151. Approaches to the Synthesis of Cytochalasans

Part 10[1])

Cuprates as Reagents for the Formation of C–C Bonds

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Based upon our novel concept for the total synthesis of cytochalasans, the model lactams **2**–**9** were treated with $Bu_2Cu(CN)Li_2$. The results of these conversions vary much from those obtained with $Ph_2Cu(CN)Li_2$, demonstrating the uncertainty of predictions in cuprate chemistry. The bicyclic compound **20** was prepared in good yield. However, all attempts to convert *p*-toluenesulfonate **20** into the Ph-substituted derivative **21**, an intermediate for the synthesis of cytochalasin B (**1**), have failed so far.

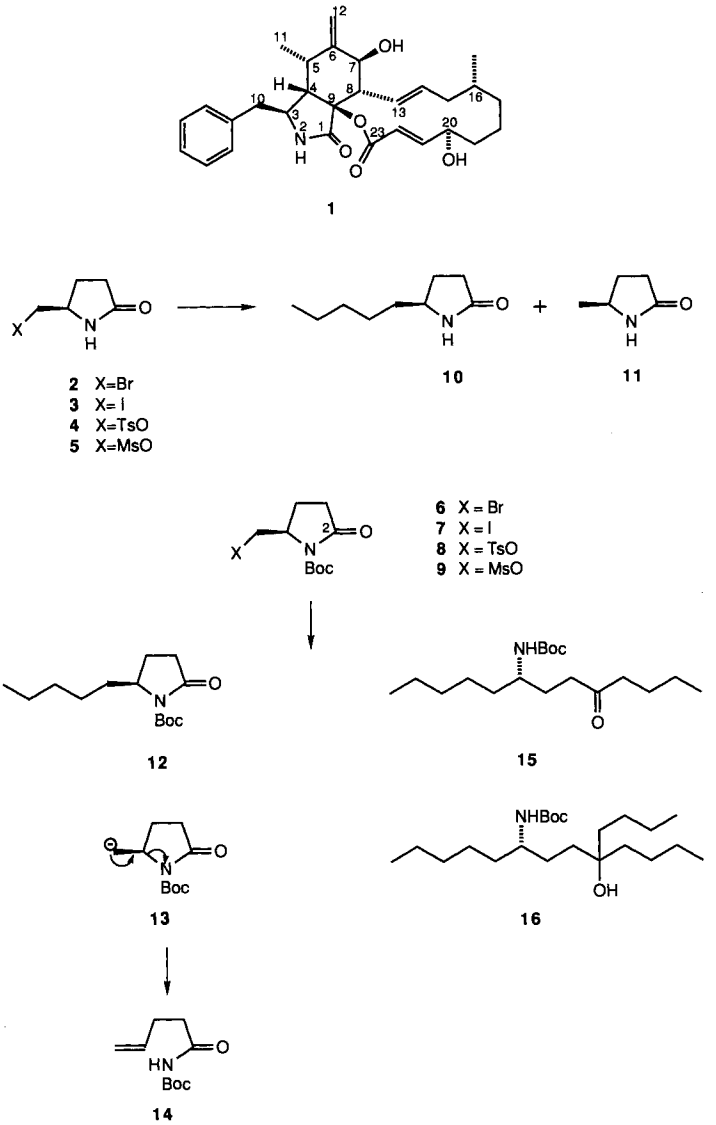
In [1], we have presented a versatile concept, leading to all structural types of cytochalasans, *e.g.* cytochalasin B (**1**), whereby the desired substituent at C(10) is attached after formation of the bicyclic system. We have already described the reactions with the monocyclic γ-lactams **2**–**9** serving as models with $Ph_2Cu(CN)Li_2$ in order to establish the best conditions for the introduction of a Ph group (*Scheme*). We now wish to report the results of the conversion of **2**–**9** with $Bu_2Cu(CN)Li_2$, a typical aliphatic cuprate. These experiments were carried out to establish the influence of the cuprate upon the reactivity, and to gain information on the optimal conditions for the introduction of an aliphatic group which is required for the construction of many naturally occurring and synthetic cytochalasans.

In a first set of experiments, the *N*-unprotected γ-lactams **2**–**5** were treated with $Bu_2Cu(CN)Li_2$ applying three different methods (*cf. Table 1*) as described in [1].

