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Synthesis of Mono- and Diunsaturated Esters of TADDOL

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Abstract: The synthesis of fourteen new mono- and diesters of (4R,5R)-2,2-dimethyl- $\alpha,\alpha,\alpha',\alpha'$ -tetraphenyl-1,3-dioxolane-4,5-dimethanol (TADDOL) is reported. This study shows that esterifications of TADDOL (1) with acid chlorides, derived from normal and α,β -unsaturated carboxylic acids, in the presence of *n*-butyllithium (BuLi) can lead to both mixtures of the corresponding mono- and diesters, the latter in higher yield, and to just the diesters, depending on the structure of the starting acids. These reactions take place in most cases in good to excellent overall yields (57–95%). The reaction between a dichloro derivative of TADDOL and the silver salts of α,β -unsaturated acids also gives the corresponding unsaturated diesters of TADDOL in good yields.

Key words: TADDOL, α , β -unsaturated esters, butyllithium, unsaturated acid silver salts

Unsaturated esters of (4R,5R)-2,2-dimethyl- $\alpha,\alpha,\alpha',\alpha'$ tetraphenyl-1,3-dioxolane-4,5-dimethanol (TADDOL),¹ like TADDOL dimethacrylate (**9**), have been synthesized and successfully employed in stereoselective cyclopolymerizations.^{2,3} In the course of our investigations, we considered it of interest to study some reactions of unsaturated esters of TADDOL. However, although the synthesis of diester **9** was reported in 1997² we were not able to find any reference to other unsaturated esters of TADDOL in the chemical literature. This prompted us to carry out a study on the synthesis of this type of TADDOL esters.

To begin with we studied the esterification of butanoic and benzoic acids with TADDOL (1). All the attempts we made to carry out the esterifications of these acids using the N,N'-dicyclohexylcarbodiimide (DCC)/4-(dimethylamino)pyridine (DMAP) method failed.

We then used the reaction between TADDOL (1) and the corresponding acyl chlorides in the presence of *n*-butyl-lithium (BuLi) in hexane and methyllithium (MeLi) in diethyl ether, according to Scheme 1. In this scheme, it can be seen that whereas the reaction of diol 1 with butanoyl chloride in the presence of BuLi at -78 °C, followed by warming the reaction mixture to room temperature, leads to monoester 2 as the only product in 70% yield, the reaction of 1 with benzoyl chloride in the presence of MeLi at -78 °C followed by warming to room temperature leads to

SYNTHESIS 2005, No. 15, pp 2491–2496 Advanced online publication: 04.08.2005 DOI: 10.1055/s-2005-872123; Art ID: M01005SS © Georg Thieme Verlag Stuttgart · New York a 95% overall yield of a mixture of the diester **3** and monoester **4**, the former in much higher yield. It is noteworthy that Seebach used acetyl chloride under similar conditions to obtain the corresponding monoester as the only product (84%) of the reaction, even when using a large excess of acetyl chloride.³



Scheme 1

Taking into account these results, we investigated the synthesis of unsaturated esters of TADDOL. Again, using the DCC/DMAP method we were unable to obtain any products of esterification. However, through the reaction of TADDOL (1) and BuLi with the chlorides of α , β -unsaturated acids at 0 °C we succeeded in obtaining a series of new unsaturated mono- and diesters of TADDOL **5–16**, as shown in Scheme 2, in good to excellent overall yields. The reactions were carried out by mixing diol 1 in tetrahydrofuran with BuLi in hexane and then adding the acid chlorides to the mixture at 0 °C; the reaction mixtures were then heated at reflux temperature (refluxing times are included in Table 1) and left at room temperature for 12 hours.

As shown in Scheme 2, these reactions can lead in some cases to the diesters, e.g. 5 and 6, as the only products and in other cases to a mixture of diesters (major product) and monoesters (minor product), e.g. 7-16. Taking into account that in all cases a large excess of the corresponding acid chloride was used, the formation of the mixtures might be related to structural factors. The average overall yield for all of the reactions was 78.5%. We found that complete separation of the mixtures of mono- and diesters, as well as their purification, could be performed in



Scheme 2

all cases by column chromatography using neutral alumina as adsorbent. It should be noted that in several cases we were not able to achieve good separation using silica gel.

