High-Pressure Aminolysis of Lactones to Hydroxy Amides

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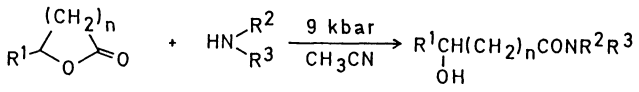
The preparation of hydroxy amides from a wide variety of lactones and amines has been achieved at 9 kbar and 30 or 65 °C. The yields of hydroxy amides were moderate to excellent. Some limitations were encountered in the reaction of 6-hexanolide; for example, diethylamine gave only a 15% yield of the corresponding amide at 8 kbar and 60 °C. 4-Pentanolide did react with extremely unreactive amines such as 4-nitroaniline and diphenylamine, and the product was a mixture of the hydroxy amide and 3-aminobutyric acid.

Particular attention has been directed to certain hydroxy amides that can serve as novel types of surfactants,[1a] (metal) chelating agents,[1b] liquid crystals,[1c] and protecting groups,[1d] as well as important intermediates for the synthesis of pharmacologically intriguing substances.[1e] Although one of the most convenient and simplest methods for preparing hydroxy amides would consist in the direct nucleophilic ring opening of lactones with amines, this conversion is generally limited either to strained three-membered lactones such as 3-propanolide[2] and 3-butanolide[3] or to relatively highly nucleophilic amines.[4] Specifically, the reactions of 4-substituted 4-butanolides with amines were reported to be sluggish,[5] and 3-butanolide did not react with 4-nitroaniline in refluxing acetonitrile.[3] Since we have previously demonstrated that secondary amines reacted in high yields at moderate temperatures with a variety of nonactivated esters to produce the corresponding acid amides if the reactions were performed under a few kbar,§[6] the same technique was expected to effect aminolysis of lactones by nucleophilic displacement at the carbonyl group.[7,8]

In this paper we wish to report in full detail the preparation of hydroxy amides by the aminolysis of lactones under high pressure.[9] The representative results are summarized in Table 1.

The structures of the amides **3** were confirmed on the basis of their analytical and ^{1}H and ^{13}C NMR spectroscopic data (see Experimental). Neither an inert atmosphere nor dry solvents were required. Alkyl-, aryl-, and aralkylamines **2** react with a wide variety of lactones **1** in moderate to excellent yields at 9 kbar and at room temperature to 65 °C affording the corresponding hydroxy amides **3**. For example, 4-butanolide (**1a**), 4-pentanolide (**1b**), and 5-pentanolide (**1d**) underwent aminolysis with piperidine (**2a**) at 30 °C to give the corresponding hydroxy amides **3aa**, **3ba**, and **3da** in 99, 95, and 96% yields, respectively, whereas no appreciable reaction was observed in refluxing acetonitrile at 1 bar. Similarly, diethylamine (**2b**) reacted smoothly with **1a**, **1b**, and **1d** at 9 kbar and



1 **2** **3**

1	n	R^1
a	2	H
b	2	CH_3
c	2	n-C_6H_{13}
d	3	H
e	4	H
f	1	CH_3

2	R^2	R^3
a	-$(CH_2)_5$-	
b	C_2H_5	C_2H_5
c	$C_6H_5CH_2$	H
d	C_6H_5	H
e	p-$NO_2C_6H_4$	H
f	C_6H_5	C_6H_5

Table 1. Reactions of Lactones **1** with Amines **2** at 9 kbar

Product	Reaction conditions		Yield	Mp
	Temp/°C	Time/d	%	θ_m/°C
3aa	30	7	99	Oil
3ab	30	4	100	Oil
3ad	55	5	8	69—70
	65	7	47	
3ba	30	7	95	Oil
3bb	30	4	95	Oil
3bc	30	7	100	Oil
3bd	55	5	19	88—89
	65	7	39	
3ca	30	7	96	Oil
3cb	30	10	93	Oil
3da	30	4	96	Oil
3db	30	4	94	Oil
3dd	55	7	94	67—68
3ea	30	1	40[a]	Oil
	30	4	86[b]	
3eb	55	7	15	Oil
3fe	60	7	40(+60[c])	142—143
	60[d]	7	50(+50[c])	
3ff	60	7	35(+28[e])	98—99
	60[f]	7	8(+8[e])	(99—100)
5a	30	7	87	79—80
5b	30	7	100	Oil
7a	30	7	77	80—90
7b	30	7	88	Oil

a) At 5 kbar for 12 h, **10** (oil) was obtained in 13% yield. b) A 3% yield of **10**. c) The yield of **11e**. d) In THF. e) The yield of **11f**. f) In toluene.

