), 24.4–22.8

In order to establish the migration of the HOOC group, we prepared **1a** labeled with ^{13}C at C(3) by condensation of benzaldehyde-1-^{13}C with isobutyric acid. When **1a**-3-^{13}C was submitted to treatment with HSO_3F/SO_2ClF at 0 °C, the ^{13}C label appeared in the 2 position (δ 122.1) of protonated **2a** as well as in that of **3** (δ 94.2); it was equally visible in the ^{1}H spectra by coupling of ^{13}C with the protons of the methyl groups of protonated **2a** (δ 2.62, ^3J = 4.6 Hz, and δ 2.07, ^3J = 5.0 Hz) and of **3** (δ 2.85 and 2.47, ^3J = 6.0 Hz); similar values had been found for labeled **2c**.[9]

Definite proof for the HOOC group migration in the superacid comes from use of **1a** doubly ^{13}C labeled at C(1) (90% ^{13}C) and C(3) (69% ^{13}C).[9] In the rearranged (protonated) product **2a** the signals of the H_2OOC^+ group at 180.2 ppm and of C(2) at 122.1 ppm (both increased by enrichment) are split into two doublets by direct ^{13}C,^{13}C coupling ($^1J_{CC}$ = 68.7 Hz). Furthermore, in quenching experiments starting with **1a**-$^{13}C_2$, the label appeared only in the positions 1 and 2 of (nonprotonated) **2a**, isolated and purified; ^{13}C NMR (acetone-d_6) δ 170.4 (d, $^1J_{CC}$ = 71.4, C(1)), 132.0 (d, $^1J_{CC}$ = 70.5, C(2)). We conclude that the only reaction path available for the transformation **1a** → **2a** is a 1,2 shift of the HOOC group.[17]

In order to test whether the reaction is *inter*molecular (for instance via a decarbonylation–carbonylation process[18]), we conducted a cross experiment using a 1:1 mixture of doubly labeled and unlabeled **1a**. There was no increase of monolabeled product in either the ^{13}C NMR spectra (judged by the amount of ^{13}C,^{13}C-coupling between C(1) and C(2)) or in the mass spectra of isolated **2a**; this confirms the *intra*molecular character of the HOOC migration.

We attribute the preference for HOOC over Me migration to a difference in stability of the rearranged carbocations: if a Me group had been shifted, the positive charge would have appeared α to the carboxyl group, thus destabilizing this intermediate.

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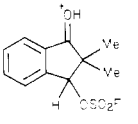
Registry No. 1a, 23985-59-3; **2a**, 4412-08-2; **4**, 81158-98-7.

Supplementary Material Available: All ^{1}H and ^{13}C NMR spectra mentioned in the text (19 pages). Ordering information is given on any current masthead page.

(14) Other peaks observed in the reaction mixture correspond to **4** formed



4

from **1** (or from its fluorosulfate ester) by a Friedel–Crafts type cyclization and replacement of OH by by OSO_2F. The same peaks turned up upon treatment of authentic 3-hydroxy-2,2-dimethylindanone[15] with HSO_3F/SO_2ClF. This was the main product formed from **1a** with HSO_3F in the absence of a solvent when the temperature was raised rapidly.

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(16) By following the reaction of **1a** with the superacid from −100 to +10 °C by ^{1}H and ^{13}C NMR spectroscopy we observed spectral changes analogous to those observed[9] with **1b** and **1c** and which we interprete as the consecutive transformation into the oxonium ion, the fluorosulfate, and (partially) the fluoride $PhCHXCMe_2COOH_2^+$, X = OH_2^+, OSO_2F and F.

(17) It is not possible, however, to decide whether COOH migrates in its protonated or unprotonated form (though it might be felt that protonation would make the group too poor in electrons), nor can other transient species be excluded, e.g., a mixed anhydride (though their presence in the reaction mixture could not be detected).

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Specific Peptide Sequences for Metal Ion Coordination. 1. Solid-Phase Synthesis of *cyclo*-(Gly-His)$_3$

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Synthetic cyclic peptides[1,2] have been used to model various aspects of protein conformation and active sites.[3-8] The advantages of cyclic peptides[3] over linear peptides are the constrained geometry and the absence of free COO^- and NH_3^+ terminals. Thus, a flexible polypeptide can be limited to a few desirable

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