gel with ethanol–ether (1:1) and afforded 3.0 mCi of **4**, which was both chemically and radiochemically pure by TLC (ether) and GC (2.5% Carbowax 20M on 100–120 Varaport-30, 6 ft × $^1/_8$ in. column, 140 °C, $N_2$ flow 30 mL/min, $t_R$ 3.6 min). The material had specific activity of 39.5 mCi/mmol.

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## Activated Anhydrides of Tartaric and Malic Acids

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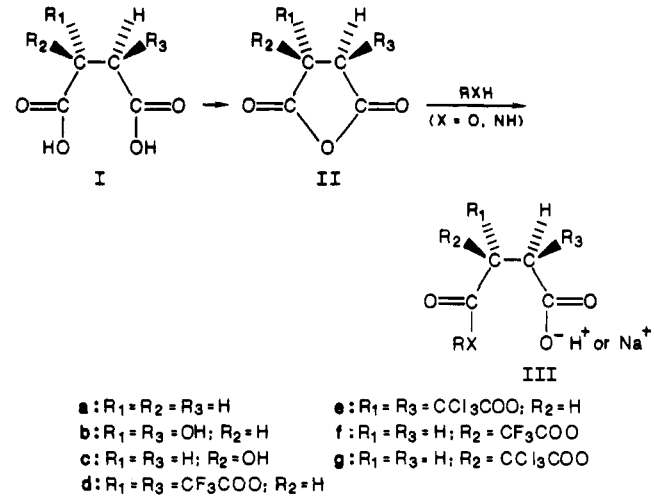
The monoesterification of dicarboxylic acids can often be achieved by preliminary intramolecular anhydride formation. Thus, monoesters (IIIa, X = O) of succinic acid (Ia) can be made[2] by reacting 1 equiv of alcohol with succinic anhydride (IIa). Application of this approach to tartaric (Ib) and malic (Ic) acids has been limited. Their anhydrides (IIb and IIc) are known, but they are either difficult to make or impossible to isolate.[3] Stable derivatives of these anhydrides are known wherein the hydroxyls have been esterified.[4] However, these derivatives are useless for forming esters with free hydroxyls in the acid moiety since deprotection of the hydroxyls would also cleave the esters. We report below the syntheses and characterizations of anhydrides IId-g and their use for the syntheses of IIIb and IIIc.

Of the four compounds IId–g, only IIf was a known material before the start of our work. There are two reports of its use as a reactive intermediate in the synthesis of malate half acid/half amides[5b] and half acid/half esters.[5a] Though no detailed study of its reactivity was reported, it was clear that the trifluoroacetate (TFA) group activated the anhydride toward nucleophile attack. Partial




a: $R_1 = R_2 = R_3 = H$
b: $R_1 = R_3 = OH$; $R_2 = H$
c: $R_1 = R_3 = H$; $R_2 = OH$
d: $R_1 = R_3 = CF_3COO$; $R_2 = H$
e: $R_1 = R_3 = CCl_3COO$; $R_2 = H$
f: $R_1 = R_3 = H$; $R_2 = CF_3COO$
g: $R_1 = R_3 = H$; $R_2 = CCl_3COO$

TFA removal also consumed added nucleophilic reagent, so excess alcohol or amine was used. Nevertheless, these reactions proceeded with good regiochemical integrity and acceptable yields of ester or amide. The goals of our work were to extend this approach to tartrate derivatives and to improve it by the use of trichloroacetate (TCA) instead of TFA (IIe and IIg). We reasoned that TCA should also activate the ring-opening process but not be as labile to nucleophilic attack as TFA. This would permit the use of only 1 equiv of nucleophile. TCA removal could also be achieved under conditions that would not cleave a simple ester. We therefore set out to develop efficient syntheses for these trihaloacetylated anhydrides.

