Concave Reagents. 20. Sterically Shielded *m*-Terphenyls as Selective Agents in General Protonations[1]

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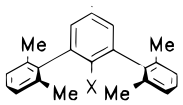
New *m*-terphenyls with acidic substituents in the 2′-position have been used in general protonations leading to reagent-controlled selectivity enhancements: up to 96:4 for the γ/α-protonation of unsymmetrically substituted allyl anions, up to 97:3 for the protonation of cyclohexyl anions generating preferentially the thermodynamically less stable *cis*-products. In order to allow a general, reagent-controlled protonation the acidity of the protonating agent should be as low as possible.

Most asymmetrically substituted carbon atoms have a hydrogen atom as one of the four different substituents. If this hydrogen atom could be attached selectively to a prochiral carbon atom, for instance by a reagent-controlled protonation, many enantio- and stereoselectivity problems would be solved. But there are always two mechanistic pathways possible for a kinetically controlled protonation: the *general* and the *specific protonation* (see Figure 1 and ref 2). The proton can either be transferred directly from the acid to the substrate (reagent control, *general protonation*) or the acid is only the source for the protons that are transferred to the substrate by the solvent or a cosolvent (shuttle mechanism, *specific protonation*). Therefore, reagents and reaction conditions have to be worked out to allow *general protonation* exclusively.

Selective protonations have been investigated thoroughly. Some progress has been made toward enantioselectivity[3] but even the problem of diastereoselective or regioselective protonation is not solved yet.[4] To increase the selectivities of protonations, concave acids and other sterically extremely shielded acids have been developed.[5] Concave acids (and the conjugate acids of concave bases) have been used to govern the diastereoselectivity[6] and the regioselectivity of the protonation of nitronate ions (C- vs O-protonation, "soft Nef-reaction"[7,8]).

In this work, we introduce 2′-substituted *m*-terphenyls as selective proton donors for diastereoselective and regioselective protonations.

Our concept of concave reagents[5,9,10] has taken the geometry of enzymes and has transferred it to standard reagents of organic chemistry like acids and bases.[11] In these reagents a macrocycle is spanned by a bridge carrying a functional group in such a way that a reaction only can occur on the inside of the bimacrocycle. The nature of this bridge is very important because conformations that allow the functional group to undergo reactions on the convex outside must be avoided. Bis-*ortho*-substituted phenyl derivatives ensure this, and very useful building blocks are 2′-substituted *m*-terphenyls such as **1**−**10**, especially if the outer aryl rings are also *ortho*-substituted.



	X
1	MgBr
2	I
3	Li
4	COOH
5	SOOH
6	SH
7	CH_2OH
8	SAc
9	SO_2Cl
10	CHO

Hart[12] developed a method to synthesize *m*-terphenyls that may be substituted in all *ortho*-positions of the outer aryl rings and developed ways to incorporate these into polymacrocycles. The key intermediate of Hart's method is the 2′-Grignard compound **1**, which can be quenched by iodine to give the 2′-iodide **2**.

Starting from the iodide **2**, we have synthesized various 2′-substituted *m*-terphenyls via the lithium compound **3**: open chain tetra-*o*-methyl derivatives **4**−**10**,[13] bimac-

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(1) Concave Reagents. 19. Ross, H.; Lüning, U. *Tetrahedron* **1996**, *52*, 10879−10882.

(2) For general and specific acid catalysis see: Maskill, H. *The Physical Basis of Organic Chemistry*; Oxford University Press: New York, 1993. For general and specific protonation see ref 20.

(3) Review: (a) Waldmann, H. *Nachr. Chem. Tech. Lab.* **1991**, *39*, 413−418. Recent examples: (b) Fehr, C.; Galindo, J. *Angew. Chem.* **1994**, *106*, 1967−1969; *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1888−1889. (c) Ishihara, K.; Kaneda, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 11179−11180. (d) Fuji, K.; Kawabata, T.; Kuroda, A.; Taga, T. *J. Org. Chem.* **1995**, *60*, 1914. (e) See the references in refs 3a−d, 4c.

