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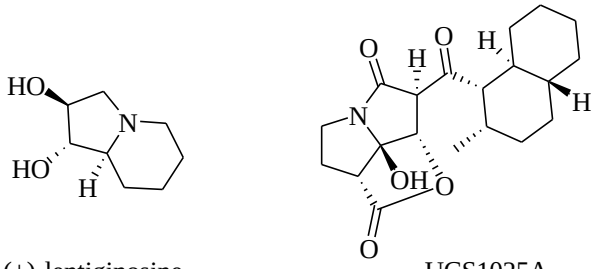
Abstract
Unexpected hydrolysis of diacyl tartaric acids during their reaction with primary amines yielded new monoacyl tartrimides.

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] Dicaffeoyl- 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]



(+)-lentiginosine UCS1025A

Figure 1. Lentiginosine and UCS1025A potential anticancer agent.

Diacyl tartrimides 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 tartrimides. A preparation of *O*-benzoyl-*N*-methyltartrimide raises doubts.[13] Patent information concerns a rather specific *N*-substituent, 5-sulfamoyl-1,3,4-thiadiazol-2-yl, of *O*-acetyl- and *O*-pivaloyltartrimides; no spectroscopic data are given.[14]

Results and Discussion

Motivated by the diverse and important applications of tartrimides, we sought an effective synthesis of this group of organic compounds. Our goal was to obtain various diacyltartrimides via the reaction of an appropriate acid[15] or anhydride[4] with a primary amine.

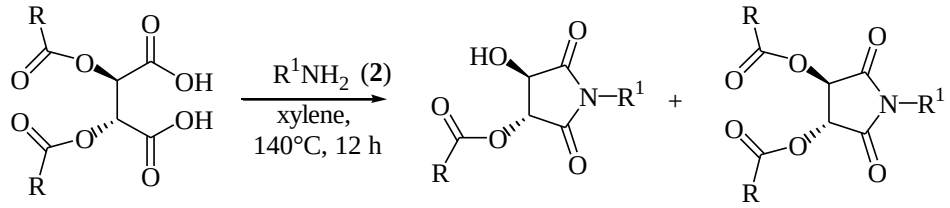
First, we examined the reaction of dibenzoyltartaric acid **1a**, the most commonly used derivative of tartaric acid, with benzylamine **2f**, refluxed in a few aromatic solvents with the azeotropic distillation of water. Unexpectedly, we isolated *O*-monobenzoyl-*N*-benzyltartrimide **3f** (38% in toluene 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** monobenzoyltartrimide **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 diacyltartrimides or mixtures thereof were obtained (Table 2).

Table 1. Synthesis of *O*-monobenzoyl-*N*-benzyltartrimide (**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)



1 **3** **4**

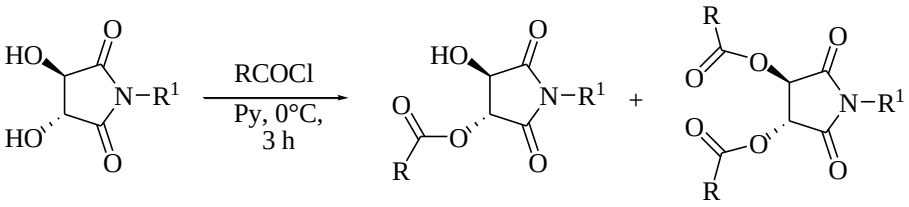
Entry	R (**1**)	R^1 (**2**)	Yield[a] ( )[b] (%) Mono (**3**)	Di (**4**)
a	Ph	*i*-Pr	43 (17)	39
b		*n*-Bu	2	83 (35)
c		Ph	46 (42)	26 (2)
d		4-Cl-C_6H_4	1 (1)	78 (62)
e		4-Cl-3-F-C_6H_3	44 (43)	13
f		$PhCH_2$	46 (46)	30
g		4-Me-C_6H_4	1	74 (53)
h		2-MeO-C_6H_4	48 (45)	11 (2)
i	2-Cl-C_6H_4 4-MeO-C_6H_4	Ph	12	80 (53)
j		$PhCH_2$	61 (49)	24 (1)
k		*i*-Pr	7	94 (66)
l		*n*-Bu	6	56 (44)
m		Ph	4	79 (65)
n		4-Cl-3-F-C_6H_3	-	65 (51)
o		$PhCH_2$	7	70 (68)

[a]NMR yield. [b]isolated yield.