Syntheses of the anhydrides were each achieved by heating the diacids with trifluoroacetic anhydride or trichloroacetic anhydride in dioxane at 75 °C. Completion of cyclic anhydride formation was monitored by noting the disappearance of diacid crystals; the cyclic anhydrides are very soluble in dioxane while the diacids are only sparingly soluble. We also ascertained that neat reaction of TFA anhydride and tartaric acid (pressure bottle, 75 °C) leads to formation of IId. Thus, while the dioxane solvent simplifies the procedure by allowing the use of an open system with only a reflux condenser, its use can be avoided. In either case, vacuum removal of trihaloacetic acid and unreacted trihaloacetic anhydride (and dioxane) leaves virtually clean anhydrides IId–g (crude yields >95%). Sublimation gives (>85% yields) analytically pure material. These sharp-melting, white, crystalline solids were characterized by their specific rotations, IR and NMR ($^1H$ and $^{13}C$) spectra, and elemental analyses. The absence of epimerization during anhydride formation was demonstrated by hydrolysis back to Ib and Ic and comparison of the rotations to those of the acids.

The ring openings of IId–g were compared to that of IIa and to each other. Each of the anhydrides was dissolved at room temperature in $CD_3OD$ and its reaction was monitored by NMR. Tartrate anhydrides were completely consumed in <90 s and malate anhydrides showed >80% ring opening in <90 s and complete reaction in <5 min. In contrast, IIa was 39% reacted in 3 h and 90% in 19 h.

The $CD_3OD$ reactions also shed light on the trihaloacetyl removal process. While more than half of the malate TFA was removed in 40 min and 88% in 3 h, there was only 6% TCA removal in 3 h. A similar trend is seen for the two tartrate trihaloacetyl groups. After 5 min there was 25% loss of one of the tartrate TCA groups vs. 66% loss of one TFA group and 21% loss of both TFA groups. Similarly, 87% double deacylation takes 3 h with TFA and 19 h with TCA.

(1) NIH Research Career Development Awardee (1983–1988).
(2) Zingg, M.; Meyer, K. *Pharm. Acta Helv.* **1957**, *32*, 393.
(3) (a) Malic anhydride was first reported in 1913 (Denham, W. S.; Woodhouse, H. *J. Chem. Soc.* **1913**, *103*, 1861–1870). Its synthesis requires formation of the disilver salt of malic acid and gives anhydride in 50% yield. Recent reports of its use are the following: Matsoukas, J. M.; Burnell, D. J.; Theodoropoulos, D. *Spectrosc. Lett.* **1983**, *16*, 933. Cordopatis, P.; Matsoukas, J.; Michel, A.; Janen, J.; Theodoropoulos, D. *Experientia* **1983**, *39*, 353–355. (b) There is one literature report that infers the existence of tartaric anhydride as a reactive intermediate; neither its isolation nor its direct characterization is reported: Higuchi, T.; Uno, H.; Shimada, I. *J. Pharm. Sci.* **1965**, *54*, 302. A second possible report of tartaric anhydride is suggested in *Chem. Abstr.* **1979** *91*, 221691; however, the original paper itself makes no mention of tartaric anhydride: Pankratova, V. N.; Goreva, T. F.; Krasnov, Yu. N. *Khim. Elementoorg. Soedin.* **1978**, *6*, 20. Hence we conclude that IIb has never been isolated or characterized.
(4) (a) Other than IIf,[5] the acetyl, propionyl, stearyl, and palmityl derivatives of IIc are known. The first reported and still most prominent derivative is the acetyl compound: Perkin, W. H. *Ber.* **1881**, *14*, 2540–2549. Anschutz, R. *Ber.* **1881**, *14*, 2789–2792. An improved preparation of this material appears in Jones, B. *J. Chem. Soc.* **1933**, 788–796. (b) At least nine dicarboxylated derivatives of IIb are in the literature, with the dibenzoyl and diacetyl the most prominent. An early report of both of them is Anschutz, R.; Pictet, A. *Ber.* **1880**, *13*, 1175–1178. An improved synthesis of the dibenzoyl compound is found in Butler, C. L.; Cretcher, L. H. *J. Am. Chem. Soc.* **1933**, *55*, 2605. A useful reference to the preparation of the diacetyl anhydride is Shriner, R.L.; Furrow, C. L. *Organic Syntheses*; Wiley: New York; 1963; Collect. Vol. IV, p 242.
(5) (a) Miller, M. J.; Bajwa, J. S.; Mattingly, P. G.; Peterson, K. *J. Org. Chem.* **1982**, *47*, 4928. (b) Rajashekhar, B.; Kaiser, E. T. *J. Org. Chem.* **1985**, *50*, 5480.