(4) Examples for diastereoselective protonations of cyclic carbanions: (a) Hünig, S.; Keita, Y.; Peters, K.; v. Schnering, H. G. *Chem. Ber.* **1994**, *127*, 1495−1500. (b) Gerlach, U.; Haubenreich, T.; Hünig, S.; Keita, Y. *Chem. Ber.* **1993**, *126*, 1205−1215. (c) Krause, N. *Angew. Chem.* **1994**, *106*, 1845−1847; *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1764−1765 and references cited therein. For diastereoselective protonations of nitronate ions: (d) Zimmerman, H. E. ; Mariano, P. S. *J. Am. Chem. Soc.* **1968**, *90*, 6091−6096. (e) Zimmerman, H. E. *Acc. Chem. Res.* **1987**, *20*, 263−268. (f) See ref 6. Examples for regioselective protonations: (g) Tanaka, J.; Nojima, M.; Kusabayashi, S.; Nagase, S. *J. Chem. Soc., Perkin Trans. 2* **1987**, 673−678. (h) Ikeda, Y.; Ukai, J.; Ikeda, N.; Yamamoto, H. *Tetrahedron* **1987**, *43*, 743−753.

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(8) Review for the Nef-reaction: Pinnick, H. W. *Org. React.* **1990**, *38*, 655−792.

(9) Lüning, U. *Liebigs Ann. Chem.* **1987**, 949−955.

(10) Our concept of concave reagents has been adopted, and "reaction bowls" have been synthesized: Goto, K.; Tokitoh, N.; Okazaki, R. *Angew. Chem.* **1995**, *107*, 1202−1203; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1124−1126.

(11) Recent reviews for enzyme mimics: (a) Kirby, A. J. *Angew. Chem.* **1996**, *108*, 769−790; *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 705−724. (b) Murakami, Y.; Kikuchi, J.; Hisaeda, Y.; Hayashida, O. *Chem. Rev.* **1996**, *96*, 721−758.

(12) Hart, H.; Vinod, T. K. *Top. Curr. Chem.* **1994**, *172*, 119−178.

(13) Lüning, U.; Baumgartner, H. *Synlett* **1993**, 571−572.

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rocyclic *m*-terphenyl carboxylic acids,[14] a bimacrocyclic sulfinic acid,[15] and a bimacrocyclic thiol acetate.[13] Other nonmacrocyclic *m*-terphenyl-2′-carboxylic acids have been investigated by Siegel[16] and others.[12,17]

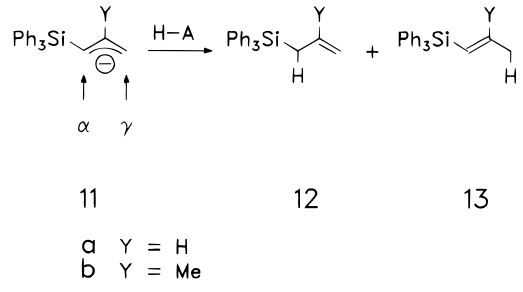
In the bimacrocyclic 2′-substituted *m*-terphenyls as well as in the open-chain precursors the functional groups are sterically well shielded. Although in bimacrocylic *m*-terphenyls the shielding of a functional group in the 2′-position is much larger than in the open-chain precursors (see methyl carboxylate cleavages[14b]), a tetra-*o*-substitution of a 2′-substituted *m*-terphenyl has still a strong steric effect (for reaction retardations of a sulfonyl chloride and a carbaldehyde oxime see ref 13, for cleft molecules see ref 18).

We have therefore investigated tetra-*o*-methyl-*m*-terphenyls carrying an acidic function in the 2′-position in protonation reactions. In addition to the 2′-carboxylic and sulfinic acids **4** and **5** for which the acidities have been determined,[15,16] also the 2′-thiol **6** and the 2′-carbinol **7** can also be used as proton sources if the pK_a of the anion to be protonated is large enough.

In two model reactions (protonation of the anions **11** and **16**) we have investigated *m*-terphenyl derivatives as acids and compared them to other acids.