For comparison, we examined the reaction of *N*-benzyl- and *N*-phenyltartrimide 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*-

phenyltartrimide (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.

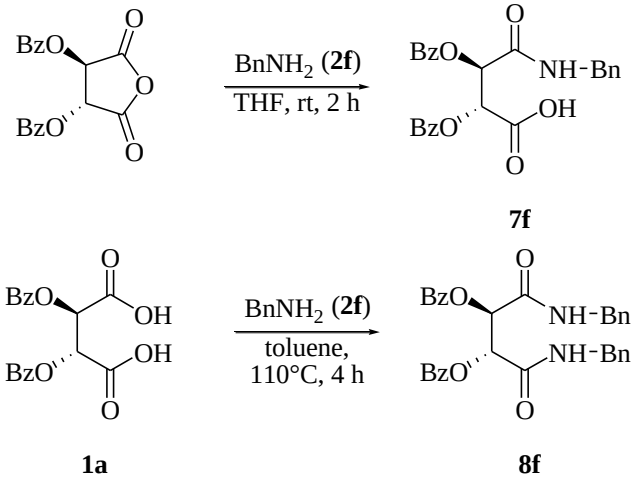
Table 3. Acylation of tartrimides with acyl chlorides



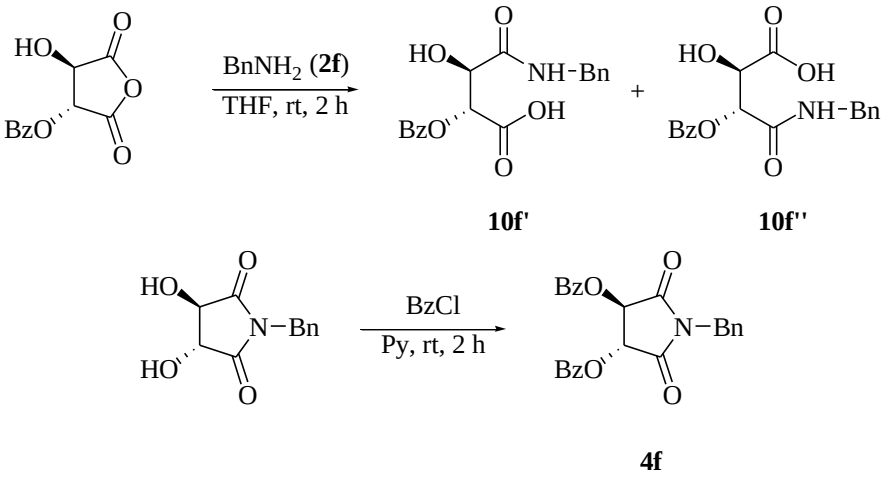
3 **4**

Entry	R^1	R	Yield[a] ( )[b] (%)	
			Mono (**3**)	Di (**4**)
1	Ph	Ph	59	15
2		2-Cl-C_6H_4	51	16
3		2-F-C_6H_4	55	20
4	$PhCH_2$	Ph	46	28
5		2-Cl-C_6H_4	54	25
6		2-F-C_6H_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*-benzyltartrimide **4f**[19] from *N*-benzyltartrimide.



1a **8f**



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*-benzyltartrimide **3f**, dibenzoyl-*N*-benzyltartrimide **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 tartrimide **4f** present and a slightly faster increase in the amount of tartrimide **3f**. Traces of isomeric monobenzoyl-*N*-benzyltartaric monoamide **10f′**, **10f″** and of tartaric diamide **8f** were also visible.