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**Table I. Anhydride Syntheses**

| anhydride | acid, g | $(CX_3CO)_2O$, mL (equiv) | diox, mL | sublimation °C/mm (% yld) | analyses obsd/calcd C | H | X |
|---|---|---|---|---|---|---|---|
| TFA/IId | 14.5 | 46.6 (3.3) | 30.0 | 50/0.03 (89) | 29.59/29.65 | 0.62/0.62 | 34.81/35.17 |
| TFA/IId | 3.5 | 24.2 (5.0) | | 50/0.03 (80) | | | |
| TCA/IIe | 0.5 | 2.0 (3.3) | 1.5 | 140/0.05 (85) | 22.84/22.73 | 0.67/0.48 | 50.27/50.31 |
| TFA/IIf | 2.0 | 4.6 (2.2) | 5.0 | 95/0.04 (97) | 34.07/33.98 | 1.34/1.43 | 27.11/26.87 |
| TCA/IIg | 0.4 | 1.2 (2.2) | 3.0 | 115/0.07 (92) | 27.35/27.56 | 1.19/1.16 | 41.12/40.68 |

**Table II. Anhydride Characterization**

| anhydride | mp, °C | $[\alpha]_D$[b] | $^1$H NMR[a] ($\delta$) $R_1$ | $R_2$ | $R_3$[d] | H | $^{13}$C NMR[a] ($\delta$) C=O | | | $CX_3$ | $CR_1R_2$ | $CR_3H$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| TFA(+)-tartrate/IId | 54–5 | +40.4 | | 6.20 | | 6.20 | 159.8 | 156.2 | | 114.0 | 73.2 | 73.2 |
| TCA(+)-tartrate/IIe | 176–7 | +64.6 | | 4.68 | | 4.68 | 160.8 | 160.1 | | 87.9 | 73.9 | 73.9 |
| TFA(−)-malate/IIf[c] | 77–8 | −50.5 | 5.83 | | 3.48 | 3.13 | 165.4 | 164.8 | 156.3 | 114.1 | 69.6 | 34.5 |
| TCA(−)-malate/IIg | 167–9 | −26.1 | 5.86 | | 3.57 | 3.23 | 166.6 | 166.2 | 160.7 | 88.3 | 71.0 | 33.8 |

[a] $CDCl_3$ solvent (except IIg $^{13}$C NMR in dioxane; IIe $^1$H NMR and $^{13}$C NMR in $C_6D_6$). [b] $CHCl_3$ solvent (except IIe which was done in benzene); *c* 1.00. [c] Lit.[5a] (±)-IIf mp 44–6 °C; $^1$H NMR (acetone-$d_6$) 6.29, 3.60. [d] Arbitrarily differentiated from H for malate $CH_2$.

Reaction of the anhydrides with stoichiometric amounts of 1-octanol in both THF and in $CD_3CN$ confirmed that deacylation of the TFA system was competitive with anhydride opening; excess alcohol is needed to guarantee complete anhydride opening. However, TCA anhydrides can be opened with <1.2 equiv of alcohol or amine and the monoesters/monoamides (IIIe/IIIg) are obtained. Removal of the TCA from the malate system is barely detected (<5%) under these conditions and <15% of one of the TCA groups is lost from the tartrates.

Monoesters and monoamides (IIIb/IIIc; R = *n*-octyl[6]) were obtained (70–90% yields) as follows. Reaction of 1-octanol with IId in dry THF at room temperature was complete in <4 h; IIf was allowed to react overnight. Comparable reactions of IIe and IIg were refluxed overnight. Corresponding reactions with *n*-octylamine were rapid even at reduced temperature. TFA removal occured during the initial reaction with alcohol or amine. TCA removal was done with water at room temperature. In all cases, condensation and trihaloacetyl removal were followed by sodium salt formation with dilute NaOH. Since the esters show significant hydrolysis at pH >10, excess base should be avoided.