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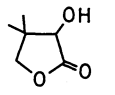
§ 1 bar=10^5 Pa.

30 °C to produce **3ab**, **3bb**, and **3db** in 100, 95, and 94% yield, respectively, while at 5 kbar and 30 °C only a 36% yield of **3bb** was obtained, thus demonstrating a considerable pressure effect in this reaction. It is rather surprising that the reaction of 4-pentanolide (**1b**) with benzylamine (**2c**) took place quantitatively at 9 kbar since some of the original lactone was always recovered even under the vigorous conditions at 1 bar and 190 °C for several days that resulted in much decomposition.[4] Furthermore, **1a** and **1b** did react with aniline (**2d**) at 9 kbar and 65 °C affording **3ad** and **3bd** albeit in moderate yields (47 and 39%). Aniline, with a pK_a of 4.69, is one million times less basic than a typical primary alkylamine and is therefore reported to be inert to **1b** upon heating to 180 °C.[4] 5-Pentanolide (**1d**) was more reactive than 4-butanolide (**1a**), thus 94% yield of the hydroxy amide **3dd** was obtained at 9 kbar and 55 °C.

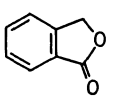
Other examples of five membered lactones include 4-decanolide (**1c**) and 4,5-dihydro-3-hydroxy-4,4-dimethyl-2(3*H*)-furanone (**4**) that reacted with **2a** and **2b** under similar conditions giving the hydroxy amides **3ca**, **3cb**, **5a**, and **5b**, respectively. The most versatile reagents for the mild aminolysis of esters[10] and lactones[11] are the dialkylaluminum amides. However, the hydrolysis procedure employed in this method often leads to recyclization to the original lactones as exemplified in the reaction of 1(3*H*)-isobenzofuranone (**6**) with diethylaluminum dimethyl amide.[11] This is not the case in the present method;



4

$HOCH_2C(CH_3)_2CH(OH)CONR^2R^3$

5a, b



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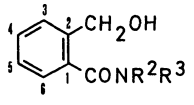
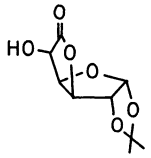


7a, b

for instance, **6** with **2a** at 9 kbar and 30 °C produced the hydroxy amide **7a** in 77% yield.

In contrast to **1a** and **1b**, a bicyclic lactone, 1,2-*O*-isopropylidene-α-D-glucofuranurono-6,3-lactone (**8**) underwent facile aminolysis with **2a** and **2c** at 1 bar and room temperature to give the corresponding amides **9a** and **9c** in 87 and 100% yields, respectively.



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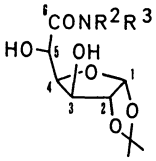


9a, c

This is presumably because of the bicyclic ring strain or the more constrained *cis*-ester structure.[12]

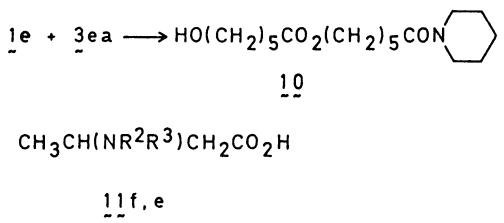
The reaction of 6-hexanolide (**1e**) with the amines was more complicated. For example, **1e** with **2a** at 9