Interestingly, in the case of methacryloyl chloride, when we lowered the reaction temperature to -78 °C we exclusively obtained the corresponding TADDOL monoester **10** in 65% yield, even when using an excess of acid chloride (Scheme 3). It is noteworthy that all attempts we made to obtain exclusively the monoesters of the other unsaturated acids under these reaction conditions failed.

In order to obtain mixed unsaturated esters of TADDOL, we attempted the reaction of monoester **10** in the presence of BuLi with acryloyl chloride at 0 and -78 °C. To our





surprise, instead of the expected TADDOL mixed acrylate methacrylate diester, we obtained in both cases monounsaturated diester **17** as the only product in over 50% yield. The formation of diester **17** could be explained in terms of the monoester **10** reacting with BuLi in such a fashion that 1,4-addition to the monoester takes precedence over the competing deprotonation of **10**.

Unsaturated diesters of TADDOL can also be obtained from the reaction between silver salts of the unsaturated acids and (4R,5R)-4,5-bis[chloro(diphenyl)methyl]-2,2dimethyl-1,3-dioxolane (18),⁴ as shown in Scheme 4. Thus, the reaction between the silver salts of acrylic and methacrylic acid and the dichloride 18 in toluene under reflux led to the corresponding unsaturated diesters 7 and 9, respectively, as the only products in good yields (70 and 79%, respectively). One point of interest concerned the synthesis of the starting dichloride 18. Following the technique given in the literature,⁴ i.e. the reaction of 1 and thionyl chloride in the presence of triethylamine, dichloride 18 is obtained pure with an average yield of 50%. We were able to improve the yield by halogenation of 1 using phosphorus pentachloride in chloroform and in the presence of calcium carbonate. Using this method, the average yield of **18** rose to 60%.



Scheme 4

In summary, fourteen new mono- and diesters of TAD-DOL have been synthesized. Esterification of TADDOL (1) with acid chlorides derived from normal and α,β -unsaturated carboxylic acids is performed at low temperatures followed by warming to room temperature or reflux of the reaction mixture, respectively. This reaction leads both to mixtures of the corresponding mono- and diesters, with the latter as the major product, and to just the diesters, depending on the structure of the starting acids. It is also shown that by using this method, the esterification of monounsaturated esters of TADDOL, which should lead to mixed unsaturated esters, is not possible. This is because nucleophilic addition of BuLi to the unsaturated ester group in the starting TADDOL derivative takes place before the attack of the unsaturated acid chloride, as demonstrated by the formation of a mixed saturated-unsaturated diester. The reaction between a dichloro derivative of TADDOL and the silver salts of α , β -unsaturated acids gives the corresponding unsaturated diesters of TADDOL in good yields.

Reaction conditions, yields, and some selected physical and spectroscopic data for those compounds synthesized are summarized in Table 1; ¹H and ¹³C NMR spectroscopic data are given in Table 2.

The NMR spectra were obtained using a Bruker ARX 300 instrument. Infrared spectra were recorded with a Nicolet Nexus FT spectrometer. Mass spectra were obtained using an ESI-TOF Bruker BIOTOF II spectrometer at Santiago de Compostela University (Spain). Melting points were determined on a Kofler hot stage and are uncorrected. Specific rotations were measured with a Polar L- μ P, IBZ Messtechnik. All the solvents and reagents used were analytical reagent grade.