## Experimental Section

$^1$H NMR and $^{13}$C NMR (Varian XL-200) are reported as ppm ($\delta$) downfield from $Me_4Si$. IR spectra were recorded on a PE 1420 spectrometer ($cm^{-1}$, Nujol). Rotations were measured on a PE 141 polarimeter. Mass spectra were obtained at the Midwest Center for Mass Spectrometry. A Thomas-Hoover melting point apparatus was used. Elemental analyses were done by Galbraith Laboratories.

*d*-Tartaric acid, *l*-malic acid, trifluoroacetic anhydride, trichloroacetic anhydride, 1-octanol, *n*-octylamine, $CD_3OD$, and $CD_3CN$ were all used as received from Aldrich. Succinic anhydride was obtained from MCB. THF and 1,4-dioxane were freshly distilled under nitrogen from sodium metal.

**Syntheses of Anhydrides IId–g.** Preparation of these materials involved mixing the indicated amounts (Table I) of trihaloacetic anhydride, dry dioxane, and diacid in a flask equipped with a magnetic stirring bar, a nitrogen inlet, and a reflux condenser. Heating this slurry at 75 °C for no more than 2 h gave a clear solution. Vacuum removal (w/o heating) of dioxane, unreacted trihaloacetic anhydride, and trihaloacetic acid gave the desired anhydride. This material, protected from extended exposure to atmospheric moisture, could be used for further synthetic manipulations. Analytically pure samples were obtained by sublimation. An alternative preparation of IId omitted the dioxane and involved heating the reagents (6 h, 75 °C) in a pressure bottle, followed by vacuum removal of TFA anhydride/acid.

**Additional Spectral Characterization.** (1) The proton-decoupled $^{13}$C NMR spectra of IId and IIf (reported in Table II) showed C–F coupling of 45–46 Hz as a quartet for the carbonyls of the trifluoroacetyl groups ($\delta$ 156.2 and 156.3) and a quartet with $J$ = 285 Hz for the $CF_3$ groups. (2) IR spectra of the anhydrides are listed below in order of decreasing band intensity ($cm^{-1}$). IId: 1810, 1180, 1230, 1135, 1120, 1070, 995, 1075, 1890; IIe: 1203, 1785, 1230, 1010, 848, 825, 932, 1895; IIf: 1142, 1230, 1184, 1775, 1792, 1085, 958, 1870, 722, 775; IIg: 1228, 1755, 1720, 1245, 840, 827, 1795, 688, 677, 1870.

**Anhydride Optical Purity.** To verify that neither anhydride formation nor sublimation had compromised the optical purity of the tartrate or malate units, each was dissolved in 1 mL of $H_2O$, and rotations were compared with the rotations of comparable quantities of authentic acids at 589 nm. IIe and IIg were dissolved in $H_2O$ and stirred overnight to insure complete hydrolysis of both the anhydride and the TCA groups. Rotations of hydrolyzed IId and IIf were obtained after 1 h in water. The specific rotations of these samples were compared with those of authentic diacids by measuring the rotations of the authentics in the presence of 1 or 2 equiv of the appropriate trihaloacetic acid. The specific rotations in water were as follows (hydrolyzed anhydride/authentic diacid): IId (*c* 1.00) +12.2°/+12.5°; IIe (c 1.00) +15.1°/+14.4°; IIf (*c* 2.68) −2.0°/−1.9°; IIg (c 2.68) −1.7°/−1.7°.

**NMR Assessment of Anhydride Ring-Opening and Deacylation Processes.** Direct monitoring of anhydride opening was done in pure $CD_3OD$ and in $CD_3CN$ containing 1 or 3 equiv of 1-octanol. The reactions were done in 5-mm NMR tubes and followed by $^1$H NMR.

Reaction of each of the anhydrides in $CD_3OD$ was done by weighing a solid sample of the anhydride directly into a 5-mm NMR tube and diluting the sample with 0.5 mL of $CD_3OD$ from a freshly opened ampule (concentration of anhydride, 0.08 M). Spectra were taken after about 90 s and again at 5, 20, 40, 90, and 180 min. Less reactive samples had spectra recorded after 19, 48, and 72 h as well. The reported results are based on integration of these spectra.