Table 2. Eluents of Chromatography and Elemental Analysis

Compd No	Chromato. Solv.[a]	Found/%			Calcd/%			Formula
		C	H	N	C	H	N	
3aa	E	63.17	10.29	8.16	63.13	10.01	8.18	$C_9H_{17}NO_2$
3ab	E/A(g)	60.03	11.03	8.75	60.35	10.76	8.80	$C_8H_{17}NO_2$
3ad	E/T(7/3)	66.97	7.37	7.72	67.02	7.31	7.82	$C_{10}H_{13}NO_2$
3ba	E	64.40	10.42	7.48	64.83	10.34	7.56	$C_{10}H_{19}NO_2$
3bb	E/A(g)	62.14	11.34	8.09	62.39	11.05	8.09	$C_9H_{19}NO_2$
3bc	E	69.79	8.37	6.77	69.54	8.27	6.76	$C_{12}H_{17}NO_2$
3bd	E/T(7/3)	68.16	7.83	7.35	68.37	7.82	7.25	$C_{11}H_{15}NO_2$
3ca	E/T(7/3)	70.80	11.70	5.68	70.54	11.45	5.48	$C_{15}H_{29}NO_2$
3cb	E/T(7/3)	69.10	12.26	5.80	69.09	12.01	5.76	$C_{14}H_{29}NO_2$
3da	E/A(1/1)	64.73	10.41	7.36	64.83	10.34	7.56	$C_{10}H_{19}NO_2$
3db	E/A(g)	62.01	11.26	7.98	62.39	11.05	8.09	$C_9H_{19}NO_2$
3dd	E/T(7/3)	68.48	7.85	7.25	68.37	7.82	7.25	$C_{11}H_{15}NO_2$
3ea	E/A(g)	66.13	10.87	7.27	66.30	10.62	7.03	$C_{11}H_{21}NO_2$
3eb	E/A(g)	63.87	11.55	7.35	64.13	11.30	7.48	$C_{10}H_{21}NO_2$
3fe	B/E(g)	53.82	5.54	12.36	53.57	5.39	12.49	$C_{10}H_{12}N_2O_4$
3ff	B/E(g)	74.96	6.80	5.43	75.27	6.71	5.49	$C_{16}H_{17}NO_2$
5a	E/T(7/3)	61.39	10.01	6.45	61.37	9.83	6.51	$C_{11}H_{21}NO_3$
5b	E/T(7/3)	58.81	10.69	6.65	59.09	10.41	6.89	$C_{10}H_{21}NO_3$
7a	E/T(7/3)	71.38	7.85	6.37	71.21	7.81	6.39	$C_{13}H_{17}NO_2$
7b	E/T(7/3)	69.28	8.36	6.75	69.54	8.27	6.76	$C_{12}H_{17}NO_2$
10a		64.10	9.93	4.52	64.19	9.76	4.68	$C_{16}H_{29}NO_4$
11e		53.54	5.45	12.39	53.57	5.39	12.49	$C_{10}H_{12}N_2O_4$
11f		75.38	6.74	5.33	75.27	6.71	5.49	$C_{16}H_{17}NO_2$

a) In this column are shown eluents of a column chromatography on silica gel to isolate the product: E=ethyl acetate, A=acetone, B=benzene, T=toluene; and in the parentheses the solvent ratio or g=gradient fashion.

kbar and 30 °C gave an 86% yield of **3ea** along with 6-oxo-6-piperidinohexyl 6-hydroxyhexanoate (**10**, 3%), the formation of which can be explained in terms of acyl-oxygen fission of **1e** with **3ea**. At the lower pressure (5 kbar) and employing the shorter reaction time (12 h), the yield of **10** increased to 13% while that of **3ea** decreased to 40%. Under higher pressure and a longer reaction time, **10** apparently undergoes further aminolysis to give **3ea**. Diethylamine (**2b**) was almost inert to **1e** at 8 kbar and 30 °C. However, the reaction took place at 8 kbar and 60 °C, producing a complex mixture of products from which the amide **3eb** was isolated only in 15% yield.