Table 1	Reaction Conditions,	Yields, and Some S	Selected Physical	and Spectroscopic	Data for Compounds 2-17
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Product	Method ^a	Refluxing Time (h)	Yield (%)	Mp (°C)	$\left[\alpha\right]_{D}^{25}$	IR (KBr) (cm ⁻¹)	ESI-HRMS $m/z [M + Na]^+$
2	А	b	70	158–160	-75.6 (<i>c</i> 0.48, CHCl ₃)	3491, 3060, 3055, 2966, 2928, 1739, 1495, 1448, 1172, 1079, 889, 757, 703	calcd for C ₃₅ H ₃₆ O ₅ : 559.2460; found: 559.2455
3	A*	b	80	135–137	–78.7 (<i>c</i> 0.40, CHCl ₃)	3056, 3029, 2978, 2928, 1724, 1600, 1499, 1445, 1102, 1067, 881, 714, 695	calcd for C ₄₅ H ₃₈ O ₆ : 697.2566; found: 697.2561
4	A*	b	15	185–187	-64.3 (<i>c</i> 0.42, CHCl ₃)	3584, 3056, 3021, 2978, 2956, 1732, 1596, 1491, 1448, 1106, 1071, 885, 761, 703	calcd for C ₃₈ H ₃₄ O ₅ : 593.2307; found: 593.2299
5	В	1	65	170–172	-120.5 (<i>c</i> 0.44, CHCl ₃)	3056, 3029, 2959, 2928, 1720, 1650, 1495, 1448, 1130, 1071, 881, 726, 699	calcd for C ₄₁ H ₄₂ O ₆ : 653.2879; found: 653.2874
6	В	2.5	57	181–183	-47.2 (<i>c</i> 0.43, CHCl ₃)	3056, 3025, 2959, 2932, 1716, 1631, 1495, 1445, 1110, 1072, 881, 761, 695	calcd for $C_{51}H_{46}O_6$: 777.3192; found: 777.3187
7	С	4	70	160–162	-129.2 (<i>c</i> 0.42, CHCl ₃)	3056, 3025, 2986, 2932, 1728, 1631, 1499, 1405, 1172, 1079, 889, 747, 707	calcd for C ₃₇ H ₃₄ O ₆ : 597.2256; found: 597.2248
7	В	1	70				
8	В	1	20	144–146	–96.7 (<i>c</i> 0.30, CHCl ₃)	3584, 3056, 3029, 2932, 2858, 1735, 1634, 1495, 1448, 1176, 1071, 889, 749, 699	calcd for C ₃₄ H ₃₂ O ₅ : 543.2147; found: 543.2142
9	С	4	79	166–168	-103.2 (<i>c</i> 1.0, CHCl ₃)	3055, 3052, 2990, 2928, 1728, 1638, 1495, 1448, 1149, 1071, 885, 753, 697	с
9	В	1	74				c
10	В	1	15	187–189	–97.4 (<i>c</i> 0.42, CHCl ₃)	3600, 3052, 3051, 2982, 2928, 1732, 1638, 1495, 1448, 1153, 1075, 881, 746, 703	calcd for C ₃₅ H ₃₄ O ₅ : 557.2303; found: 557.2299
11	В	2	75	197–199	–92.8 (<i>c</i> 0.43, CHCl ₃)	3052, 3050, 2974, 2897, 1732, 1658, 1491, 1440, 1165, 1075, 893, 757, 691	calcd for C ₃₉ H ₃₈ O ₆ : 625.2566; found: 625.2561
12	В	2	10	145–147	-69.2 (<i>c</i> 0.40, CHCl ₃)	3603, 3056, 3029, 2928, 2854, 1732, 1646, 1499, 1444, 1168, 1075, 893, 757, 699	calcd for C ₃₅ H ₃₄ O ₅ : 557.2303; found: 557.2299
13	В	2	63	175–177	-42.0 (<i>c</i> 0.40, CHCl ₃)	3056, 3021, 2990, 2928, 1716, 1634, 1491, 1448, 1161, 1071, 885, 745, 699	calcd for C ₄₉ H ₄₂ O ₆ : 749.2879; found: 749.2874
14	В	2	7	178–180	-48.0 (<i>c</i> 0.40, CHCl ₃)	3590, 3058, 3032, 2931, 2873, 1725, 1624, 1490, 1445, 1170, 1071, 891, 762, 699	calcd for C ₄₀ H ₃₆ O ₅ : 619.2460; found: 619.2455

 Table 1
 Reaction Conditions, Yields, and Some Selected Physical and Spectroscopic Data for Compounds 2–17 (continued)