When no NaH was added (*Method A*), only bromide **2** gave the desired Bu-substituted product **10** in a satisfactory yield as previously described by *Winkler* and *Hershberger* [2]. This result is in contrast to the reaction with $Ph_2Cu(CN)Li_2$ [1] in which bromide **2**, iodide **3**, and *p*-toluenesulfonate **4** had given good-to-excellent yields of the desired Ph-substituted product. However, it has to be mentioned that, using $Bu_2Cu(CN)Li_2$, the temperature could not be raised above −40°. Otherwise, decomposition of the cuprate took place. Especially the very low reactivity of **4** was unexpected, because it had been proved to be the most suitable substrate for the reaction with $Ph_2Cu(CN)Li_2$ [1]. With $Bu_2Cu(CN)Li_2$, compound **3** was found to be the most reactive substrate. Unfortunately, the desired product **10** could be isolated only as a by-product of the main compound **11**. It is interesting to note that **11** had not been isolated even in traces using $Ph_2Cu(CN)Li_2$

[1]) Part 9: [1].

Scheme



instead of $Bu_2Cu(CN)Li_2$. We suppose that **11** is produced by reduction of **3** *via* an SET reaction as proposed by *Ashby* and *Coleman* for similar cases [3]. As for the conversion with $Ph_2Cu(CN)Li_2$, no significant acceleration of the reaction could be observed upon adding NaH (*Method B* and *C*). This result indicates that we were once again unable to confirm the hypothesis of aziridine formation promoted by NaH, as postulated by *Knapp* and *Levorse* [4].

Table 1. *Yields of the Reaction of* **2–5** *with* $Bu_2Cu(CN)Li_2$

	Starting material	X	Conditions	Yield [%]		
				10	**11**	Recovered educt
Method A[a])	**2**	Br	−42°, 24 h	41	0	58
	3	I	−78°, 4 h	17	83	0
	4	TsO	−42°, 24 h	26	0	72
	5	MsO	−42°, 24 h	6	0	65
Method B[b])	**2**	Br	−42°, 24 h	26	0	65
	3	I	−78°, 4 h	12	73	2
	4	TsO	−42°, 24 h	18	0	73
	5	MsO	−42°, 24 h	< 3	0	70
Method C[c])	**2**	Br	−42°, 24 h	35	0	62
	3	I	−78°, 4 h	9	41	8
	4	TsO	−42°, 24 h	20	0	63
	5	MsO	−42°, 24 h	< 3	0	63

[a]) 5 equiv. of $Bu_2Cu(CN)Li_2$.
[b]) 5 equiv. of $Bu_2Cu(CN)Li_2$, 0.2 equiv. of NaH.
[c]) 5 equiv. of $Bu_2Cu(CN)Li_2$, 1 equiv. of NaH.

In a second set of experiments, the *N*-Boc-protected γ-lactams **6–9** were treated with $Bu_2Cu(CN)Li_2$ (*Table 2*). Again, only the Br derivative gave the Bu-substituted lactam **12** in moderate yield. As for the *N*-unprotected lactams **2–5**, the I derivative **7** proved to be the most reactive substance. However, as for the iodide **3**, the desired Bu substitution occurred only as a side reaction. In this case, **14** was isolated in high yield. We suppose that **14** was produced *via* the consecutive transfer of two-electrons, yielding carbanion **13** as intermediate, with subsequent spontaneous elimination. This result is in contrast to the conversion of **7** with $Ph_2Cu(CN)Li_2$ where exclusively the Ph-substituted product was obtained in high yield [1]. In the case of bromide **6** and *p*-toluenesulfonate **8**, nucleophilic ring opening at C(2) occurred as side reaction, followed by nucleophilic substitution leading to **15**, or by nucleophilic substitution and nucleophilic addition yielding **16**.

Summarizing these observations, it has to be concluded that the results of the conversion of **2–5** and **6–9** with $Bu_2Cu(CN)Li_2$ vary from those with $Ph_2Cu(CN)Li_2$ to a large extent. It has been found that leaving groups that are suitable for the reaction with $Ph_2Cu(CN)Li_2$ are unsuitable for conversions with $Bu_2Cu(CN)Li_2$ and *vice versa*. In addition, other types of products were formed using $Bu_2Cu(CN)Li_2$.