Regioselective Protonation of Allyl Anions

If an unsymmetrical allyl anion is protonated, two products are possible because the proton can attack the α- or the γ-position. Using the (triphenylsilyl)allyl anion **11a**[19] as a model compound, specific reagents and reaction conditions for a selective protonation have been found to produce the allyl or the vinyl compounds **12a** or **13a** selectively in large excesses.[20] While most acids led to a mixture of **12a** and **13a**, 2,6-di-*tert*-butylphenol (**14a**) formed the vinyl compound **13a** with a 9:1 selectivity presumably caused by steric control.



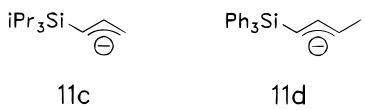


Table 1. Regioselectivities of the Protonation of the Allyl Anions 11a and 11b by Various Acids[22]

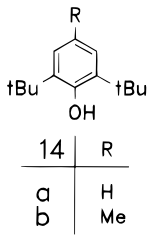
acid	12a:13a	12b:13b	ref
14b (R = Me)	3:97		*a*
6 (X = SH)	4:96		*a*
14a (R = H)	7:93	21:79	20/*a*
4 (X = COOH)	9:91		*a*
7 (X = CH_2OH)	10:90		*a*
thiophenol	20:80		*a*
5 (X = SOOH)	20:80		*a*
2,2,5,5-tetramethylcyclopentanol[23]	25:75		*a*
2′-hydroxy-5′-nitro-*m*-terphenyl[24]	32:68		25
2,6-dimethylphenol	34:66		*a*
tert-butyl alcohol	36:64		
benzoic acid	37:63		*a*
benzyl alcohol	39:61		
15[14a]	53:47		*a*
diethyl malonate	90:10	80:20	20/*a*

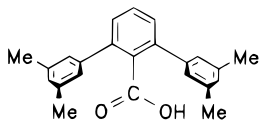
[a] This work.

A reversed regioselectivity was observed when malonates were used as protonating species. The α-protonated product **12a** was formed in excesses of up to 9:1.[20] An explanation for this reversed selectivity may be the formation of complexes between the malonates and the lithium ions in the contact ion pairs prior to the proton transfer from the malonate to the anion **11a**.

The nature of lithium−**11a** aggregates plays an important role for α- and γ-selectivity of the protonation. The reaction is very sensitive to solvent or stoichiometry changes and to the addition of co-solvents. With diethyl ether as solvent and a 1:2:2.5 stoichiometry of **12**:HMPT:*n*-BuLi, reagent-controlled protonations were possible.[20] This stoichiometry has been used in this work, as well (see Table 1).

Variation of the substituents at the silicon atom (**11c**) or in the γ-position of the allyl anion (**11d**) led to substrate-controlled α/γ-selectivities. Change of the proton sources from 2,6-di-*tert*-butylphenol (**14a**) to diethyl malonate had no influence on the α/γ-selectivities: <10:>90 for **11c**, >90:<10 for **11d**.[21]





We have now applied *m*-terphenyls carrying acidic functionalities in the 2′-position in the protonation of **11a** and a second allyl anion **11b**. The regioselectivities are compared in Table 1.

Table 1 clearly shows that the preference of the γ-protonation cannot only be achieved by changing the methyl groups of 2,6-dimethylphenol to *tert*-butyl groups (**14**[20]). The **13**/**12**-selectivity of other acids is also strongly increased when the acidic function (thiol, carboxylic acid, or methanol) is located in the 2′-position of a tetra-*o*-

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(19) (a) Corriu, R.; Masse, J. *J. Organomet. Chem.* **1973**, *57*, C5−C8. (b) Corriu, R. J. P.; Masse, J.; Samate, D. *J. Organomet. Chem.* **1975**, *93*, 71−80.

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(21) Meynhardt, B. Diploma Thesis, Universität Kiel, 1995.

(22) **13a** can be formed as the *cis*- or *trans*-isomer, but only *trans*-**13a** has been detected.

