

Tartaric acid and its *O*-acyl derivatives. Part 8. Direct synthesis of novel *N*-substituted mono- and diacyltartrimides: unusual reaction course

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Abstract

Unexpected hydrolysis of diacyl tartaric acids during their reaction with primary amines yielded new monoacyl tartrimides.

Keywords: Acylation, amines, carboxylic acids, diols, imides

Introduction

Tartrimides belong to the group of easy available tartaric acid derivatives. Two chiral carbons with hydroxyl substituent and rigid heterocyclic structure cause that tartrimides are excellent starting materials in asymmetric synthesis. So, diacetyl-*N*-*p*-methoxybenzyltartrimide is an intermediate in the diastereoselective synthesis of 3,4-dihydroxyglutamic acids, which can play agonists role of mGluR1.¹ It is also a precursor in the synthesis of 3-hydroxyoxiracetam, the API of a useful nootropic drug in treatment of dementia.² Dicafeoyl- and digalloyl-tartrimide derivatives were examined as inhibitors of the integrase of the HIV virus.³ *N*-substituted diacyl tartrimides were used in synthesis of lentiginosine derivatives.⁴⁻⁷ Lentiginosine itself was used as α -glucosidase and amyloglucosidase inhibitor a potential anticancer and antiviral agent. In the total synthesis of UCS1025A, which is an active agent against cancer human cells by the inhibition of telomerase, the starting materials were diacyl tartrimides (Figure 1).⁸

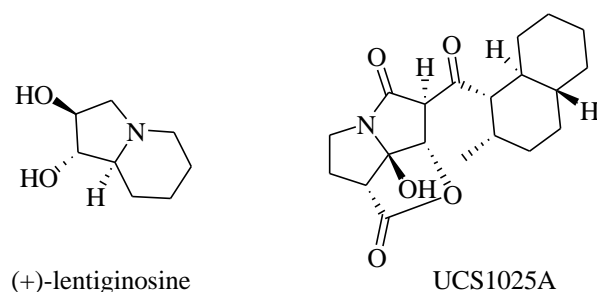


Figure 1. Lentiginosine and UCS1025A potential anticancer agent.

Diacyl tartrimites are easily converted to enantiomeric vicinal difluoro-,⁹ diamino-,¹⁰ or dihydroxypyrrolidines.⁹⁻¹¹ These valuable compounds were used as chiral ligands, for example, in the asymmetric epoxidation of allyl alcohols,^{9,12} or the enantioselective addition of diethylzinc to aromatic aldehydes.^{9,11}

We have found only two references regarding monoacyl tartrimites. A preparation of *O*-benzoyl-*N*-methyltartrimitide raises doubts.¹³ Patent information concerns a rather specific *N*-substituent, 5-sulfamoyl-1,3,4-thiadiazol-2-yl, of *O*-acetyl- and *O*-pivaloyltartrimites; no spectroscopic data are given.¹⁴

Results and Discussion

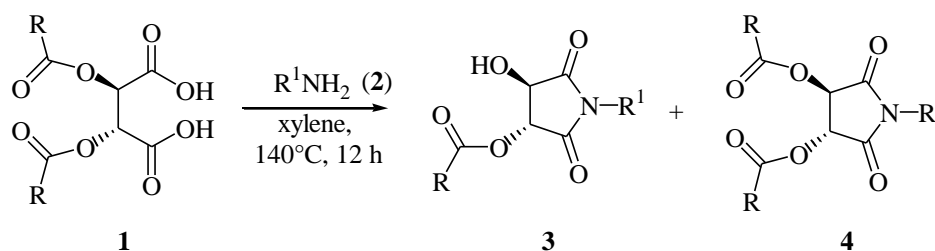
Motivated by the diverse and important applications of tartrimites, we sought an effective synthesis of this group of organic compounds. Our goal was to obtain various diacyltartrimites via the reaction of an appropriate acid¹⁵ or anhydride⁴ with a primary amine.

First, we examined the reaction of dibenzoyltartaric acid **1a**, the most commonly used derivative of tartaric acid, with benzylamine **2f**, refluxed in a few aromatic solvents with the azeotropic distillation of water. Unexpectedly, we isolated *O*-monobenzoyl-*N*-benzyltartrimitide **3f** (38% in toluene after 8 h, 42% in xylene after 12 h). Extending the reaction time beyond 12 h did not increase the yield. At lower temperatures the reaction did not proceed with the previously observed yield (Table 1). Similarly, in the reaction of dibenzoyltartaric anhydride and **2f** monobenzoyltartrimitide **3f** was isolated with 41% yield.

Under optimal conditions we performed the reaction between three different diacyl tartaric acids and eight primary amines (1:1 mol/mol, azeotropic distillation of water, 12 h). Depending on the kind of substrates used, mono- or diacyltartrimites or mixtures thereof were obtained (Table 2).