Three-membered lactones, like 3-propanolide and 3-butanolide, readily undergo aminolysis, but presumably because of the effect of ring strain, alkyl-oxygen fission is also observed. The course of the

Table 3. ^{1}H NMR Data of Hydroxy Amides **3**, **5**, **7**, **9**, **10**, and **11**[a]

3aa	1.61 (bs, 6H, $^{3',4',5'}CH_2$), 1.72—2.00 (m, 2H, $^{3}CH_2$), 2.47 (t, J=6.9 Hz, 2H, $^{2}CH_2$), 3.3—3.8 (m, 7H, $^{4,2'6'}CH_2$+OH)
3ab	1.11, 1.19 (each t, J=7.0 Hz, 6H, CH_2CH_3×2), 1.72—2.00 (m, 2H, $^{3}CH_2$), 2.48 (t, J=6.9 Hz, 2H, $^{2}CH_2$), 3.33, 3.34 (each q, J=7.0 Hz, 4H, CH_2CH_3×2), 3.65 (bt, J=5.7 Hz, 2H, $^{4}CH_2$), 4.2 (bs, 1H, OH)
3ad	1.78—2.05 (m, 2H, $^{3}CH_2$), 2.48 (t, J=7.0 Hz, 2H, $^{2}CH_2$), 3.5—3.8 (m, 3H, $^{4}CH_2$+OH), 7.0—7.6 (m, 5H, C_6H_5), 8.38 (bs, 1H, NH)
3ba	1.16 (d, J=5.4 Hz, 3H, $^{5}CH_3$), 1.58 (bs, 6H, $^{3',4',5'}CH_2$), 1.6—1.9 (m, 2H, $^{3}CH_2$), 3.3—3.6 (m, 4H, $^{2',6'}CH_2$), 3.6—4.0 (m, 2H, ^{4}CH+OH)
3bb	1.10, 1.19 (each t, J=7.0 Hz, 6H, CH_2CH_3×2), 1.20 (d, J=6.2 Hz, 3H, $^{5}CH_3$), 1.6—1.9 (m, 2H, $^{3}CH_2$), 2.49 (t, J=7.0 Hz, 2H, $^{2}CH_2$), 3.34, 3.37 (each q, J=7.0 Hz, 4H, CH_2CH_3×2), 3.6—4.2 (m, 2H, ^{4}CH+OH)
3bc	1.12 (d, J=6.3 Hz, 3H, $^{5}CH_3$), 1.5—1.9 (m, 2H $^{3}CH_2$), 2.30 (t, J=7.0 Hz, 2H, $^{2}CH_2$), 3.49 (bs, 1H, OH), 3.6—4.0 (m, 1H, ^{4}CH), 4.32 (d,J=5.7 Hz, 2H, $CH_2C_6H_5$), 6.9 (bs, 1H, NH), 7.1—7.3 (m, 5H, C_6H_5)
3bd	1.19 (d, J=6.2 Hz, 3H, $^{5}CH_3$), 1.6—1.9 (m, 2H, $^{3}CH_2$), 2.49 (t, J=6.9 Hz, 2H, $^{2}CH_2$), 3.43 (bs, 1H, OH), 3.6—4.0 (m, 1H, ^{4}CH), 6.9—7.6 (m, 5H, C_6H_5), 8.35 (bs, 1H, NH)
3ca[b]	0.88 (t, J=7 Hz, 3H, $^{10}CH_3$), 1.3—1.9 (m, 18H, $^{3,5,6,7,8,9,3',4',5'}CH_2$), 2.50 (t, J=7.0 Hz, 2H, $^{2}CH_2$), 3.4—3.6 (m, 6H, ^{4}CH+OH+$^{2',6'}CH_2$)
3cb[b]	0.88 (t, J=7.0 Hz, 3H, $^{10}CH_3$), 1.11, 1.19 (each t, J=7.0 Hz, 6H, CH_2CH_3×2), 1.2—1.5 (m, 10H, $^{5,6,7,8,9}CH_2$), 1.6—2.0 (m, 2H, $^{3}CH_2$), 2.3—2.6 (m, 2H, $^{2}CH_2$), 3.33, 3.36 (each q, J=7.0 Hz, 4H, CH_2CH_3×2), 3.6 (bs, 1H, OH)
3da	1.6 (bs, 10H, $^{3,4,3',4'5'}CH_2$), 2.36 (t, J=7.0 Hz, 2H, $^{2}CH_2$), 3.3—3.8 (m, 7H, $^{5,2',6'}CH_2$+OH)
3db	1.10, 1.18 (each t, J=7.0 Hz, 6H, CH_2CH_3×2), 1.4—1.9 (m, 4H, $^{3,4}CH_2$), 2.35 (bt, J=6.8 Hz, 2H, $^{2}CH_2$), 3.33, 3.36 (each q, J=7.0 Hz, 4H, CH_2CH_3×2), 3.60 (t, J=6 Hz, 2H, $^{5}CH_2$), 3.96 (bs, 1H, OH)
3dd	1.3—1.9 (m, 4H, $^{3,4}CH_2$), 2.33 (bt, J=6.7 Hz, 2H, $^{2}CH_2$), 3.4—3.8 (m, 3H, $^{5}CH_2$+OH), 6.9—7.6 (m, 5H, C_6H_5), 8.58 (bs, 1H, NH)