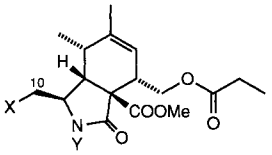
These results clearly show that the reactivity of the 5-substituted γ-lactams towards cuprates not only depends upon the leaving group and the *N*-protecting group, but also

Table 2. *Yields of the Reaction of* **6–9** *with* $Bu_2Cu(CN)Li_2$

Starting material	X	Conditions	Yield [%]				
			12	**14**	**15**	**16**	Recovered educt
6	Br	−42°, 16 h	46	8	9	0	12
7	I	−78°, 2 h	2	86	0	0	0
8	TsO	0°, 16 h	15	0	0	9	17
9	MsO	−78°, 4 h	0	0	0	0	0

on the nature of the cuprate. It is, therefore, risky to draw conclusions for a planned reaction with a cuprate on the basis of a similar case described in the literature. Nevertheless, it can be summarized that iodides, bromides, and *p*-toluenesulfonates may serve as suitable leaving groups at least in some cases, whereas mesylates are throughout unsuitable. The use of the *N*-Boc-protecting group is not beneficial, because side reactions as *e.g.* ring-opening of γ-lactams may occur. In general, iodides have proved to be very reactive, but in some cases undesired compounds were formed as main products.

We attempted to use these conclusions for the total synthesis of cytochalasin B (**1**). The *N*-unprotected *p*-toluenesulfonate **20** was chosen as starting material for the introduction of the Ph group using $Ph_2Cu(CN)Li_2$ as nucleophile, because the corresponding model compound had been proved to be very suitable. Substrate **20** was prepared from **17** by cleavage of the silyl ether with TsOH in MeOH (→ **18**), tosylation with TsCl in pyridine (→ **19**, 44% yield starting from **17**) followed by cleavage of the *N*-protecting



17 X = (*t*-Bu)Me_2SiO, Y = Boc
18 X = OH, Y = Boc
19 X = TsO, Y = Boc
20 X = TsO, Y = H
21 X = Ph, Y = H
22 X = Br, Y = H
23 X = I, Y = H

group using CF_3COOH in CH_2Cl_2 (→ **20**, 96% yield). Subsequently, **20** was treated with $Ph_2Cu(CN)Li_2$. Unfortunately, all attempts to isolate the desired **21** failed so far. We were only able to isolate a mixture of several by-products which could not be seperated by column chromatography. In that mixture, no ester groups could be detected using ^{1}H-NMR, whereas the Ts group was still present. Due to the high reactivity of the ester groups, nucleophilic substitution at C(10) seems to be difficult, if the leaving group is not especially suitable. It is planned to use now the compounds **22** and **23** as substrates for the introduction of the Ph group. The results will be reported in due time.

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Experimental Part

General. See [1].

(5S)-5-Pentylpyrrolidin-2-on (**10**) *and (5S)-5-Methylpyrrolidin-2-on* (**11**). *Method A* (no NaH). A suspension of 100 mg (1.12 mmol) of CuCN in 2.5 ml of abs. THF was cooled to −78°, then 1.33 ml (2.24 mmol) of BuLi (1.68M) were added. The cooling bath was removed, until a clear soln. was obtained which was immediately recooled to −78°, followed by dropwise addition of 0.22 mmol of a soln. of the γ-lactams **2**–**5** in 2 ml of abs. THF. The mixture was then stirred at −78° (for **3**) or at −42° (for **2**, **4**, and **5**) for 4 h (for **3**) or for 24 h (for **2**, **4**, and **5**), quenched by adding 5 ml of a sat. NH_4Cl/conc. NH_4OH soln. 9:1, and extracted with 5 portions of 10 ml of CH_2Cl_2. The org. extracts were dried and evaporated, and the residue was purified by CC (Et_2O/i-PrOH 10:1). From **2**: 14 mg (41%) of **10** and 23 mg (58%) of educt; from **3**: 6 mg (17%) of **10** and 18 mg (83%) of **11**; from **4**: 9 mg (26%) of **10** and 43 mg (72%) educt; from **5**: 2 mg (6%) of **10** and 28 mg (65%) educt were obtained.