Reaction of the anhydrides in $CD_3CN$ was done with 3 equiv of 1-octanol and also with 1 equiv of alcohol for IIe and IIg. Anhydrides IIa and IId-g (0.06 mmol) were each dissolved in 300 $\mu$L of $CD_3CN$ at room temperature and 3 equiv of 1-octanol were added. These samples were heated to 70 °C and monitored by $^1$H NMR. IIa showed 42% reaction after 2 days at 70 °C. IId and IIf showed concomitant anhydride opening and deacylation. Complete disappearance took 20 min for IId and 2.5 h for IIf. The corresponding reaction with IIg showed clean anhydride opening after 16 h. IIe showed some TCA removal prior to complete anhydride opening, which took 30 min. This deacylation was slow and was still only partially complete after >2 days. Anhydride opening with only 15% monodeacylation was achieved for IIe by repeating the $CD_3CN$ reaction using only 1 equiv of 1-octanol. Formation of IIIe and IIIg (X = O) required 19 h and 2 days, respectively. There was no deacylation of the TCA malate system and only a small amount for the TCA tartrate. This allowed us

to record $^1H$ NMR spectra for IIIe and IIIg. IIIe (X = O): ($CD_3CN$) 5.98 (s, 2 H), 4.23 (t, 2 H, $J$ = 6.5 Hz), 1.68 (m, 2 H), 1.31 (m, 10 H), 0.92 (t, 3 H, $J$ = 6.2 Hz). IIIg (X = O): ($CD_3CN$) 5.61 (m, 1 H), 4.23 (t, 2 H, $J$ = 6.5 Hz), 3.05 (m, 2 H), 1.67 (t, 2 H, $J$ = 6.5 Hz), 1.34 (m, 10 H), 0.93 (t, 3 H, $J$ = 6.5 Hz).

**Preparations of *n*-Octyl Esters and Amides. Octyl Tartrate (IIIb, X = O).** 1-Octanol, anhydride IId or IIe, and freshly distilled dry THF were mixed at room temperature in a dry flask equipped with a magnetic stirring bar, condenser, and nitrogen inlet. A large-scale preparation with the TFA system used 44.9 g (285 mmol) of octanol, 40 mL of THF, and 30.8 g (95 mmol) of IId. A smaller scale reaction with the TCA system used octanol (31 mg, 0.24 mmol) and IIe (50 mg, 0.12 mmol) in 1 mL of THF. The TFA reaction was stirred at room temperature for 4 h and the TCA reaction was heated at reflux overnight. In both cases the THF was removed by vacuum. TCA hydrolysis was effected by overnight stirring in 2 mL water and both reactions were processed by adding 3 equiv of cold 3 N NaOH. The NaOH solution did not dissolve all of the white solid product. This slurry was washed 3 times with diethyl ether and lyophilized to dryness. The solid crude sodium salt was contaminated with sodium trihaloacetate which could be removed by washing with cold water followed by recrystallization from a 95/5 mixture of THF/water. The large-scale reaction gave a near quantitative yield of crude product and 88% of recrystallized material. The crude yield from the TCA preparation was 88%: $^1H$ NMR ($D_2O$) 4.49 (d, 1 H, $J$ = 2.1 Hz), 4.25 (d, 1 H, $J$ = 2.1 Hz), 4.09 (t, 2 H, $J$ = 6.5 Hz), 1.53 (t, 2 H, $J$ = 6.5 Hz), 1.17 (m, 10 H), 0.74 (t, 3 H, $J$ = 6.5 Hz); $^{13}C$ NMR ($D_2O$) 177.31, 174.37, 74.15, 73.23, 66.56, 32.20, 29.56 (2 C's), 28.82, 26.11, 22.93, 14.16; IR 3520–3050, 1737, 1620, 1068, 1142, 1210, 723. Conversion of the salt to the acid with dilute HCl was followed by continuous extraction into ether. After drying with $MgSO_4$, ether removal left the solid acid, mp 51–51.5 °C: $[\alpha]_D$ ($CHCl_3$, $c$ 2.00) +7.4°; MS (70 eV, M + H) calcd $C_{12}H_{23}O_6$ 263.1495, found 263.1488.