Table 1. Synthesis of *O*-monobenzoyl-*N*-benzyltartramide (**3f**)

Entry	Solvent	Temperature (°C)	Time (h)	Yield (%)
1	benzene	80	8	-
2	toluene	110		23
3	xylene	140	4	28
4			8	38
5			12	42
6			68	39

Table 2. Synthesis of *N*-substituted mono- **3** and di- **4** acyltartrimides (xylene, 140 °C, 12 h)

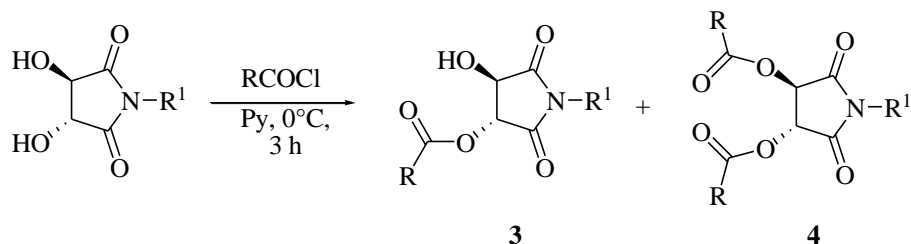
Entry	R (1)	R ¹ (2)	Yield ^a () ^b (%)	
			Mono (3)	Di (4)
a	Ph	<i>i</i> -Pr	43 (17)	39
b		<i>n</i> -Bu	2	83 (35)
c		Ph	46 (42)	26 (2)
d		4-Cl-C ₆ H ₄	1 (1)	78 (62)
e		4-Cl-3-F-C ₆ H ₃	44 (43)	13
f		PhCH ₂	46 (46)	30
g		4-Me-C ₆ H ₄	1	74 (53)
h		2-MeO-C ₆ H ₄	48 (45)	11 (2)
i	2-Cl-C ₆ H ₄ 4-MeO-C ₆ H ₄	Ph	12	80 (53)
j		PhCH ₂	61 (49)	24 (1)
k		<i>i</i> -Pr	7	94 (66)
l		<i>n</i> -Bu	6	56 (44)
m		Ph	4	79 (65)
n		4-Cl-3-F-C ₆ H ₃	-	65 (51)
o		PhCH ₂	7	70 (68)

^aNMR yield. ^bisolated yield.

For comparison, we examined the reaction of *N*-benzyl- and *N*-phenyltartramide with acyl chlorides (1:1 molar ratio) in pyridine. In spite of the low temperature, mixtures of mono- and diacylproducts were formed. The highest yield and selectivity was observed for monobenzoyl-*N*-

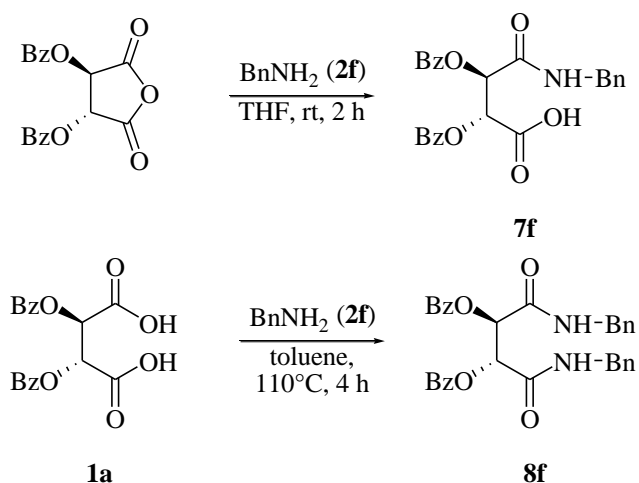
phenyltartramide (59%, according to HPLC, Table 3). However, due to the difficult resolution by crystallization and the necessity of column chromatography, this method is of little preparative importance as a source of monoacyl-*N*-substituted tartrimides.

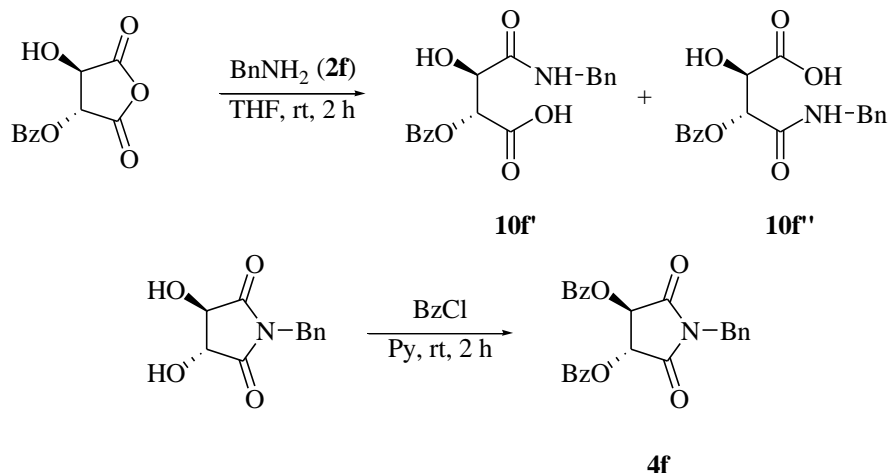
Table 3. Acylation of tartrimides with acyl chlorides



Entry	R ¹	R	Yield ^a () ^b (%)	
			Mono (3)	Di (4)
1	Ph	Ph	59	15
2		2-Cl-C ₆ H ₄	51	16
3		2-F-C ₆ H ₄	55	20
4	PhCH ₂	Ph	46	28
5		2-Cl-C ₆ H ₄	54	25
6		2-F-C ₆ H ₄	42	34

To check the reaction course of diacyltartaric acids with primary amines, we synthesized the compounds which may occur in the reaction system of dibenzoyltartaric acid **1a** and benzyl amine **2f**, i. e. dibenzoyl-*N*-benzyl-tartaric monoamide **7f**¹⁶ from dibenzoyltartaric anhydride,¹⁷ dibenzoyl-*N,N'*-dibenzyltartaric diamide **8f**¹⁶ from **1a**,¹⁷ mixture of isomeric monobenzoyl-*N*-benzyltartaric monoamides **10f'** and **10f''**¹⁷ from monobenzoyltartaric anhydride,¹⁸ and dibenzoyl-*N*-benzyltartramide **4f**¹⁹ from *N*-benzyltartramide.