3ea	1.2—2.0 (m, 12H, $^{3,4,5,3',4',5'}CH_2$), 2.33 (t, J=7.0 Hz, 2H, $^{2}CH_2$), 2.88 (bs, 1H, OH), 3.3—3.8 (m, 6H, $^{5,2',6'}CH_2$)
3eb	1.10, 1.17 (each t, J=7.1 Hz, 6H, CH_2CH_3×2), 1.2—1.9 (m, 6H, $^{3,4,5}CH_2$), 2.31 (t, J=7.2 Hz, 2H, $^{2}CH_2$), 2.48 (bs, 1H, OH), 3.30, 3.37 (each q, J=7.1 Hz, 4H, CH_2CH_3×2), 3.65 (t, J=6 Hz, 2H, $^{6}CH_2$)
3fe[c]	1.19 (d, J=6.2 Hz, 3H, $^{4}CH_3$), 2.46 (d, J=5.8 Hz, 1H, ^{2}CHH), 2.49 (d, J=7.1 Hz, 1H, ^{2}CHH), 4.0—4.4 (m, 1H, ^{3}CH), 4.70 (bd, J=4.6 Hz, 1H, OH), 7.85, 8.15 (ABq, J=9.5 Hz, 4H, C_6H_4), 8.8 (bs, 1H, NH)
3ff	1.0—1.4 (m, 3H, $^{4}CH_3$), 2.0—2.9 (m, 2H, $^{2}CH_2$), 5.32 (bq, J=6 Hz, 1H, ^{3}CH), 4.5—4.9 (m, 1H, OH), 6.8—7.3 (m, 10H, C_6H_5×2)
5a	0.90, 0.96, 1.07, 1.20 (each s, 6H, CH_3×2), 1.4—1.8 (m, 6H, $^{3',4',5'}CH_2$), 2.7—2.9 (m, 2H, $^{2',6'}CHH$), 3.46 (bs, 2H, $^{2',6'}CHH$), 3.3—3.9 (m, 2H, OH×2), 4.01 (d, J=9 Hz, 1H, ^{2}CH), 4.29 (s, 2H, $^{4}CH_2$)
5b	0.94, 0.98 (each s, 6H, CH_3×2), 1.16, 1.22 (each t, J=7.0 Hz, 6H, CH_2CH_3×2), 3.1—4.1 (m, 8H, $^{4}CH_2$+OH×2+CH_2CH_3×2), 4.39 (d, J=9 Hz, 1H, ^{2}CH)
7a	1.3—1.8 (m, 6H, $^{3',4',5'}CH_2$), 2.7—3.8 (m, 4H, $^{2',6'}CH_2$), 4.53 (bs, 2H, CH_2), 5.32 (s, 1H, OH), 7.2—8.0 (m, 4H, C_6H_4)
7b	1.16, 1.36 (each t, J=7.3 Hz, 6H, CH_2CH_3×2), 3.21, 3.57 (each q, J=7.3 Hz, 4H, CH_2CH_3×2), 4.50 (s, 2H, CH_2), 7.6—8.0 (m, 4H, C_6H_4)
9a	1.30, 1.45 (each s, 6H, CH_3×2), 1.6 (bs, 6H, $^{3',4',5'}CH_2$), 3.4—3.8 (m, 6H, $^{2',6'}CH_2$+OH×2), 4.02 (dd, J=8.0, 3.6 Hz, 1H, ^{4}CH), 4.46 (d, J=14.8 Hz, 1H, ^{1}CH), 4.46, 4.71 (ABq, J=8.0 Hz, 2H, $^{2,3}CH$), 5.95 (d, J=3.6 Hz, 1H, ^{5}CH)
9c	1.29, 1.45 (each s, 6H, CH_3×2), 3.6—4.2 (m, 3H, NH+OH×2), 4.2—4.6 (m, 7H, $^{1,2,3,4}CH$+NH+CH_2), 5.92 (d, J=3.6 Hz, 1H, ^{5}CH), 7.1—7.4 (bs, 5H, C_6H_5)
10a	1.2—1.9 (m, 18H, $^{3,4,5,2',3',4',3'',4'',5''}CH_2$), 2.2—2.5 (m, 5H, $^{2,6}CH_2$+OH), 3.3—3.7 (m, 6H, $^{5',2'',6''}CH_2$), 4.07 (bt, J=6 Hz, 2H, $^{1'}CH_2$)
10b	1.10, 1.17 (each t, J=7.2 Hz, 6H, CH_2CH_3×2), 1.1—1.9 (m, 10H,$^{3,4,5,2',3'}CH_2$), 2.2—2.5 (m, 4H, $^{2,4'}CH_2$), 3.30, 3.41 (each q, J=7.2 Hz, 4H, CH_2CH_3×2), 3.63 (bt, J=6 Hz, 2H, $^{3}CH_2$), 4.06 (bt, J=6 Hz, 4H, $^{6,1'}CH_2$)
11e	1.36 (d, J=6.5 Hz, 3H, $^{4}CH_3$), 2.19 (s, 1H, OH), 2.64 (dd, J=5.4, 1.8 Hz, 2H, $^{2}CH_2$), 3.9—4.2 (m, 1H, ^{3}CH), 6.56, 8.06 (ABq, J=9.0 Hz, 4H, C_6H_4), 7.7 (bs, 1H, NH)
11f	1.13 (d, J=6.4 Hz, 3H, $^{4}CH_3$), 2.36 (d, J=5.4 Hz, 2H, $^{2}CH_2$), 3.94 (bs, 1H, OH), 4.0—4.4 (m, 1H, ^{3}CH), 7.1—7.5 (m, 10H, C_6H_5×2)