Method B (0.2 equiv. of NaH). At 0°, 2 mg (0.05 mmol) of a NaH dispersion (55% in oil) were washed with 1 ml of hexane, then 1 ml of abs. THF was added. A soln. of 0.22 mmol of the γ-lactams **2**–**5** in 2 ml of THF was added dropwise. After evolution of H_2 had ceased, the mixture was cooled to −78°, and a cold (−78°) soln. of $Bu_2Cu(CN)Li_2$, prepared from 100 mg (1.12 mmol) of CuCN and 1.33 ml (2.24 mmol) of BuLi (1.68M) as described in *Method A* was added. The mixture was then stirred at −78° (for **3**) or at −42° (for **2**, **4**, and **5**) for 4 h (**3**) or for

24 h (**2**, **4**, and **5**), quenched by adding 5 ml of a sat. NH_4Cl/conc. NH_4OH soln. 9:1, and extracted with 5 portions of 10 ml of CH_2Cl_2. The org. extracts were dried and evaporated, and the residue was purified by CC (Et_2O/i-PrOH 10:1). From **2**: 9 mg (26%) of **10** and 26 mg (65%) of educt; from **3**: 4 mg (12%) of **10**, 16 mg (73%) of **11**, and 1 mg (2%) of educt; from **4**: 6 mg (18%) of **10** and 44 mg (73%) of educt; from **5**: < 1 mg (3%) of **10** and 30 mg (70%) of educt were obtained.

Method C (1 equiv. of NaH). At 0°, 10 mg (0.23 mmol) of a NaH dispersion (55% in oil) were washed with hexane (3 × 1 ml), then 1 ml of abs. THF was added. A soln. of 0.22 mmol of the λ-lactams **2**–**5** in 2 ml of THF was added dropwise. After evolution of H_2 had ceased, the mixture was cooled to −78°, and a cold (−78°) soln. of $Bu_2Cu(CN)Li_2$, prepared from 100 mg (1.12 mmol) of CuCN and 1.33 ml (2.24 mmol) of BuLi (1.68M) as described in *Method A* was added. The mixture was then stirred at −78° (for **3**) or at −42° (for **2**, **4**, and **5**) for 4 h (for **3**) or for 24 h (for **2**, **4**, and **5**), quenched by adding 5 ml of a sat. NH_4Cl/conc. NH_4OH soln. 9:1 and extracted with 5 × 10 ml of CH_2Cl_2. The org. extracts were dried and evaporated, and the residue was purified by CC (Et_2O/i-PrOH 10:1). From **2**: 12 mg (35%) of **10** and 25 mg (62%) of educt; from **3**: 3 mg (9%) of **10**, 9 mg (41%) of **11**, and 4 mg (8%) of educt; from **4**: 7 mg (20%) of **10** and 38 mg (63%) of educt; from **5**: < 1 mg (3%) of **10** and 27 mg (63%) of educt were obtained.

Data of **10**: $[\alpha]_D^{22} = -9.7$ ($c = 0.78$, EtOH). IR (film): 3220 (NH); 2960, 2930, 2860 (CH); 1695 (C=O). ^{1}H-NMR (400 MHz): 0.88–0.93 (*m*, CH_3); 1.24–1.37 (*m*, $CH_3CH_2CH_2CH_2$); 1.40–1.56, 1.66–1.77, 2.20–2.38 (3*m*, CH_2(3), CH_2(4), CH_2–C(5)); 3.59–3.69 (*m*, H–C(5)); 6.16 (br. *s*, NH). ^{13}C-NMR (101 MHz): 13.90 (CH_3); 22.5 (CH_3CH_2); 25.5 ($CH_3CH_2CH_2CH_2$) 27.3 (C(4)); 30.1 (C(3)); 31.6 ($CH_3CH_2CH_2$); 36.7 (CH_2–C(5)); 54.5 (C(5)); 178.2 (C(2)). EI-MS: 155 (6, M^+), 84 (100).