Then, we examined the reaction of dibenzoyltartaric acid with benzyl amine (1:1 molar ratio) (HPLC) under azeotropic distillation of water. Immediately after adding benzylamine **2f** to the solution of dibenzoyl tartaric acid **1a** in xylene a suspension appeared, most probably composed of mono- **5** and/or diaminium salt **6** of dibenzoyltartaric acid, which dissolved after 2.5 h as the salts were converted to highly soluble in hot xylene amides and imides (Figure 2). Meanwhile, the evolution of water was observed. After 3 h **1a** was totally consumed. It was converted mostly into dibenzoyl-*N*-benzyltartaric monoamide **7f**, monobenzoyl-*N*-benzyltartramide **3f**, dibenzoyl-*N*-benzyltartramide **4f**, and benzoic acid **9** as a byproduct. During further heating, the monoamide **7f** vanished and there was a slow increase in the amount of tartramide **4f** present and a slightly faster increase in the amount of tartramide **3f**. Traces of isomeric monobenzoyl-*N*-benzyltartaric monoamide **10f'**, **10f''** and of tartaric diamide **8f** were also visible.

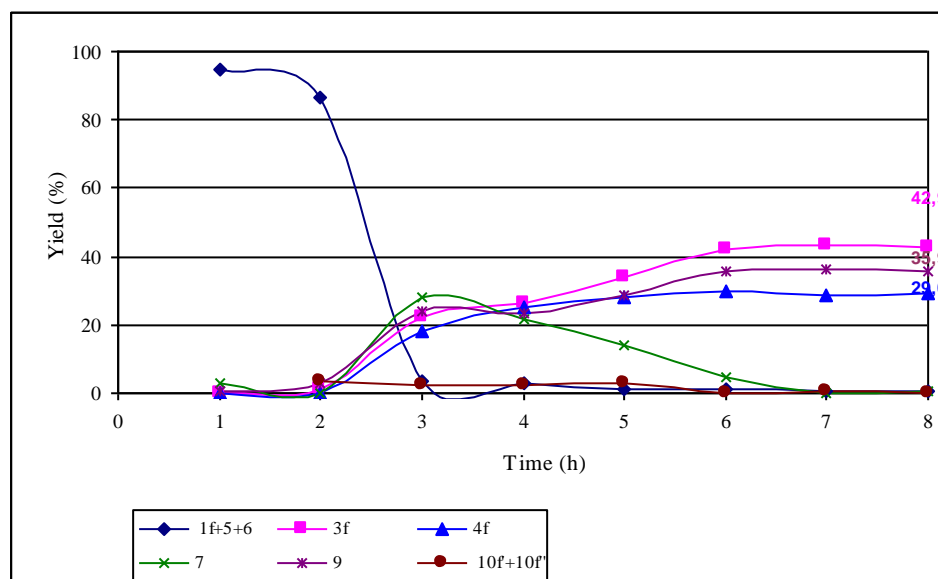
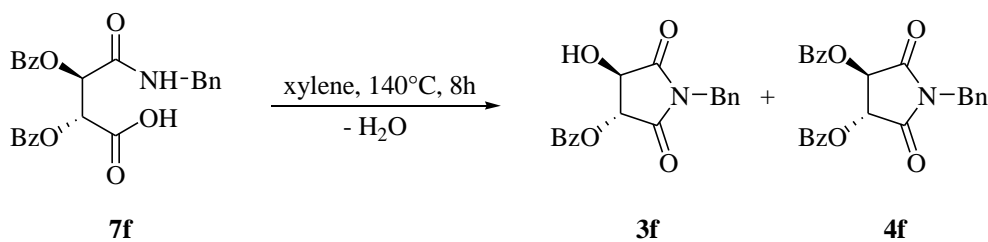
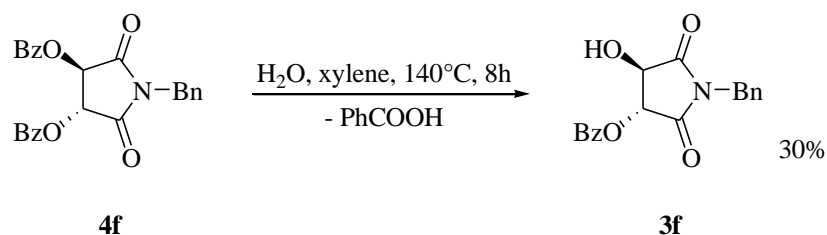