a) 90 MHz in $CDCl_3$. Superscripts indicate the position of carbons. b) 200 MHz. c) In DMSO-d_6 at 40 °C.

reaction is believed to be sensitive to the reaction conditions.[2,3] The reaction of 3-butanolide (**1f**) with unreactive amines, such as 4-nitroaniline (**2e**) and diphenylamine (**2f**), further demonstrates the utility and generality of the method, since no reaction of **1f** with **2e** at 1 bar in refluxing acetonitrile was

Table 4. ^{13}C NMR Data of Hydroxy Amides **3**, **5**, **7**, **9**, **10**, and **11** in $CDCl_3$

	C=O	$-CH_2-$ and $R^1CH(OH)$	R^2 and/or R^3
3aa	171.3(C-1)	29.9(C-2) 27.6(C-3) 61.4(C-4)	42.4 46.3(C-2′,6′) 25.1 26.0(C-3′,5′) 24.0(C-4′)
3ab	172.0(C-1)	29.4(C-2) 27.5(C-3) 61.1(C-4)	39.6 41.5($\underline{C}H_2$) 12.4 13.6($\underline{C}H_3$)
3ad	172.4(C-1)	34.4(C-2) 28.1(C-3) 61.8(C-4)	137.9(C-1′) 120.2(C-2′,6′) 128.8(C-3′,5′) 124.3(C-4′)
3ba	171.1(C-1)	33.5(C-2) 29.1(C-3) 66.0(C-4) 22.8(C-5)	41.9 46.0(C-2′,6′) 24.8 25.7(C-3′,5′) 23.7(C-4′)
3bb	173.0(C-1)	34.1(C-2) 29.8(C-3) 67.3(C-4) 23.6(C-5)	40.4 42.3($\underline{C}H_2$) 13.0 14.3($\underline{C}H_3$)
3bc	173.9(C-1)	34.3(C-2) 32.7(C-3) 66.8(C-4) 23.1(C-5)	43.1($\underline{C}H_2$) 138.1(C-1′) 127.0(C-4′) 127.3(C-2′,6′) 128.3(C-3′,5′)
3bd	172.6(C-1)	34.2(C-2) 34.0(C-3) 67.3(C-4) 23.5(C-5)	138.0(C-1′) 120.2(C-2′,6′) 128.8(C-3′,5′) 124.2(C-4′)
3ca	171.5(C-1)	37.2(C-2) 31.9(C-3) 70.5(C-4) 31.3(C-5) 29.4 28.9 25.2(C-6,7,8) 22.1(C-9) 13.5(C-10)	42.2 46.2(C-2′,6′) 25.1 26.0(C-3′,5′) 24.0(C-4′)
3cb	172.7(C-1)	37.6(C-2) 32.0(C-3) 71.0(C-4) 31.6(C-5) 29.5 29.1 25.5(C-6,7,8) 22.3(C-9) 14.0(C-10)	40.1 41.9($\underline{C}H_2$) 12.7 13.8($\underline{C}H_3$)
3da	171.0(C-1)	32.3(C-2) 21.0(C-3) 31.6(C-4) 60.9(C-5)	42.0 46.1(C-2′,6′) 24.9 25.9(C-3′,5′) 23.8(C-4′)
3db	172.0(C-1)	32.1(C-2) 21.0(C-3) 31.8(C-4) 61.1(C-5)	39.6 41.6($\underline{C}H_2$) 12.5 13.8($\underline{C}H_3$)
3dd	172.4(C-1)	36.7(C-2) 21.9(C-3) 31.6(C-4) 61.7(C-5)	138.0(C-1′) 120.2(C-2′,6′) 128.7(C-3′,5′) 124.1(C-4′)