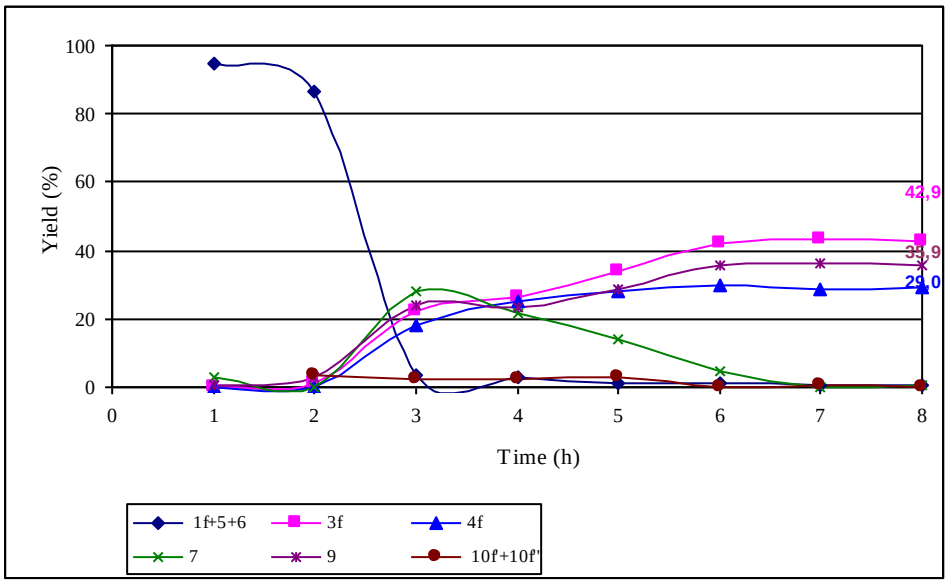
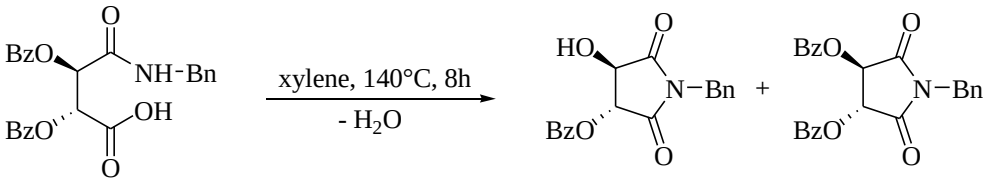


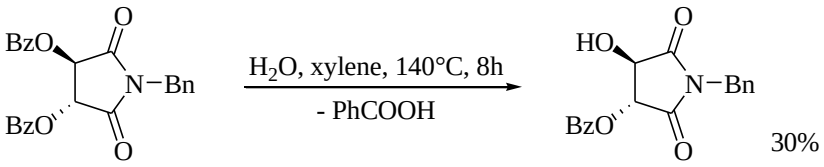
Figure 2. Products composition **1f**, **3f**, **4f**, **7f**, **9**, **10f′**, **10f″** in the reaction of dibenzoyltartaric acid with benzylamine (1:1 mol/mol, in xylene, 140 °C, HPLC yield).

To finally clarify the reaction course, some model reactions were performed under conditions of monobenzoyl-*N*-benzyltartrimide **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.