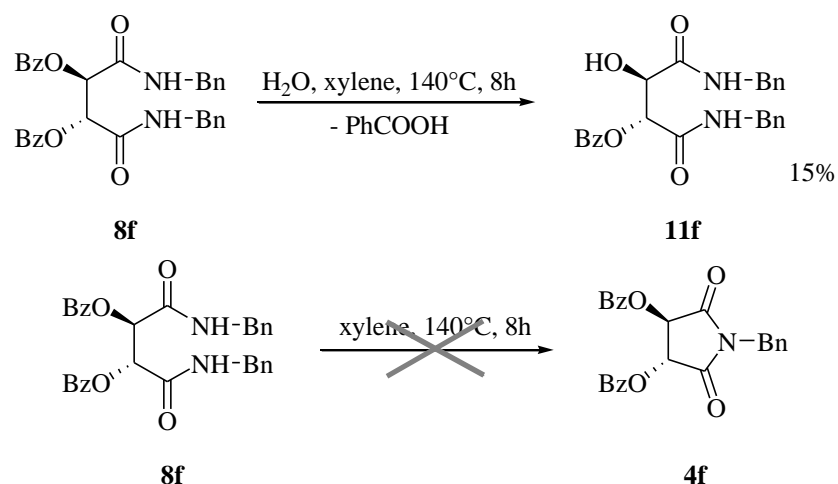
Figure 2. Products composition **1f**, **3f**, **4f**, **7f**, **9**, **10f'**, **10f''** in the reaction of dibenzoyltartaric acid with benzylamine (1:1 mol/mol, in xylene, 140 °C, HPLC yield).

To finally clarify the reaction course, some model reactions were performed under conditions of monobenzoyl-*N*-benzyltartramide **3f** synthesis (xylene, 140 °C, 8 h). The heating of **7f** resulted in a mixture of mono- **3f** and di- **4f** benzoyltartrimides. Thus, the reaction of either dibenzoyltartaric acid or anhydride with benzylamine resulted in the same mixture of products.

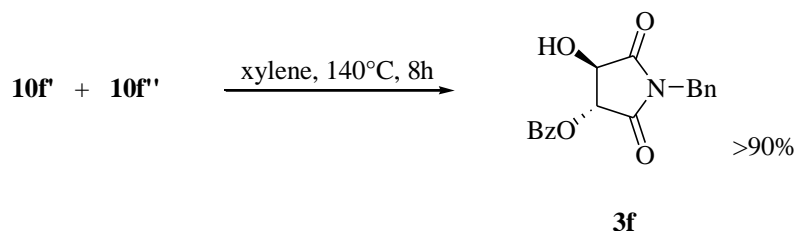


The hydrolysis of one benzoyl group of dibenzoyltartramide **4f** and of tartaric diamide (**8f**) proceeded slowly and with moderate or even small yield (30% and 15%, according to HPLC), respectively. No formation of **4f** in the latter case was observed.





In contrast, the cyclization of monobenzoyltartaric monoamides **10f'**, **10f''** to monobenzoyltartramide **3f** proceeded quickly and with very high yield (>90% HPLC). This might be the reason why we did not isolate **10f'**, **10f''** during heating of dibenzoyl-*N*-benzyltartaric monoamide **7f**, because the hydrolysis of **7f** (synthesis of **10f'**, **10f''**) is much slower than the following cyclization (synthesis of **3f**).