Data of **11**: $[\alpha]_D^{21} = -9.9$ ($c = 0.97$, EtOH). IR (film): 3440 (NH); 3010, 2980, 2940 (CH); 1695 (C=O); 1420, 1210, 725. ^{1}H-NMR (400 MHz): 1.23 (*d*, $J = 6$, CH_3–C(5)); 1.61–1.73, 2.22–2.39 (2*m*, CH_2(3), CH_2(4)); 3.79 (*qt*, $J = 6$, 6, H–C(5)); 6.45 (br. *s*, NH). ^{13}C-NMR (101 MHz) [5]: 22.0 (CH_3); 29.0 (C(4)); 30.4 (C(3)); 50.0 (C(5)); 178.7 (C(2)). EI-MS: 99 (35, M^+), 84 (100), 56 (28), 55 (16), 44 (36), 43 (10), 42 (23), 41 (85).

tert-*Butyl (5S)-2-Oxo-5-pentylpyrrolidine-1-carboxylate* (**12**) *and* N-*[(*tert-*butoxy)carbonyl]pent-4-enamide* (**14**), *and* tert-*Butyl* N-*[(1S)-4-Oxo-1-pentyloctyl]carbamate* (**15**) *and* tert-*Butyl* N-*[(1S)-4-Butyl-4-hydroxy-1-pentyloctyl]carbamate* (**16**). *General Procedure for the Reaction of* **6**–**9** *with* $Bu_2Cu(CN)Li_2$. A suspension of 81 mg (0.90 mmol) CuCN in 2 ml of abs. THF was cooled to −78°, then 1.10 ml (1.80 mmol) of BuLi (1.63M) were added. The cooling bath was removed, when a clear soln. was obtained, which was immediately recooled to −78°, followed by dropwise addition of a soln. of 0.18 mmol of the **6**–**9** in 1.5 ml of abs. THF. The mixture was then stirred at −42° for 16 h (for **6**), −78° for 2 h (for **7**), 0° for 16 h (for **8**) or −78° for 4 h (for **9**), and quenched by either adding 5 ml of a sat. NH_4Cl/conc. NH_4OH soln. 9:1 for **6**, **7**, and **8**, or by injecting (syringe) the mixture into 5 ml of sat. NH_4Cl/conc. NH_4OH soln. 9:1 for **9**. Then, 100 ml of Et_2O were added, the org. phase washed twice with H_2O, dried, and evaporated. The residue was purified by CC (Et_2O/Pentan 1:3 → Et_2O). From **6**[2]: 21 mg (46%) of **12**, 3 mg (8%) **14**, 5 mg (9%) **15**, and 6 mg (12%) of educt; from **7**: 1 mg (2%) of **12** and 31 mg (86%) of **14**; from **8**: 7 mg (15%) of **12**, 6 mg (9%) of **16**, and 11 mg (17%) of educt; from **9**: neither products nor educt, were obtained.

Data of **12**: $[\alpha]_D^{22} = +61.8$ ($c = 1.31$, $CHCl_3$). IR (film): 2960, 2940, 2860 (CH); 1790, 1750 (C=O, Boc); 1715 (C=O, lactam); 1460, 1370, 1310, 1155. ^{1}H-NMR (400 MHz): 0.90 (*t*, $J = 6$, CH_3CH_2); 1.23–1.42 (*m*, $CH_3CH_2CH_2CH_2$); 1.53 (*s*, *t*-BuO); 1.73–1.82, 2.06–2.14, 2.37–2.65 (3*m*, CH_2(3), CH_2(4), CH_2–C(5)); 4.07–4.14 (*m*, H–C(5)). ^{13}C-NMR (101 MHz): 13.7 (CH_3CH_2); 22.2, 22.3, 25.1, 31.2, 31.4, 33.4 (C(3), C(4), $CH_3CH_2CH_2CH_2CH_2$); 27.8 ($(CH_3)_3C$); 58.0 (C(5)); 82.6 ($(CH_3)_3C$); 150.2 (*t*-BuO*C*O); 174.9 (C(2)). FAB-MS: 256 (10, $[M + H]^+$), 200 (100), 182 (10), 156 (3), 84 (4), 57 (28).