Product	Method ^a	Refluxing Time (h)	Yield (%)	Mp (°C)	$\left[\alpha\right]_{D}^{25}$	IR (KBr) (cm ⁻¹)	ESI-HRMS $m/z [M + Na]^+$
15	В	1	73	205–207	–91.9 (<i>c</i> 0.41, CHCl ₃)	3052, 3025, 2988, 2935, 1716, 1623, 1495, 1448, 1168, 1075, 877, 761, 699	calcd for C ₆₁ H ₅₀ O ₆ : 901.3504; found: 901.3499
16	В	1	21	214–216	–52.0 (<i>c</i> 0.40, CHCl ₃)	3588, 3052, 3025, 2928, 2868, 1724, 1623, 1495, 1448, 1168, 1083, 881, 761, 702	calcd for C ₄₆ H ₄₀ O ₅ : 695.2772; found: 695.2768
17	B A	2 b	55 52	56–58	-60.0 (<i>c</i> 0.36, CHCl ₃)	3095, 3056, 2959, 2858, 1736, 1631, 1495, 1448, 1367, 1169, 1065, 889, 803, 699	calcd for C ₄₂ H ₄₆ O ₆ : 669.3192; found: 669.3187

^a Method A: ratio of [TADDOL (1)/BuLi/acid chloride] 1.0:2.2:2.5; -78 °C; A*: ratio of [TADDOL (1)/MeLi/acid chloride] 1.0:2.2:2.5; -78 °C; B: ratio of [TADDOL (1)/BuLi/acid chloride] 1.0:2.4:3.0; 0 °C. C: ratio of (18/silver salt) 1.0:2.2; r.t. ^b Conducted at r.t.

^c See ref. 2.