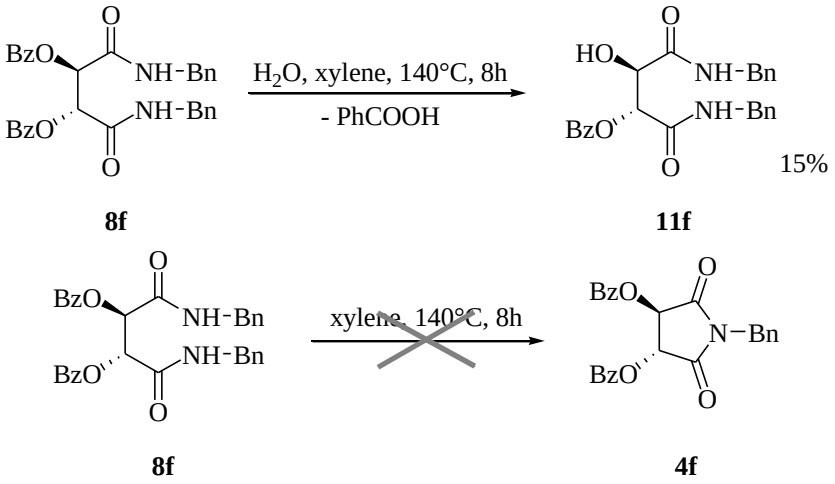


7f **3f** **4f**

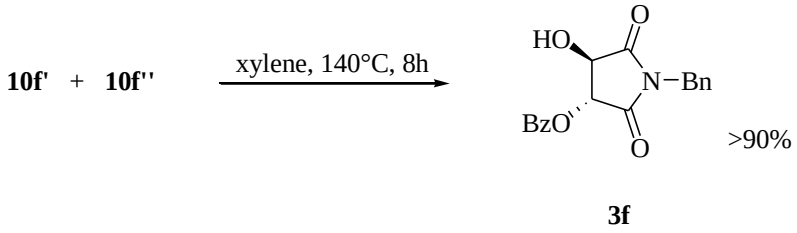
The hydrolysis of one benzoyl group of dibenzoyltartrimide **4f** and of tartaric diamide (**8f**) proceeded slowly and with moderate or even small yield (30% and 15%, according to HPLC), respectively. No formation of **4f** in the latter case was observed.



4f **3f**



In contrast, the cyclization of monobenzoyltartaric monoamides **10f′**, **10f″** to monobenzoyltartrimide **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**).