**Octyl Tartramide (IIIb, X = NH).** A two-necked flask was equipped with an addition funnel, a reflux condenser, a magnetic stirring bar, and a nitrogen inlet. It was charged with IId (27.8 g, 86 mmol) in 120 mL of freshly distilled THF and cooled to −23 °C. *n*-Octylamine (44 mL, 266 mmol) was added over 10 min. The system was kept cold and stirred under nitrogen for an hour and then allowed to warm to room temperature over an additional hour. NaOH (3 N, 300 mL) was added and the THF was removed by vacuum. The resulting material was dissolved in benzene and distilled to near dryness. The gelatinous residue was recrystallized from an 84/16 THF/water mixture to yield 9.5 g of white crystalline sodium salt: $^1H$ NMR ($D_2O$) 4.33 (d, 1 H, $J$ = 1.6 Hz), 4.20 (d, 1 H, $J$ = 1.6 Hz), 3.10 (m, 2 H), 1.40 (t, 2 H, $J$ = 6.5 Hz), 1.17 (m, 10 H), 0.74 (t, 3 H, $J$ = 6.5 Hz); $^{13}C$ NMR ($D_2O$) 178.56, 174.53, 74.03, 40.22, 32.48, 29.88 (2 C's), 29.80, 27.62, 23.21, 14.43; IR 3320, 3295, 3275, 3210, 3570–3060, 1620, 1657, 1543, 1144, 727. Concentration of the mother liquor and trituration of the residue with ether allowed recovery of another 7.5 g of product (combined yield 70%). This fraction was dissolved in 1 N HCl and the protonated form of IIIb was recovered by continuous extraction with ether, mp 150–151 °C; $[\alpha]_D$ (EtOAc, $c$ 0.5) +32.2°; $^1H$ NMR ($Me_2SO$-$d_6$) 7.63 (t, 1 H, $J$ = 6.6 Hz), 4.30 (d, 1 H, $J$ = 2.0 Hz), 4.15 (d, 1 H, $J$ = 2.0 Hz), 3.05 (m, 2 H), 1.42 (m, 2 H), 1.23 (m, 10 H), 0.84 (t, 3 H, $J$ = 6.7 Hz); MS (70 eV) calcd $C_{12}H_{23}NO_5$ 261.1576, found 261.1572. The comparable TCA reaction was done with IIe (50 mg, 0.12 mmol) and *n*-octylamine (31 mg, 0.24 mmol) in 1 mL of dry THF at 0 °C. After 1 h, the reaction was warmed to room temperature (over 3 h) and 3 equiv of 3 N NaOH were added. THF was removed under vacuum and the remaining aqueous layer was stirred overnight to guarantee complete TCA removal. Following washing with diethyl ether, the aqueous solution was lyophilized to a white solid residue (55 mg) of the sodium salt of the tartramide contaminated with NaTCA. The crude yield of tartramide (corrected for NaTCA) was 71%.

**Octyl Malate[6] (IIIc, X = O).** IIf (22.4 g, 106 mmol) and 1-octanol (27.6 g, 212 mmol) were added to 100 mL of dry THF in a flask equipped with a nitrogen inlet and a magnetic stirring bar. After being stirred overnight at room temperature, the THF was removed by vacuum and cold 3 N NaOH (212 mmol) was added. This solution was washed with diethyl ether and acidified. Continuous extraction with ether afforded the acid (13.01 g, 50% yield) as a slightly colored oil: $[\alpha]_D$ ($CHCl_3$, $c$ 5.0) −9.4°; $^1H$ NMR ($CDCl_3$) 5.9 (brs, 2 H), 4.49 (m, 1 H), 4.18 (t, 2 H, $J$ = 6.6 Hz), 2.86 (m, 2 H), 1.64 (m, 2 H), 1.26 (m, 10 H), 0.86 (t, 3 H, $J$ = 6.6 Hz); $^{13}C$ NMR ($CDCl_3$) 174.87, 173.19, 66.89, 65.99, 38.17, 31.48, 28.86 (2 C's), 28.12, 25.47, 22.33, 13.73; IR 3620–3050, 1800–1640, 1112, 1045, 960, 730; MS (70 eV, M + H) calcd $C_{12}H_{23}O_5$ 247.1546, found 247.1550. Alternatively, the sodium salt of IIIc was isolated by lyophilization after the ether wash: $^1H$ NMR ($D_2O$) 4.38 (m, 1 H), 4.03 (t, 2 H, $J$ = 6.5 Hz), 2.48 (m, 2 H), 1.51 (m, 2 H), 1.14 (m, 10 H), 0.71 (t, 3 H, $J$ = 6.7 Hz).