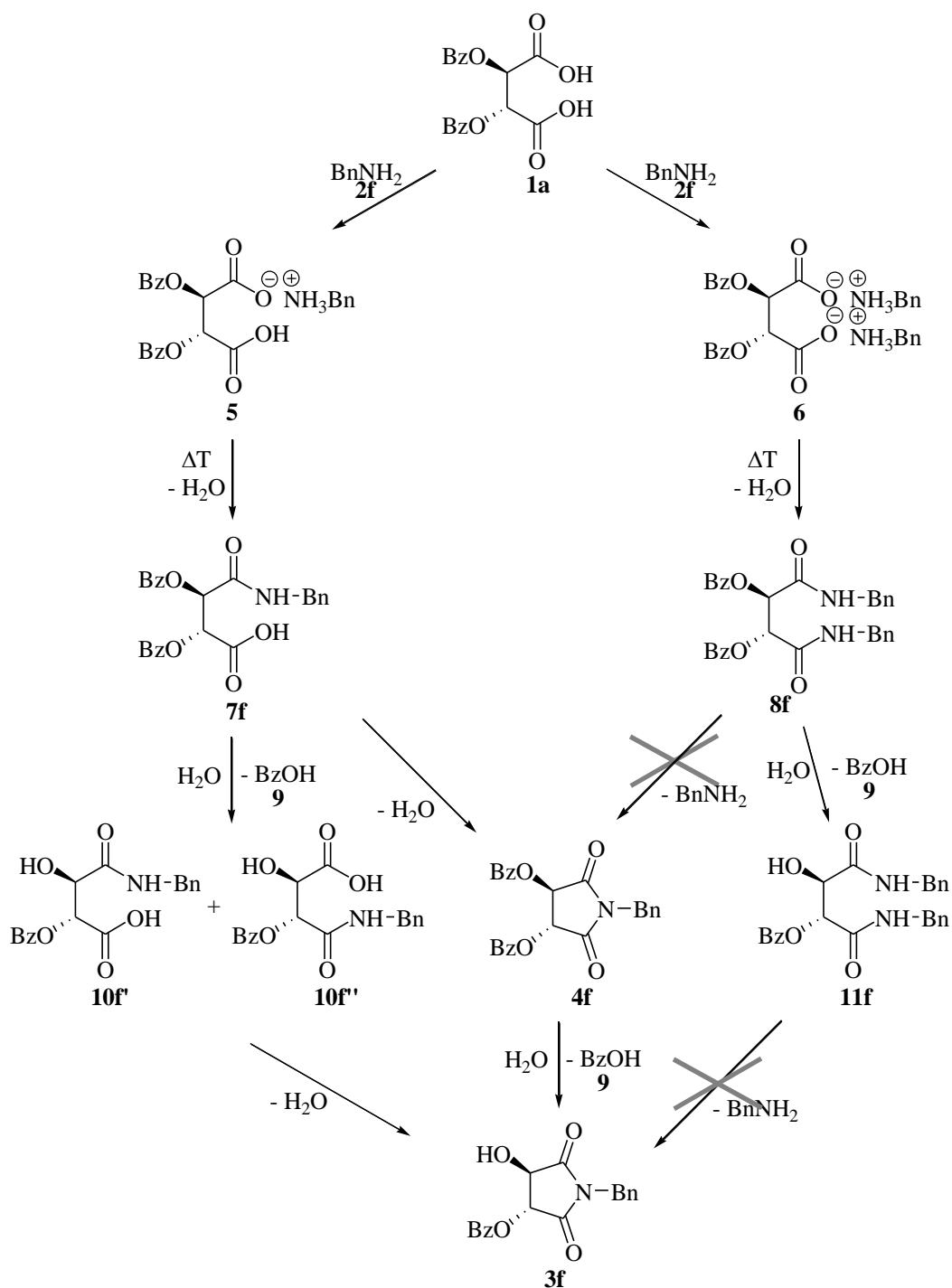


Additionally, benzoic acid was found in the reaction mixture and *N*-benzyl benzamide was not detected (GC-MS, NMR). Thus, the formation of monobenzoyltartramide proceeded via hydrolysis not aminolysis of one benzoyl group. Such a hydrolysis has not previously been reported, probably because diacyl imides were obtained from diacyl acids or anhydrides and amines under dehydration conditions caused by acetyl chloride,²⁰ acetyl anhydride,²¹ or thionyl chloride.¹³

We assume that in the formation of monobenzoyltartramide **3f** in the early stages of the reaction the hydrolysis of dibenzoyltartaric monoamide **7f** to monobenzoyltartaric monoamides **10f'**, **10f''** is faster than the hydrolysis of dibenzoyltartramide **4f**.

We propose the following formation course of *N*-substituted mono- and diacyltartrimides in the reaction of diacyltartaric acids with primary amines (1:1) (Scheme 1). In the first step mono- **5** and/or di- **6** aminium salts of diacyltartaric acid are formed, which are dehydrated to diacyltartaric monoamide **7** and/or diacyltartaric diamide **8** appropriately. Diacyltartaric monoamide **7** may hydrolyse with water to isomeric monoacyltartaric monoamides **10f'**, **10f''** or competitively cyclize to the diacyltartramide **4**. Both the following cyclization of **10f'** and **10f''** as

well as the hydrolysis of **4** result in the formation of monoacyltartramide **3**. Diacyltartaric diamide **8** may slowly hydrolyse to monoacyltartaric diamide **11**.



Scheme 1. The routes of the reaction of diacyltartaric acid **1** with primary amine **2**

Conclusions

In conclusion, the results show that the reaction of diacyltartaric acids **1** with primary amines to give the corresponding *N*-substituted monoacyltartrimides **3** and diacyltartrimides **4** is of practical importance. It was found that the diacylimide **4** occurs together with the monoacylimide **3**, which shows that the reaction proceeds via two routes (Scheme 1). After its formation, the monoamide **7** undergoes two competitive reactions, a hydrolysis of one acyl group with the formation of previously unknown isomeric monoacyltartaric monoamides **10'**, **10''** and a cyclization to the imide **4**. Both the following cyclization of **10'** and **10''** and the hydrolysis of **4** result in the formation of monoacyltartrimide **3**.

Depending on the kind of substrates used and the solubility of the products, *N*-substituted mono-**3** or diacyltartrimides **4** can be efficiently obtained and isolated. Thus, we supplied the chiral pool with six mono- and 10 diacyltartrimides, novel buildings blocks for organic chemistry. Both the presence of carboxylic acid **9** and the absence of carboxylic acid amide confirmed our earlier assumptions that the monoacyl derivatives are formed as a sequence of the hydrolysis not aminolysis of one of two acyl groups of the tartaric skeleton.

Experimental Section

General. Dibenzoyltartaric acid and dibenzoyltartaric anhydride were obtained from our pilot plant. All other reagents were obtained from commercial sources and were used without further purification. Solvents were dried over 4Å molecular sieves. HPLC was carried out with an HP 1100 (Agilent Technologies) on an RP column, using a UV-Vis detector (at 230 nm). NMR spectra were recorded with a Varian Gemini 2000 spectrometer (200 MHz for ¹H NMR, 50 MHz for ¹³C NMR) or a Varian Mercury 400 (400 MHz for ¹H NMR, 100 MHz for ¹³C NMR) and measured in CDCl₃ with TMS as the internal standard. IR spectra were recorded on a Specord M80 spectrometers using KBr pellets. The optical rotations were measured with a PolAAr 32 (Optical Activity Ltd). All the elemental analysis were measured with a Perkin Elmer 2400 Series II CHNS/O Elemental Analyzer.