3ea	171.2(C-1)	32.9(C-2) 26.2(C-3,4) 32.0(C-5) 61.7(C-5)	42.3 46.4(C-2′,6′) 24.7 25.3(C-3′,5′) 24.2(C-4′)
3eb	172.1(C-1)	32.7(C-2) 25.4 24.8(C-3,4) 32.1(C-5) 61.8(C-6)	39.9 41.8($\underline{C}H_2$) 12.8 14.1($\underline{C}H_3$)
3fe[a]	170.8(C-1)	46.8(C-2) 63.9(C-3) 23.5(C-4)	145.4(C-1′) 118.9(C-2′,6′) 124.9(C-3′,5′) 142.2(C-4′)
3ff	171.0(C-1)	49.6(C-2) 67.2(C-3) 19.6(C-4)	145.7(C-1′) 122.8(C-2′,6′) 129.2(C-3′,5′) 122.0(C-4′)
5a	172.0(C-1)	70.4(C-2) 40.0(C-3) 68.7(C-4) 19.3 21.7($\underline{C}H_3$)	43.3 47.0(C-2′,6′) 25.2 25.9(C-3′,5′) 24.0(C-4′)
5b	173.0(C-1)	71.5(C-2) 40.1(C-3) 68.8(C-4) 19.7 22.3($\underline{C}H_3$)	40.4 42.2($\underline{C}H_2$) 12.7 14.1($\underline{C}H_3$)
7a	169.5	134.7(C-1) 138.3(C-2) 125.4(C-3) 128.8(C-4) 126.7(C-5) 128.5(C-6) 62.2($\underline{C}H_2$)	42.2 48.0(C-2′,6′) 25.2 25.9(C-3′,5′) 23.9(C-4′)
7b	170.5	135.1(C-1) 137.9(C-2) 125.0(C-3) 128.6(C-4) 126.6(C-5) 128.2(C-6) 62.0($\underline{C}H_2$)	38.7 42.8($\underline{C}H_2$) 12.2 13.4($\underline{C}H_3$)
9a	170.7(C-6)	84.4(C-1) 82.4(C-2) 75.0(C-3) 65.0(C-4) 105.2(C-5) 111.6($\underline{C}$Me) 26.0 26.7(CH_3)	43.9 46.6(C-2′,6′) 25.4 26.1(C-3′,5′) 24.3(C-4′)
9c	172.3(C-6)	85.1(C-1) 81.1(C-2) 75.1(C-3) 69.5(C-4) 105.2(C-5) 112.0($\underline{C}Me_2$) 26.2 26.8($\underline{C}H_3$)	43.3($\underline{C}H_2$) 137.6(C-1′) 127.2(C-2′,6′) 128.6(C-3′,5′) 127.4(C-4′)
10a	171.0(C-1)	34.1(C-2) 62.0(C-6) 24.6 24.8 25.2 25.7 28.3 32.1 (C-3,4,5,2′,3′,4′)	64.0(C-1′) 33.0(C-5′) 173.6(C-6′) 42.5 46.5(C-2″,6″) 25.4 26.3(C-3″,5″) 24.3(C-4″)
10b	171.8(C-1)	33.9(C-2) 62.1(C-6) 24.4 24.9 25.4 25.7 27.8 32.2 (C-3,4,5,2′,3′,4′)	63.4(C-1′) 32.7(C-5′) 173.4(C-6′) 39.9 41.2($\underline{C}H_2$) 12.9 14.2($\underline{C}H_3$)
11e	176.8(C-1)	40.3(C-2) 45.3(C-3) 20.1(C-4)	152.3(C-1′) 111.4(C-2′) 126.4(C-3′) 137.6(C-4′)
11f	178.6(C-1)	39.9(C-2) 49.5(C-3) 19.2(C-4)	145.7(C-1′) 122.9(C-2′) 129.3(C-3′) 122.2(C-4′)