Fable 21H and 13C NM	R Spectroscopic Da	ta for Compounds 2-17
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Product	¹ H NMR (CDCl ₃ /TMS) δ , J (Hz)	¹³ C NMR (CDCl ₃ /TMS) δ	
2	0.75 (t, 3 H, ${}^{3}J$ = 7.6 Hz), 0.78 (s, 6 H), 1.35–1.52 (m, 2 H), 2.13 (t, 2 H, ${}^{3}J$ = 7.6 Hz), 2.74 (s, 1 H), 4.61 (d, 1 H, ${}^{3}J$ = 7.2 Hz), 5.44 (d, 1 H, ${}^{3}J$ = 7.2 Hz), 7.15–7.34 (m, 20 H)	13.71, 18.21, 27.45, 27.37, 37.66, 77.85, 78.92, 81.32, 86.20, 110.03, 127.01, 127.30, 127.44, 127.67, 128.28, 128.93, 129.07, 129.83, 139.89, 143.17, 143.45, 147.29, 171.29	
3	0.65 (s, 6 H), 5.94 (s, 2 H), 6.82–7.49 (m, 30 H)	27.65, 78.16, 88.29, 110.35, 127.11, 127.47, 127.55, 127.73, 127.96, 129.06, 129.88, 130.57, 131.09, 131.41, 132.44, 141.48, 144.24, 165.66	
4	0.69 (s, 3 H), 0.78 (s, 3 H), 2.07 (s, 1 H), 4.83 (d, 1 H, ${}^{3}J$ = 7.6 Hz), 5.77 (d, 1 H, ${}^{3}J$ = 7.6 Hz), 6.99–7.40 (m, 23 H), 7.90–7.94 (m, 2 H)	27.38, 27.65, 77.26, 78.99, 81.48, 86.97, 110.22, 127.11, 127.24, 127.40, 127.43, 127.51, 127.67, 128.23, 128.41, 128.81, 129.21, 129.75, 130.07, 132.33, 132.64, 141.46, 143.16, 147.42, 164.76	
5	0.57 (s, 6 H), 1.52 (s, 6 H), 1.61 (d, 6 H, ${}^{3}J$ = 7.0 Hz), 5.76 (s, 2 H), 6.75 (q, 2 H, ${}^{3}J$ = 7.0 Hz), 7.09–7.44 (m, 20 H)	11.21, 13.68, 26.41, 78.12, 86.40, 108.93, 125.73, 126.14, 126.20, 126.30, 126.88, 127.81, 129.87, 137.04, 140.45, 143.36, 165.78	
6	0.62 (s, 6 H), 1.79 (s, 6 H), 5.88 (s, 2 H), 7.07–7.32 (m, 30 H), 7.57 (s, 2 H)	13.44, 26.48, 78.27, 87.11, 109.16, 125.88, 126.33, 126.43, 126.49, 126.93, 127.22, 127.40, 127.96, 128.95, 129.01, 134.58, 138.91, 140.32, 143.25, 166.70	
7	1.48 (s, 6 H), 5.43 (s, 2 H), 5.68 (dd, 2 H, ${}^{3}J = 10.1$ Hz, ${}^{2}J = 1.3$ Hz), 5.98 (dd, 2 H, ${}^{3}J = 17.2$ Hz, ${}^{3}J = 10.1$ Hz), 6.24 (dd, 2 H, ${}^{3}J = 17.2$ Hz, ${}^{2}J = 1.3$ Hz), 7.12–7.36 (m, 20 H)	27.68, 78.50, 87.78, 109.81, 127.22, 127.74, 127.77, 127.99, 129.43, 130.37, 131.36, 131.40, 140.53, 143.99, 165.03	
8	0.72 (s, 3 H), 0.73 (s, 3 H), 2.42 (s, 1 H), 4.70 (d, 1 H, ${}^{3}J$ = 7.1 Hz), 5.55 (d, 1 H, ${}^{3}J$ = 7.1 Hz), 5.62 (dd, 1 H, ${}^{3}J$ = 10.3 Hz, ${}^{2}J$ = 1.3 Hz), 5.99 (dd, 1 H, ${}^{3}J$ = 17.2 Hz, ${}^{3}J$ = 10.3 Hz), 6.22 (dd, 1 H, ${}^{3}J$ = 17.2 Hz, ${}^{2}J$ = 1.3 Hz), 7.14–7.38 (m, 20 H)	27.41, 27.54, 79.01, 81.46, 86.55, 110.22, 127.04, 127.29, 127.46, 127.60, 127.63, 127.68, 128.34, 128.89, 129.16, 129.89, 130.09, 130.21, 140.47, 143.22, 143.66, 147.44, 164.05	
9	0.61 (s, 6 H), 1.68 (s, 6 H), 5.45 (d, 2 H, ${}^{2}J$ = 1.2 Hz), 5.72 (s, 2 H), 6.07 (d, 2 H, ${}^{2}J$ = 1.2 Hz), 7.13–7.27 (m, 20 H)	18.73, 27.83, 78.03, 88.20, 110.43, 127.23, 127.32, 127.76, 127.79, 127.88, 129.31, 130.79, 138.41, 141.57, 144.55, 166.74	
10	0.68 (s, 3 H), 0.71(s, 3 H), 1.85 (s, 3 H), 2.06 (bs, 1 H), 4.72 (d, 1 H, ${}^{3}J$ = 7.1 Hz), 5.42 (d, 1 H, ${}^{2}J$ = 1.5 Hz), 5.62 (d, 1 H, ${}^{3}J$ = 7.1 Hz), 6.02 (d, 1 H, ${}^{2}J$ = 1.5 Hz), 7.11–7.38 (m, 20 H)	18.78, 27.38, 27.54, 78.97, 81.45, 86.45, 110.29, 124.71, 127.03, 127.20, 127.26, 127.32, 127.60, 127.62, 127.66, 128.30, 128.66, 129.31, 129.91, 138.45, 141.30, 142.81, 144.24, 147.76, 165.41	
11	0.75 (s, 6 H), 1.76 (dd, 6 H, ${}^{3}J$ = 6.8 Hz, ${}^{4}J$ = 1.5 Hz), 5.58 (s, 2 H), 5.76 (dd, 2 H, ${}^{3}J$ = 13.7 Hz, ${}^{4}J$ = 1.5 Hz), 6.84 (dq, 2 H, ${}^{3}J$ = 13.7 Hz, ${}^{3}J$ = 6.8 Hz), 7.13–7.45 (m, 20 H)	17.93, 27.31, 78.11, 87.01, 109.34, 125.75, 126.69, 127.16, 127.25, 127.44, 128.98, 130.14, 140.56, 143.99, 144.14, 164.78	