General procedure for the synthesis of *N*-substituted mono- and diacyltartrimides

The appropriate diacyl acid (15 mmol) was dissolved in 50 ml xylene and placed in a three-necked flask equipped with a Dean-Stark trap and refluxed until the azeotropic distillation of crystalline water was completed. The appropriate amine (15 mmol) was added and reaction mixture refluxed for 12 h under azeotropic distillation of water. After cooling to r. t., the reaction mixture was filtered under reduced pressure. Crude products were crystallized from methanol and dried (60°C, 6 h).

(3*R*,4*R*)-*N*-Isopropyl-4-benzoyloxy-3-hydroxypyrrolidine-2,5-dione (3a). Yield 17%, white solid, mp 117–119 °C. [α]_D²² +43.7 (*c* 0.1, CHCl₃). IR (ν_{max} , cm⁻¹): 3476, 1794, 1704. ¹H NMR

(200 MHz, CDCl₃) δ 8.08 (m, 2H), 7.61 (m, 1H), 7.46 (m, 2H), 5.48 (d, $J = 5.3$ Hz, 1H), 4.82 (d, $J = 5.4$ Hz, 1H), 4.43 (m, 1H), 1.41 (dd, $J = 3.1$ Hz, $J = 6.9$ Hz, 6H). ¹³C NMR (50 MHz, CDCl₃) δ 170.4, 169.7, 165.5, 134.4, 130.4, 128.8, 128.5, 128.2, 76.8, 62.5, 37.8, 21.3, 21.2. Anal. Calcd. for C₁₄H₁₅NO₅: C, 60.64, H 5.45, N 5.05; Found: C 60.72, H 5.39, N 4.99.

(3R,4R)-N-Phenyl-4-benzoyloxy-3-hydroxypyrrolidine-2,5-dione (3c). Yield 42%, pale yellow solid, mp 158–160 °C. $[\alpha]_D^{22} +12.0$ (c 0.1, CHCl₃). IR (ν_{\max} , cm⁻¹): 3268, 1772, 1704. ¹H NMR (200 MHz, CDCl₃) δ 8.07 (m, 2H), 7.67–7.26 (m, 8H), 5.67 (d, 1H, $J = 4.8$ Hz), 4.52 (d, 1H, $J = 4.8$ Hz). ¹³C NMR (50 MHz, CDCl₃) δ 167.7, 167.5, 165.5, 140.5, 134.3, 130.4, 128.9, 128.8, 128.6, 124.7, 120.4, 73.4, 60.2. Anal. Calcd. for C₁₇H₁₃NO₅: C 65.59, H 4.21, N 4.50; Found: C 65.64, H 4.20, N 4.53.

(3R,4R)-N-(3-Chloro-4-fluorophenyl)-4-benzoyloxy-3-hydroxypyrrolidine-2,5-dione (3e). Yield 42%, white solid, mp 146–147 °C. $[\alpha]_D^{22} +51.1$ (c 0.1, CHCl₃). IR (ν_{\max} , cm⁻¹): 3276, 1784, 1704. ¹H NMR (200 MHz, CDCl₃) δ 8.06–7.18 (m, 8H), 5.55 (d, 1H, $J = 4.8$ Hz), 4.61 (d, 1H, $J = 4.8$ Hz). ¹³C NMR (50 MHz, CDCl₃) δ 167.7, 167.4, 165.4, 156.6, 138.1, 134.4, 130.3, 128.8, 128.6, 122.8, 121.4, 120.9, 117.1, 73.6, 60.0. Anal. Calcd. for C₁₇H₁₁ClFNO₅: C 56.14, H 3.05, N 3.85; Found: C 56.18, H 3.09, N 3.88.

(3R,4R)-N-Benzyl-4-benzoyloxy-3-hydroxypyrrolidine-2,5-dione (3f). Yield 46%, white solid, mp 168–169 °C. $[\alpha]_D^{22} +67.3$ (c 0.1, CHCl₃). IR (ν_{\max} , cm⁻¹): 3284, 1780, 1716. ¹H NMR (200 MHz, CDCl₃) δ 8.06 (m, 2H), 7.61–7.28 (m, 8H), 5.51 (d, 1H, $J = 5.0$ Hz), 4.84 (d, 1H, $J = 5.0$ Hz), 4.74 (s, 2H). ¹³C NMR (50 MHz, CDCl₃) δ 169.1, 168.3, 165.5, 134.7, 134.2, 130.5, 128.9, 128.8, 128.6, 128.4, 128.3, 73.1, 59.8, 44.0. Anal. Calcd. for C₁₈H₁₅NO₅: C 66.46, H 4.65, N 4.31; Found: C 66.41, H 4.62, N 4.34.

(3R,4R)-N-(2-Methoxyphenyl)-4-benzoyloxy-3-hydroxypyrrolidine-2,5-dione (3h). Yield 45%, white solid, mp 171–174 °C. $[\alpha]_D^{22} +22.5$ (c 0.1, CHCl₃). IR (ν_{\max} , cm⁻¹): 3468, 1808, 1704. ¹H NMR (200 MHz, CDCl₃) δ 8.01 (m, 2H), 7.55–7.26 (m, 4H), 7.12–6.87 (m, 3H), 5.71 (d, 1H, $J = 4.5$ Hz), 4.58 (d, 1H, $J = 4.6$ Hz), 3.82 (s, 3H). ¹³C NMR (50 MHz, CDCl₃) δ 167.6, 167.2, 165.5, 151.7, 134.5, 130.3, 128.9, 128.6, 125.9, 125.4, 121.2, 115.1, 73.7, 59.9, 56.0. Anal. Calcd. for C₁₈H₁₅NO₆: C 63.34, H 4.43, N 4.10; Found: C 63.41, H 4.42, N 4.08.