**Octyl Malamide (IIIc, X = NH).** IIf (22.4 g, 106 mmol) was dissolved in 100 mL of dry distilled THF in a flask equipped with a septum and a nitrogen inlet. The flask was cooled to 0 °C and *n*-octylamine (27.46 g, 212 mmol) was added over 5 min. The reaction was stirred for 1 h at 0 °C and then warmed to room temperature overnight. Solvent was removed by vacuum and cold 6 N NaOH (233 mmol) was added. The aqueous mixture was exhaustively washed with ether. The product was recrystallized from the solution that was obtained by adding 200 mL of THF to this aqueous slurry. This gave the pure sodium salt of IIIc (X = NH) as white flakes (73% yield): $^1H$ NMR ($D_2O$) 4.25 (m, 1 H), 3.06 (t, 2 H, $J$ = 6.8 Hz), 2.39 (m, 2 H), 1.36 (m, 2 H), 1.13 (m, 10 H), 0.70 (t, 3 H, $J$ = 6.7 Hz); $^{13}C$ NMR ($D_2O$) 179.59, 176.28, 70.57, 42.67, 40.10, 32.46, 29.88, 29.82 (2 C's), 27.56, 23.21, 14.47; IR 3430, 3330, 3300, 3230, 3240, 3207, 3180, 3150, 3550–3050, 728, 1715, 1590, 1633, 1090. A subsequent small-scale preparation using IIf gave a crude yield of 92%. The same material was made from IIg (100 mg, 0.38 mmol) and octylamine (54 mg, 0.42 mmol). The only difference in procedure was to stir the aqueous solution overnight before the ether wash to insure complete TCA removal; yield (corrected for NaTCA contamination) 81%. A sample of the protonated half acid was obtained by acidification with dilute HCl and continuous extraction into ether. After drying with $MgSO_4$, ether removal left the acid: mp 83–84 °C; $[\alpha]_D$ (EtOAc, $c$ 2.0) −16.5°; $^1H$ NMR ($Me_2SO$-$d_6$) 7.80 (t, 1 H, $J$ = 5.9 Hz), 4.18 (m, 1 H), 3.38 (brs, 2 H), 3.03 (m, 2 H), 2.45 (m, 2 H), 1.23 (m, 12 H), 0.84 (t, 3 H, $J$ = 6.7 Hz); MS (70 eV) calcd $C_{12}H_{23}NO_4$ 245.1627, found 245.1626.

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(6) Octyl malate is mentioned in a British patent that is reported in *Chem. Abstr.* **1964**, *60*, 15741b.

## Novel Polyquinanes from a Caged Hexacyclic [4.4.2]Propellane System

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Recently, we have reported a new Lewis acid catalyzed rearrangement of the pentacyclic dione **1** to the trishomocubane system **2**.[1] Earlier we had also described the facile 2 + 2 cycloreversion of **1** to triquinane bis-enone **3** under flash vacuum pyrolysis (FVP) conditions[1b] (Scheme I). These interesting and useful observations with **1** prompted us to investigate the carbonium ion mediated

(1) (a) Mehta, G.; Reddy, A. V.; Tacreiter, W.; Cameron, T. S. *J. Chem. Soc., Chem. Commun.* **1983**, 441. (b) Mehta, G.; Srikrishna, A.; Reddy, A. V.; Nair, M. S. *Tetrahedron* **1981**, *37*, 4543. (c) Mehta, G.; Reddy, A. V.; Srikrishna, A. *J. Chem. Soc., Perkin Trans. 1* **1986**, 291.

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