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Product	¹ H NMR (CDCl ₃ /TMS) δ , <i>J</i> (Hz)	¹³ C NMR (CDCl ₃ /TMS) δ	
12	0.81 (s, 6 H), 1.73 (dd, 3 H, ${}^{3}J$ = 6.8 Hz, ${}^{4}J$ = 1.2 Hz), 2.76 (s, 1 H), 4.77 (d, 1 H, ${}^{3}J$ = 7.2 Hz), 5.65 (d, 1 H, ${}^{3}J$ = 7.2 Hz), 5.73 (dd, 1 H, ${}^{3}J$ = 15.4 Hz, ${}^{4}J$ = 1.2 Hz), 6.82 (m, 1 H, ${}^{3}J$ = 15.4 Hz, ${}^{3}J$ = 6.8 Hz), 7.12–7.46 (m, 20 H)	17.82, 27.28, 27.39, 78.76, 81.48, 86.06, 109.90, 124.17, 126.85, 127.08, 127.13, 127.22, 127.40, 127.49, 128.07, 128.72, 128.92, 129.71, 140.23, 143.27, 143.50, 144.11, 147.19, 164.04	
13	0.70 (s, 6 H), 5.63 (s, 2 H), 6.23 (d, 2 H, ${}^{3}J$ = 16.0 Hz), 6.97– 7.33 (m, 30 H), 7.43 (d, 2 H, ${}^{3}J$ = 16.0 Hz)	27.76, 78.48, 87.92, 110.02, 120.87, 127.21, 127.68, 127.77, 127.95, 128.46, 128.99, 129.45, 130.50, 130.67, 134.38, 141.13, 144.45, 145.23, 165.97	
14	0.76 (s, 3 H), 0.81 (s, 3 H), 2.62 (s, 1 H), 4.73 (d, 1 H, ${}^{3}J$ = 7.2 Hz), 5.62 (d, 1 H, ${}^{3}J$ = 7.2 Hz), 6.23 (d, 1 H, ${}^{3}J$ = 16.2 Hz), 7.18 (d, 1 H, ${}^{3}J$ = 16.2 Hz), 7.10–7.41 (m, 25 H)	27.39, 27.58, 78.96, 81.59, 86.58, 110.02, 119.71, 127.06, 127.12, 127.37, 127.41, 127.45, 127.59, 127.68, 128.27, 128.28, 128.89, 128.96, 134.58, 140.44, 143.67, 143.78, 144.47, 147.03, 164.83	
15	0.84 (s, 6 H), 6.31 (s, 2 H), 7.02–7.65 (m, 40 H), 8.16 (s, 2 H)	27.82, 78.54, 89.01, 110.88, 126.80, 127.49, 127.60, 127.64, 127.99, 128.44, 129.37, 129.90, 130.74, 130.95, 134.41, 135.76, 141.29, 141.90, 144.07, 167.33	
16	0.64 (s, 3 H), 0.66 (s, 3 H), 2.25 (s, 1 H), 4.53 (d, 1 H, ${}^{3}J$ = 7.2 Hz), 5.63 (d, 1 H, ${}^{3}J$ = 7.2 Hz), 6.89–7.36 (m, 30 H), 7.68 (s, 1 H)	27.46, 78.98, 81.68, 86.92, 110.45, 126.86, 127.24, 127.33, 127.38, 127.51, 127.65, 127.75, 128.24, 128.33, 128.84, 129.02, 129.20, 129.43, 129.74, 129.81, 130.87, 134.24, 134.76, 136.83, 140.24, 141.22, 142.62, 144.15, 147.92, 165.55	
17	0.72 (s, 3 H), 0.82 (t, 3 H, ${}^{3}J = 6.9$ Hz), 0.88 (s, 3 H), 0.92 (t, 3 H, ${}^{3}J = 7.1$ Hz), 1.04–1.51 (m, 8 H), 2.42 (m, 1 H), 5.05 (d, 1 H, ${}^{3}J = 7.7$ Hz), 5.06 (d, 1 H, ${}^{3}J = 7.7$ Hz), 5.72 (dd, 1 H, ${}^{3}J = 10.3$ Hz, ${}^{2}J = 1.5$ Hz), 6.09 (dd, 1 H, ${}^{3}J = 17.1$ Hz, ${}^{3}J = 10.3$ Hz), 6.28 (dd, 1 H, ${}^{3}J = 17.1$ Hz, ${}^{2}J = 1.5$ Hz), 7.11–7.43 (m, 20 H)	14.22, 16.36, 22.72, 26.73, 27.15, 27.41, 32.18, 33.10, 39.75, 78.62, 79.69, 86.81, 87.47, 108.69, 126.88, 126.98, 127.10, 127.42, 127.75, 127.83, 129.35, 129.79, 129.88, 130.03, 130.16, 131.28, 138.34, 139.75, 142.13, 143.06, 164.27, 174.56	