(3R,4R)-N-Benzyl-4-(2-chlorobenzoyloxy)-3-hydroxypyrrolidine-2,5-dione (3j). Yield 49%, white solid, mp 152–156 °C. $[\alpha]_D^{22} +113.7$ (c 0.1, CHCl₃) IR (ν_{\max} , cm⁻¹): 3482, 1812, 1708. ¹H NMR (200 MHz, CDCl₃) δ 7.88 (m, 1H), 7.54–7.19 (m, 8H), 5.73 (d, $J = 4.6$ Hz, 1H), 4.81 (d, $J = 4.6$ Hz, 1H), 4.64 (s, 2H). ¹³C NMR (50 MHz, CDCl₃) δ 168.7, 167.5, 165.7, 134.5, 134.0, 132.8, 131.8, 131.1, 130.7, 128.5, 128.3, 128.1, 127.4, 73.3, 59.9, 43.7. Anal. Calcd. for C₁₇H₁₂ClNO₅: C 59.06, H 3.50, N 4.05; Found: C 59.10, H 3.51, N 4.03.

(3R,4R)-N-(*n*-Butyl)-3,4-dibenzoyloxy-3-hydroxypyrrolidine-2,5-dione (4b). Yield 35%, white solid, mp 96–99 °C. $[\alpha]_D^{22} +62.1$ (c 0.1, CHCl₃). IR (ν_{\max} , cm⁻¹): 1788, 1728, 1704. ¹H NMR (200 MHz, CDCl₃) δ 8.07 (m, 4H), 7.59 (m, 2H), 7.39 (m, 4H), 5.62 (s, 2H), 3.97 (m, 2H), 1.61–1.44 (m, 4H), 1.36 (dt, $J = 2.9$ Hz, $J = 7.2$ Hz, 3H). ¹³C NMR (50 MHz, CDCl₃) δ 170.4, 165.5, 132.8, 130.1, 128.8, 128.7, 128.2, 74.1, 38.6, 27.1, 23.7, 18.5. Anal. Calcd. for C₂₂H₂₁NO₆: C 66.83, H 5.35, N 3.54; Found: C 66.77, H 5.39, N 3.59.

(3R,4R)-N-(4-Chlorophenyl)-3,4-dibenzoyloxypyrrolidine-2,5-dione (4d). Yield 62%, white solid, mp 124–127 °C. $[\alpha]_{\text{D}}^{22} +34.2$ (*c* 0.1, CHCl₃). IR (ν_{max} , cm⁻¹): 1796, 1700. ¹H NMR (200 MHz, CDCl₃) δ 8.02 (m, 4H), 7.55–7.13 (m, 10H), 5.79 (s, 2H). ¹³C NMR (50 MHz, CDCl₃) δ 173.4, 165.8, 133.1, 132.6, 131.5, 130.4, 129.2, 128.7, 128.5, 128.2, 77.4. Anal. Calcd. for C₂₄H₁₆ClNO₆: C 64.08, H 3.59, N 3.11; Found: C 64.02, H 3.55, N 3.14.

(3R,4R)-N-Benzyl-3,4-dibenzoyloxypyrrolidine-2,5-dione (4f). Yield 62%, white solid, mp 113–118 °C. $[\alpha]_{\text{D}}^{22} +141.5$ (*c* 0.1, Me₂CO). IR (ν_{max} , cm⁻¹): 3008, 1796, 1716. ¹H NMR (400 MHz, CDCl₃) δ 8.09–8.06 (m, 4H), 7.64–7.60 (m, 2H), 7.49–7.45 (m, 6H), 7.38–7.32 (m, 3H), 5.93 (s, 2H), 4.83 (d, *J* = 11.6 Hz, 2H). ¹³C NMR: (100 MHz, CDCl₃) δ 169.1, 165.5, 134.6, 134.0, 130.2, 128.9, 128.8, 128.6, 128.3, 128.1, 73.4, 43.2. Anal. Calcd. for C₂₅H₁₉NO₆: C 69.92, H 4.46, N 3.26; Found: C 69.86, H 4.49, N 3.28.

(3R,4R)-N-(4-Methylphenyl)-3,4-dibenzoyloxypyrrolidine-2,5-dione (4g). Yield 53%, white solid, mp 141–142 °C. $[\alpha]_{\text{D}}^{22} +48.3$ (*c* 0.1, CHCl₃). IR (ν_{max} , cm⁻¹): 1736, 1704. ¹H NMR (400 MHz, CDCl₃) δ 8.12 (m, 4H), 7.52–7.37 (m, 10H), 5.91 (s, 2H), 2.35 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 173.1, 166.0, 135.7, 132.6, 131.5, 130.4, 129.7, 128.9, 128.6, 128.1, 77.1, 27.3. Anal. Calcd. for C₂₅H₁₉NO₆: C 69.92, H 4.46, N 3.26; Found: C 70.01, H 4.49, N 3.24.