Data of **14**: M.p. 51–53°. IR ($CHCl_3$): 3410 (NH); 3010 (olef. CH); 2880 (aliph. CH); 1750 (C=O, Boc); 1700 (C=O, amide); 1480, 1145. ^{1}H-NMR (400 MHz): 1.49 (*s*, *t*-BuO); 2.37–2.43 (*m*, CH_2(3)); 2.84 (*t*, $J = 7$, CH_2(2)); 5.01 (*ddt*, $J = 10$, 2, 2, 1 H, CH_2(5)); 5.08 (*ddt*, $J = 17$, 2, 2, 1 H, CH_2(5)); 5.86 (*ddt*, $J = 17$, 10, 6.5, H–C(4)); 7.42 (br. *s*, NH). ^{13}C-NMR (101 MHz): 28.0 ($(CH_3)_3C$); 28.1 (C(2)); 35.3 (C(3)); 82.5 ($(CH_3)_3C$); 115.4 (C(4)); 136.8 (C(5)); 150.5 (*t*-BuO*C*O); 174.0 (C(1)). FAB-MS: 200 (41, $[M + H]^+$), 144 (100), 100 (20), 83 (10), 57 (91). Anal. calc. for $C_{10}H_{17}NO_3$ (199.25): C 60.28, H 8.60, N 7.03; found: C 60.51, H 8.63, N 7.15.

Data of **15**: M.p. 36–38°. $[\alpha]_D^{20} = -5.6$ ($c = 0.45$, $CHCl_3$). IR ($CHCl_3$): 3440 (NH); 2950, 2920 (CH); 1700 (C=O); 1490, 1360, 1160. ^{1}H-NMR (400 MHz): 0.86–0.93 (*m*, CH_3(8), CH_3(5′)); 1.23–1.35, 1.51–1.59, 1.75–1.80, 2.38–2.49 (4*m*, CH_2(2), CH_2(3), CH_2(5), CH_2(6), CH_2(7), CH_2(1′), CH_2(2′), CH_2(3′), CH_2(4′)), 1.43 (*s*, *t*-BuO);

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[2]) Compounds **14** and **15** were first isolated as a mixture and could be seperated subsequently by CC (acetone/pentane 1:15).

3.48–3.52 (*m*, H–C(1)); 4.23 (br. *d*, NH). ^{13}C-NMR (101 MHz): 13.9, 14.0 (C(8), C(5′)); 22.4, 22.6, 25.6, 26.0, 29.3, 31.7, 36.1, 39.4, 42.8 (C(2), C(3), C(5), C(6), C(7), C(1′), C(2′), C(3′), C(4′)); 28.4 ((CH_3)$_3$C); 50.6 (C(1)); 79.0 ((CH_3)$_3C$); 155.9 (*t*-BuO*C*O); 211.2 (C(4)). FAB-MS: 314 (23, $[M + H]^+$), 258 (47), 214 (57), 85 (37), 57 (100).

Data of **16**: $[\alpha]_D^{20} = -4.7$ (*c* = 1.11, $CHCl_3$). IR ($CHCl_3$): 3440 (NH, OH); 2940, 2920, 2850 (CH); 1690 (C=O); 1490, 1360, 1160. ^{1}H-NMR (400 MHz): 0.87–0.93 (*m*, CH_3(8), CH_3(5′), CH_3(4″)); 1.22–1.51 (*m*, OH, CH_2(2), CH_2(3), CH_2(5), CH_2(6), CH_2(7), CH_2(1′), CH_2(2′), CH_2(3′), CH_2(4′), CH_2(1″), CH_2(2″), CH_2(3″)); 1.44 (*s*, *t*-BuO); 3.47–3.66 (*m*, H–C(1)); 4.21–4.29 (br. *d*, NH). ^{13}C-NMR (101 MHz): 14.0, 14.1 (C(8), C(5′), C(4″)); 22.6, 23.3, 25.7, 25.7, 29.4, 31.8, 34.9, 35.7, 38.8, 39.1 (C(2), C(3), C(5), C(6), C(7), C(1′), C(2′), C(3′), C(4′), C(1″), C(2″), C(3″)); 28.4 ((CH_3)$_3$C); 51.0 (C(1)); 74.1 C(4)); 78.9 ((CH_3)$_3C$); 155.9 (*t*-BuO*C*O). FAB-MS: 372 (8, $[M + H]^+$), 354 (11), 298 (100), 254 (6), 144 (29), 57 (80).