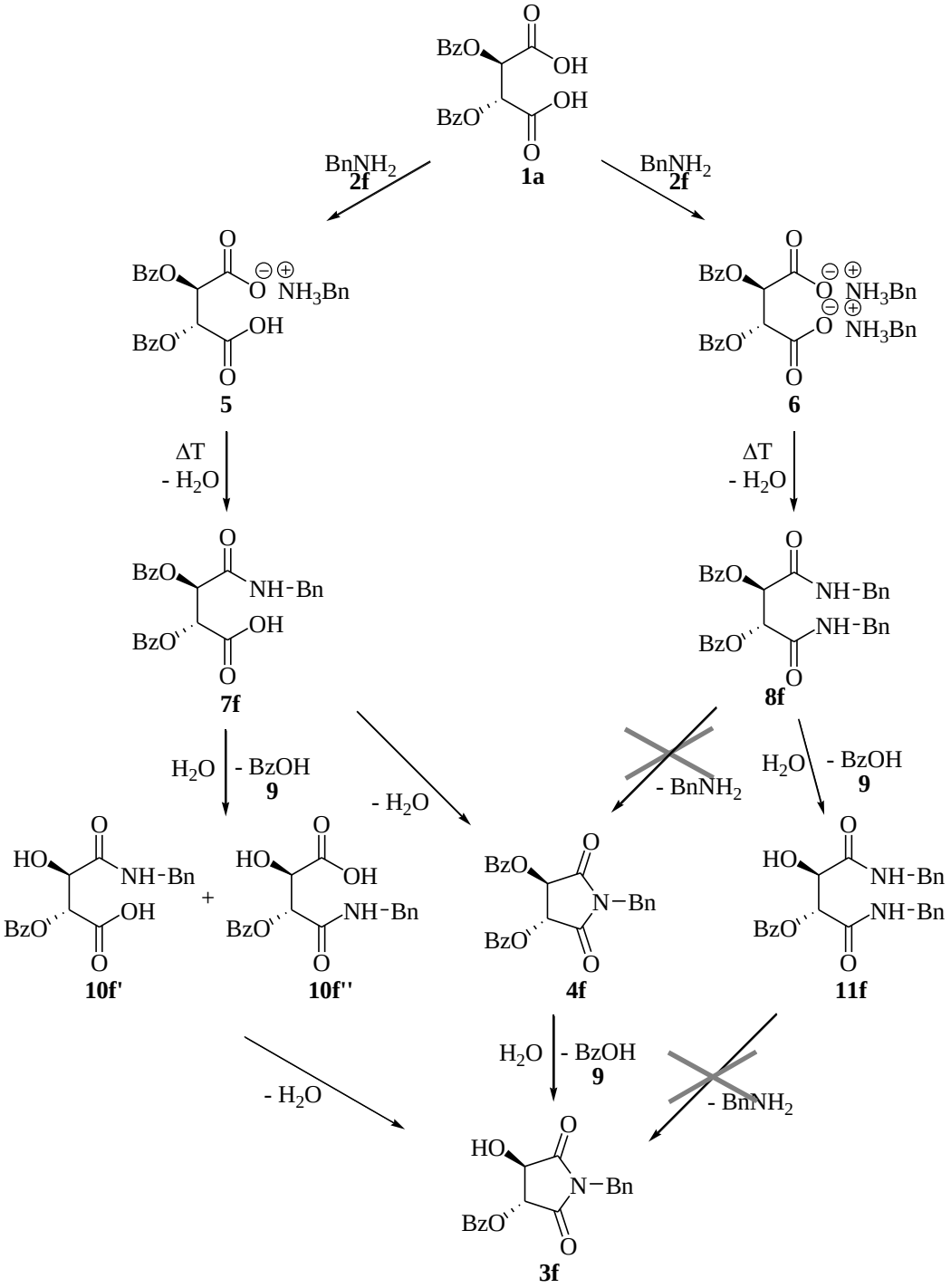


Additionally, benzoic acid was found in the reaction mixture and *N*-benzyl benzamide was not detected (GC-MS, NMR). Thus, the formation of monobenzoyltartrimide proceeded via hydrolysis not aminolysis of one benzoyl group. Such a hydrolysis has not previously been reported, probably because diacyl imides 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 monobenzoyltartrimide **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 dibenzoyltartrimide **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 **10′**, **10″** or competitively cyclize to the diacyltartrimide **4**. Both the following cyclization of **10′** and **10″** as

well as the hydrolysis of **4** result in the formation of monoacyltartrimide **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 ^{1}H NMR, 50 MHz for ^{13}C NMR) or a Varian Mercury 400 (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR) and measured in $CDCl_3$ 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 diacyltartimides

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. $[\alpha]_D^{22}$ +43.7 (*c* 0.1, $CHCl_3$). IR (ν_{max}, cm^{-1}): 3476, 1794, 1704. ^{1}H NMR

(200 MHz, $CDCl_3$) 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). ^{13}C NMR (50 MHz, $CDCl_3$) 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 $C_{14}H_{15}NO_5$: C, 60.64, H 5.45, N 5.05; Found: C 60.72, H 5.39, N 4.99.

(3*R*,4*R*)-*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, $CHCl_3$). IR (ν_{max}, cm^{-1}): 3268, 1772, 1704. ^{1}H NMR (200 MHz, $CDCl_3$) 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). ^{13}C NMR (50 MHz, $CDCl_3$) 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 $C_{17}H_{13}NO_5$: C 65.59, H 4.21, N 4.50; Found: C 65.64, H 4.20, N 4.53.

(3*R*,4*R*)-*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, $CHCl_3$). IR (ν_{max}, cm^{-1}): 3276, 1784, 1704. ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.06–7.18 (m, 8H), 5.55 (d, 1H, *J* = 4.8 Hz), 4.61 (d, 1H, *J* = 4.8 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) 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 $C_{17}H_{11}ClFNO_5$: C 56.14, H 3.05, N 3.85; Found: C 56.18, H 3.09, N 3.88.