 Table 2
 ¹H and ¹³C NMR Spectroscopic Data for Compounds 2–17 (continued)

TADDOL Monobutanoate (2); Typical Procedure (Method A): A solution of TADDOL (1; 0.93 g, 2.0 mmol) in dry THF (8.5 mL) was treated with a 1 M solution of *n*-BuLi in hexane (4.4 mL, 4.4 mmol) at -78 °C for 1 h. Butanoyl chloride (0.53 g, 5.0 mmol) was then added, and the mixture was warmed to r.t. and stirred overnight. After hydrolysis with sat. NaHCO₃ (ca. 45 mL), the organic layer was separated and the aqueous layer was extracted with Et₂O (3 × 12 mL). The combined organic extracts were washed once with H₂O and sat. NaCl, and then dried (anhyd MgSO₄). The solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica gel 60, Et₂O–hexane 10:90) to give **2** as white crystals; yield: 0.75 g (70%).

TADDOL Di-(*E*)-but-2-enoate (11); Typical Procedure (Method B):

A solution of TADDOL (1; 1.50 g, 3.2 mmol) in dry THF (14 mL) was cooled to 0 °C. Then, a 1.4 M solution of *n*-BuLi in hexane (5.5 mL, 7.68 mmol) was added slowly with a syringe. The mixture was stirred at r.t. for 30 min and cooled to 0 °C, and (*E*)-but-2-enoyl chloride (1.0 g, 0.9 mL, 9.6 mmol) was added slowly. A white precipitate (LiCl) formed immediately. The mixture was refluxed for 2 h and then stirred at r.t. overnight. After cooling to 0 °C, the reaction was quenched by the addition of sat. aq NaHCO₃ (ca. 50 mL). The organic layer was separated and the aqueous layer was extracted with Et₂O (3 × ca. 15 mL). The combined organic extracts were washed once with H₂O and sat. NaCl, and then dried (anhyd MgSO₄). The solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica gel 60, Et₂O–hexane 5:95) to give **11** as white crystals; yield: 1.45 g

(75%), and 12 as white crystals (Et_2O–hexane 7:93); yield: 0.17 g (10%).

TADDOL Diacrylate (7); Typical Procedure (Method C):

To a solution of **18** (2.02 g, 4.0 mmol) in dry toluene (40 mL) was added acrylic acid silver salt (1.50 g, 8.80 mmol). The preparation was carried out at r.t. under a nitrogen atmosphere and with magnetic stirring. The mixture was refluxed for 4 h and in the absence of light. The resulting AgCl was removed by filtration using a porous plate and washing the precipitate once with dry toluene. The filtrate was mixed with activated charcoal and then warmed up briefly in a rotatory evaporator. The solvent was distilled off under reduced pressure, and recrystallization (dry hexane) of the resulting solid gave **7** as white crystals; yield: 1.61 g (70%).

(4*R*,5*R*)-4,5-Bis[chloro(diphenyl)methyl]-2,2-dimethyl-1,3-dioxolane (18)

A solution of TADDOL (1; 6.0 g, 12.9 mmol), dry CHCl₃ (66 mL), and CaCO₃ (2.63 g, 26 mmol) was cooled to 0 °C under a nitrogen atmosphere and with magnetic stirring. Then, PCl₅ (7.14 g, 34 mmol) was added and the mixture stirred at r.t. overnight. A solution of sat. NaHCO₃ (ca. 100 mL) previously cooled to 0 °C was added to the mixture, which was then stirred vigorously until CO₂ evolution had ceased. The organic layer was separated, washed with H₂O and sat. NaCl, and then dried (MgSO₄). The filtrate was mixed with activated charcoal and then warmed up briefly in a rotatory evaporator. The solvent was distilled off under reduced pressure, and recrystallization (dry hexane) of the resulting solid gave **18** as white crystals; yield: 3.84 g (60%).

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