*2-(*tert*-Butyl) 3a-Methyl (1*R*,3a*S*,4*S*,7*S*,7a*R*)-2,3,3a,4,7,7a-Hexahydro-6,7-dimethyl-1-{[(4-methylphenyl)-sulfonyloxy]methyl}-3-oxo-4-[(propanoyloxy)methyl]-1*H*-isoindole-2,3a-dicarboxylate* (**19**). To a soln. of 211 mg (0.38 mmol) of **17** in 5 ml of MeOH, 13 mg (0.07 mmol) of TsOH were added. The mixture was stirred for 9 h at r.t., quenched by adding 10 ml of sat. $NaHCO_3$ soln. and extracted with CH_2Cl_2 (4 × 10 ml), dried, and evaporated. To the crude **18** in 3 ml of abs. pyridine, 300 mg (1.57 mmol) of TsCl were added. The mixture was stirred for 24 h at r.t., diluted with 30 ml of Et_2O, washed with 10% citric acid and sat. $NaHCO_3$ soln., dried, and evaporated. After CC (pentane/Et_2O 1:1 → 1:2) 100 mg (44%) of **19** were obtained as a colorless oil. IR ($CHCl_3$): 3060 (CH, arom.); 1785, 1730 (C=O); 1370, 1300, 1170, 1150. ^{1}H-NMR (400 MHz): 1.12 (*t*, *J* = 7.5, CH_3CH_2COO); 1.17 (*d*, *J* = 7, Me–C(7)); 1.41 (*s*, *t*-BuO); 1.73 (*s*, Me–C(6)); 2.30 (*q*, *J* = 7.5, CH_3CH_2COO); 2.44 (*s*, Me–C(4′)); 2.52 (br. *s*, H–C(7)); 2.68 (*dd*, *J* = 5, 3, H–C(7a)); 2.95 (br. *s*, H–C(4)); 3.80 (*s*, MeO); 3.81–3.84 (*m*, H–C(1)); 3.95 (*dd*, *J* = 10, 2.5, 1 H, CH_2–C(1)); 4.19 (*dd*, *J* = 10, 4.5, 1 H, CH_2–C(1)); 4.45–4.52 (*m*, CH_2–C(4)); 5.48 (br. *s*, H–C(5)); 7.35 (*d*, *J* = 8, H–C(3′), H–C(5′)); 7.75 (*d*, *J* = 8, H–C(2′), H–C(6′)). FAB-MS: 594 (0.5, $[M + H]^+$), 538 (2), 494 (31), 420 (31), 57 (100).

*Methyl (1*R*,3a*S*,4*S*,7*S*,7a*R*)-2,3,3a,4,7,7a-Hexahydro-6,7-dimethyl-1-{[(4-methylphenyl)sulfonyloxy]-methyl}-3-oxo-4-[(propanoyloxy)methyl]-1*H*-isoindole-3a-carboxylate* (**20**). To a soln. of 100 mg (0.17 mmol) of **19** in 5 ml of CH_2Cl_2, 150 µl (1.96 mmol) of CF_3COOH were added. The mixture was stirred for 30 min at r.t., quenched by adding 10 ml of sat. $NaHCO_3$ soln. and extracted with CH_2Cl_2 (4 × 10 ml), dried, and evaporated yielding 80 mg (96%) of pure **20** as a colorless solid. An anal. sample was recrystallized from CH_2Cl_2/pentane. M.p. 108–112°. ^{1}H-NMR (400 MHz): 1.12 (*t*, *J* = 7.5, CH_3CH_2COO); 1.12 (*d*, *J* = 7, Me–C(7)); 1.75 (*s*, Me–C(6)); 2.30 (*q*, *J* = 7.5, CH_3CH_2COO); 2.38–2.44 (*m*, H–C(7)); 2.47 (*s*, Me–C(4′)); 2.93–2.96 (*m*, H–C(7a)); 3.32–3.35 (*m*, H–C(4)); 3.67–3.69 (*m*, H–C(1)); 3.74 (*s*, MeO); 3.76–3.85 (*m*, 1 H, CH_2–C(1)); 4.03–4.08 (*m*, 1 H, CH_2–C(1)); 4.38–4.53 (*m*, CH_2–C(4)); 5.53 (*s*, H–C(5)); 5.80 (*s*, NH); 7.38 (*d*, *J* = 8, H–C(3′), H–C(5′)); 7.79 (*d*, *J* = 8, H–C(2′), H–C(6′)). FAB-MS: 494 (100, $[M + H]^+$), 420 (74), 360 (10), 105 (26), 91 (38), 69 (32), 57 (81).

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