(3*R*,4*R*)-*N*-Benzyl-4-benzoyloxy-3-hydroxypyrrolidine-2,5-dione (3f). Yield 46%, white solid, mp 168–169 °C. $[\alpha]_D^{22}$ +67.3 1 (*c* 0.1, $CHCl_3$). IR (ν_{max}, cm^{-1}): 3284, 1780, 1716. ^{1}H NMR (200 MHz, $CDCl_3$) 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). ^{13}C NMR (50 MHz, $CDCl_3$) 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 $C_{18}H_{15}NO_5$: C 66.46, H 4.65, N 4.31; Found: C 66.41, H 4.62, N 4.34.

(3*R*,4*R*)-*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, $CHCl_3$). IR (ν_{max}, cm^{-1}): 3468, 1808, 1704. ^{1}H NMR (200 MHz, $CDCl_3$) 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). ^{13}C NMR (50 MHz, $CDCl_3$) 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 $C_{18}H_{15}NO_6$: C 63.34, H 4.43, N 4.10; Found: C 63.41, H 4.42, N 4.08.

(3*R*,4*R*)-*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, $CHCl_3$) IR (ν_{max}, cm^{-1}): 3482, 1812, 1708. ^{1}H NMR (200 MHz, $CDCl_3$) 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). ^{13}C NMR (50 MHz, $CDCl_3$) 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 $C_{17}H_{12}ClNO_5$: C 59.06, H 3.50, N 4.05; Found: C 59.10, H 3.51, N 4.03.

(3*R*,4*R*)-*N*-(*n*-Butyl)-3,4-dibenzoyloxypyrrolidine-2,5-dione (4b). Yield 35%, white solid, mp 96–99 °C. $[\alpha]_D^{22}$ +62.1 (*c* 0.1, $CHCl_3$). IR (ν_{max}, cm^{-1}): 1788, 1728, 1704. ^{1}H NMR (200 MHz, $CDCl_3$) 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). ^{13}C NMR (50 MHz, $CDCl_3$) 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 $C_{22}H_{21}NO_6$: C 66.83, H 5.35, N 3.54; Found: C 66.77, H 5.39, N 3.59.

(3*R*,4*R*)-*N*-(4-Chlorophenyl)-3,4-dibenzoyloxypyrrolidine-2,5-dione (4d). Yield 62%, white solid, mp 124–127 °C. $[\alpha]_D^{22}$ +34.2 (*c* 0.1, $CHCl_3$). IR (ν_{max}, cm^{-1}): 1796, 1700. ^1H NMR (200 MHz, $CDCl_3$) δ 8.02 (m, 4H), 7.55–7.13 (m, 10H), 5.79 (s, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) 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 $C_{24}H_{16}ClNO_6$: C 64.08, H 3.59, N 3.11; Found: C 64.02, H 3.55, N 3.14.

(3*R*,4*R*)-*N*-Benzyl-3,4-dibenzoyloxypyrrolidine-2,5-dione (4f). Yield 62%, white solid, mp 113–118 °C. $[\alpha]_D^{22}$ +141.5 (*c* 0.1, Me_2CO). IR (ν_{max}, cm^{-1}): 3008, 1796, 1716. ^1H NMR (400 MHz, $CDCl_3$) 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). ^{13}C NMR: (100 MHz, $CDCl_3$) 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 $C_{25}H_{19}NO_6$: C 69.92, H 4.46, N 3.26; Found: C 69.86, H 4.49, N 3.28.

(3*R*,4*R*)-*N*-(4-Methylphenyl)-3,4-dibenzoyloxypyrrolidine-2,5-dione (4g). Yield 53%, white solid, mp 141–142 °C. $[\alpha]_D^{22}$ +48.3 (*c* 0.1, $CHCl_3$). IR (ν_{max}, cm^{-1}): 1736, 1704. ^1H NMR (400 MHz, $CDCl_3$) δ 8.12 (m, 4H), 7.52–7.37 (m, 10H), 5.91 (s, 2H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{25}H_{19}NO_6$: C 69.92, H 4.46, N 3.26; Found: C 70.01, H 4.49, N 3.24.