a) In DMSO-d_6.

observed and only 0.8% of the amino acid **11f** was formed in the reaction of **1f** with **2f** upon heating at 180—190 °C.[3a] The desired amides **3fe** and **3ff** were obtained in 40 and 35% yields, along with 3-(4-nitrophenylamino)- and 3-(diphenylamino)butyric acids **11e**(60%) and **11f**(28%), respectively. A slight improvement in the yield of **11e** was obtained using tetrahydrofuran as a solvent, whereas the use of more nonpolar solvents, like toluene, in the reaction of **1f** with **2f** retarded the reaction, the product ratio being little improved.

Experimental

General. Melting points are uncorrected. ^{1}H NMR spectra were measured either on a Hitachi R40(90 MHz) or JEOL FX-90Q(90 MHz) or Varian VRX-200(200 MHz) and ^{13}C NMR on a JEOL FX-90Q. The high-pressure instrument employed has been described elsewhere.[7]

High-Pressure Reaction of Lactones 1 with Amines 2. A General Procedure. A mixture of **1** (5 mmol) and **2** (10 mmol) was diluted with acetonitrile in a PTFE (8 cm^3) capsule, which was then stored for a stated time (Table 1) at 9 kbar. After evaporation of the solvent and amine (if volatile), the residue was chromatographed on silica gel, in general using ethyl acetate-acetone (or toluene or benzene) as an eluent in gradient fashion (Table 2). The results of analytical and ^{1}H and ^{13}C NMR spectroscopic data were collected in Tables 2—4.

Reaction of 1,2-*O*-Isopropylidene-α-D-glucofuranurono-6,3-lactone (8) with Piperidine (2a). A mixture of **8** (1 mmol) and **2a** (2 mmol) was stirred in acetonitrile (1 cm^3) at room temperature for 5 h. After evaporation of the solvent and amine, the residue was chromatographed on silica gel. Elution with benzene-ethyl acetate (1:3) gave *N,N*-pentamethylene-1,2-*O*-isopropylidene-α-D-glucofuranuronamide (**9a**) in 87% yield: mp 148—149 °C (see Tables 3 and 4). Found: C, 55.84; H, 7.71; N, 4.61%. Calcd for $C_{14}H_{23}NO_6$: C, 55.79; H, 7.71; N, 4.65%.

***N*-Benzyl-1,2-*O*-isopropylidene-α-D-glucofuranuronamide (9c).** The procedure was the same as described above for **9a**. **9c** was obtained quantitatively: mp 130—131 °C (see Tables 3 and 4). Found: C, 59.48; H, 6.47; N, 4.13%. Calcd for $C_{16}H_{21}NO_6$: C, 59.42, H, 6.56; N, 4.33%.

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