(3R,4R)-N-Phenyl-3,4-bis(2-chlorobenzoyloxy)pyrrolidine-2,5-dione (4i). Yield 53%, pale yellow solid, mp 127–129 °C. $[\alpha]_{\text{D}}^{22} +43.7$ (*c* 0.1, CHCl₃). IR (ν_{max} , cm⁻¹): 1812, 1708. ¹H NMR (400 MHz, CDCl₃) δ 7.90 (m, 2H), 7.58–7.21 (m, 11H), 5.71 (s, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 175.2, 166.5, 134.7, 133.1, 132.4, 130.9, 130.4, 129.4, 128.9, 128.7, 128.6, 126.7, 75.7. Anal. Calcd. for C₂₄H₁₅Cl₂NO₆: C 59.52, H 3.12, N 2.89; Found: C 59.46, H 3.14, N 2.91;

(3R,4R)-N-Isopropyl-3,4-bis(4-methoxybenzoyloxy)pyrrolidine-2,5-dione (4k). Yield 66%, white solid, mp 89–91 °C. $[\alpha]_{\text{D}}^{22} +75.6$ (*c* 0.1, CHCl₃). IR (ν_{max} , cm⁻¹): 1796, 1696. ¹H NMR (400 MHz, CDCl₃) δ 8.00 (m, 4H), 6.93 (m, 4H), 5.94 (s, 2H), 4.46 (m, 1H), 3.87 (s, 6H), 1.39 (d, *J* = 6.4 Hz, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 170.4, 165.8, 164.2, 132.5, 120.3, 113.8, 73.9, 55.8, 48.6, 20.5. Anal. Calcd. for C₂₃H₂₃NO₈: C 62.58, H 5.25, N 3.17; Found: C 62.51, H 5.22, N 3.16.

(3R,4R)-N-(*n*-Butyl)-3,4-bis(4-methoxybenzoyloxy)pyrrolidine-2,5-dione (4l). Yield 44%, white solid, mp 74–75 °C. $[\alpha]_{\text{D}}^{22} +68.1$ (*c* 0.1, CHCl₃). IR (ν_{max} , cm⁻¹): 1792, 1696. ¹H NMR (400 MHz, CDCl₃) δ 8.04 (m, 4H), 6.94 (m, 4H), 5.90 (s, 2H), 3.99 (m, 2H), 3.82 (s, 6H), 1.55–1.41 (m, 4H), 1.33 (dt, *J* = 3.2 Hz, *J* = 7.0 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 170.5, 165.8, 164.2, 132.5, 120.3, 113.8, 73.9, 55.7, 37.7, 21.2. Anal. Calcd. for C₂₄H₂₅NO₈: C 63.29, H 5.53, N 3.08; Found: C 63.34, H 5.52, N 3.10.

(3R,4R)-N-Phenyl-3,4-bis(4-methoxybenzoyloxy)pyrrolidine-2,5-dione (4m). Yield 65%, white solid, mp 132–135 °C. $[\alpha]_{\text{D}}^{22} +129.4$ (*c* 0.1, CHCl₃). IR (ν_{max} , cm⁻¹): 1782, 1696. ¹H NMR (400 MHz, CDCl₃) δ 8.05 (m, 4H), 7.69–7.21 (m, 5H), 6.96 (m, 4H), 5.79 (s, 2H), 3.87 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 170.5, 165.8, 164.2, 132.5, 131.2, 128.8, 128.3, 128.1, 120.3, 113.8, 73.9, 55.7. Anal. Calcd. for C₂₆H₂₁NO₈: C 65.68, H 4.45, N 2.95; Found: C 65.77, H 4.45, N 2.99.

(3R,4R)-N-(3-Chloro-4-fluorophenyl)-3,4-bis(4-methoxybenzoyloxy)pyrrolidine-2,5-dione (4n). Yield 51%, white solid, mp 107–108 °C. $[\alpha]_{\text{D}}^{22} +167.0$ (*c* 0.1, CHCl₃). IR (ν_{max} , cm⁻¹): 1804, 1696. ¹H NMR (400 MHz, CDCl₃) δ 8.03 (m, 4H), 7.51–7.22 (m, 3H), 6.98 (m, 4H), 5.61 (s, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 170.5, 165.8, 164.2, 155.1, 132.4, 130.9, 128.4, 124.0, 120.7, 120.3, 114.2, 113.8, 73.1, 55.7. Anal. Calcd. for C₂₆H₁₉ClFNO₈: C 59.16, H 3.63, N 2.65; Found: C 59.21, H 3.65, N 2.67.

(3R,4R)-N-Benzyl-3,4-bis(4-methoxybenzoyloxy)pyrrolidine-2,5-dione (4o). Yield 68%, white solid, mp 112–113 °C. $[\alpha]_{\text{D}}^{22} +101.7$ (*c* 0.1, CHCl₃). IR (ν_{max} , cm⁻¹): 1788, 1692. ¹H NMR (400 MHz, CDCl₃) δ 8.02 (m, 4H), 7.66–7.27 (m, 5H), 6.99–6.91 (m, 4H), 5.91 (s, 2H), 4.58 (dd, 2H), 3.88 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 169.2, 165.5, 164.2, 134.5, 132.4, 128.5, 128.3, 128.1, 120.3, 113.8, 73.5, 55.7, 43.2. Anal. Calcd. for C₂₇H₂₃NO₈: C 66.25, H 4.74, N 2.86; Found: C 66.19, H 4.75, N 2.83.

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