(3*R*,4*R*)-*N*-Phenyl-3,4-bis(2-chlorobenzoyloxy)pyrrolidine-2,5-dione (4i). Yield 53%, pale yellow solid, mp 127–129 °C. $[\alpha]_D^{22}$ +43.7 (*c* 0.1, $CHCl_3$). IR (ν_{max}, cm^{-1}): 1812, 1708. ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (m, 2H), 7.58–7.21 (m, 11H), 5.71 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{24}H_{15}Cl_2NO_6$: C 59.52, H 3.12, N 2.89; Found: C 59.46, H 3.14, N 2.91;

(3*R*,4*R*)-*N*-Isopropyl-3,4-bis(4-methoxybenzoyloxy)pyrrolidine-2,5-dione (4k). Yield 66%, white solid, mp 89–91 °C. $[\alpha]_D^{22}$ +75.6 (*c* 0.1, $CHCl_3$). IR (ν_{max}, cm^{-1}): 1796, 1696. ^1H NMR (400 MHz, $CDCl_3$) 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). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 165.8, 164.2, 132.5, 120.3, 113.8, 73.9, 55.8, 48.6, 20.5. Anal. Calcd. for $C_{23}H_{23}NO_8$: C 62.58, H 5.25, N 3.17; Found: C 62.51, H 5.22, N 3.16.

(3*R*,4*R*)-*N*-(*n*-Butyl)-3,4-bis(4-methoxybenzoyloxy)pyrrolidine-2,5-dione (4l). Yield 44%, white solid, mp 74–75 °C. $[\alpha]_D^{22}$ +68.1 (*c* 0.1, $CHCl_3$). IR (ν_{max}, cm^{-1}): 1792, 1696. ^1H NMR (400 MHz, $CDCl_3$) 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). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 165.8, 164.2, 132.5, 120.3, 113.8, 73.9, 55.7, 37.7, 21.2. Anal. Calcd. for $C_{24}H_{25}NO_8$: C 63.29, H 5.53, N 3.08; Found: C 63.34, H 5.52, N 3.10.

(3*R*,4*R*)-*N*-Phenyl-3,4-bis(4-methoxybenzoyloxy)pyrrolidine-2,5-dione (4m). Yield 65%, white solid, mp 132–135 °C. $[\alpha]_D^{22}$ +129.4 (*c* 0.1, $CHCl_3$). IR (ν_{max}, cm^{-1}): 1782, 1696. ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (m, 4H), 7.69–7.21 (m, 5H), 6.96 (m, 4H), 5.79 (s, 2H), 3.87 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{26}H_{21}NO_8$: C 65.68, H 4.45, N 2.95; Found: C 65.77, H 4.45, N 2.99.

(3*R*,4*R*)-*N*-(3-Chloro-4-fluorophenyl)-3,4-bis(4-methoxybenzoyloxy)pyrrolidine-2,5-dione (4n). Yield 51%, white solid, mp 107–108 °C. $[\alpha]_D^{22}$ +167.0 (*c* 0.1, $CHCl_3$). IR (ν_{max}, cm^{-1}): 1804, 1696. ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (m, 4H), 7.51–7.22 (m, 3H), 6.98 (m, 4H), 5.61 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{26}H_{19}ClFNO_8$: C 59.16, H 3.63, N 2.65; Found: C 59.21, H 3.65, N 2.67.

(3*R*,4*R*)-*N*-Benzyl-3,4-bis(4-methoxybenzoyloxy)pyrrolidine-2,5-dione (4o). Yield 68%, white solid, mp 112–113 °C. $[\alpha]_D^{22}$ +101.7 (*c* 0.1, $CHCl_3$). IR (ν_{max}, cm^{-1}): 1788, 1692. ^1H NMR (400 MHz, $CDCl_3$) 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). ^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{27}H_{23}NO_8$: C 66.25, H 4.74, N 2.86; Found: C 66.19, H 4.75, N 2.83.

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