(23) Synthesis: Beckwith, A. L. J.; Lawrence, T. *J. Chem. Soc. Perkin Trans. 2* **1979**, 1535−1539. We thank Dr. M. Gelbert for a sample.

(24) Synthesis: Johnson, B. P.; Gabrielsen, B.; Matulenko, M.; Dorsey, J. G.; Reichardt, C. *Anal. Lett.* **1986**, *19*, 939−962.

(25) Wangnick, C. Ph.D. Thesis, Universität Freiburg, 1991.

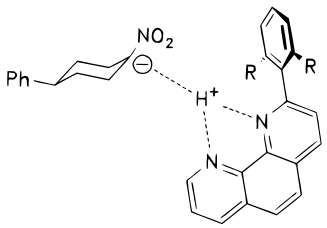
methyl-*m*-terphenyl (**6**, **4**, **7**). 2′-Hydroxy-5′-nitro-*m*-terphenyl and the 3,3″,5,5″-substituted acid **15** only formed **13a** and **12a** in a 2:1 and 1:1 ratio, respectively. The tetra-*ortho*-substitution is necessary to obtain **13**/**12**-selectivities of >90:<10. Thiol **6** was the most selective *m*-terphenyl, reflecting the slightly higher selectivity of thiophenol in comparison to benzoic acid and benzyl alcohol.

The selectivity increase can be rationalized by the geometry of the tetra-*ortho*-substituted *m*-terphenyls **4**, **6**, and **7**. The tetra-*ortho*-substitution leads to an almost perpendicular twist between the aryl rings of the *m*-terphenyl.[16b]

It is remarkable that the **13**/**12**-selectivities obtained with the *m*-terphenyls **4**, **6** and **7** do not vary much although the acidity of the functional group in the 2′-position varies from alcohol (**7**) to carboxylic acid (**4**). Only the use of the most acidic proton source, the sulfinic acid **5**, leads to a smaller selectivity. Whether this is a result of its acidity or of its hygroscopic behavior cannot be answered. But the almost nonexisting acidity dependence of the selectivities is in contrast to the results observed for the protonation of the cyclohexyl anion **16** where a strong dependence of the selectivities on the acidity of the proton source was observed.

Diastereoselective Protonation of Cyclohexyl Anions

If a carbanion is part of a ring system that carries appropriate substituents protonation can lead to *cis*- and *trans*-isomers.[4] The *cis*/*trans*-ratio should be controllable if a general protonation was possible. By using buffers of substituted 1,10-phenanthrolines, a *cis*-selective general protonation of cyclic nitronate ions is possible.[6] Due to the concave wrapping of the proton transferred from the protonated 1,10-phenanthroline to the nitronate ion, the thermodynamical less stable *cis*-products were formed in large excess (>12:1). This contrathermodynamic protonation is favored because the smallest substituent in the product, the proton, is a very large pseudosubstituent in the transition state when it is still partly bound to the shielded 1,10-phenanthroline.



We have tried to extend this selective protonation to ester stabilized cyclic carbanions for which diastereoselective protonations have already been investigated by Hünig et al.[4b] (see Table 2). In the case of the methyl ester they found remarkable "uniform" *cis*/*trans*-selectivities (max 73:27).

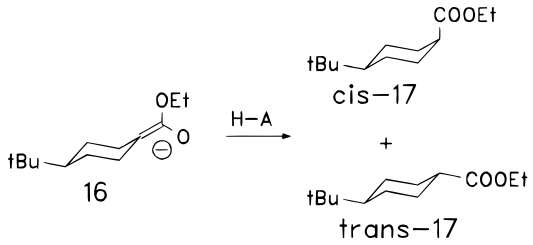
The protonations of the *tert*-butyl-substituted ester enolate **16**[26] with the *m*-terphenyl acid **4** or even the *m*-terphenyl thiol **6** hardly showed any selectivities.

(26) To deprotonate **17** LDA was used, although problems in selective deuterations have been encountered when LDA has been used: (a) Seebach, D. *Angew. Chem.* **1988**, *100*, 1685−1715; *Angew Chem., Int. Ed. Engl.* **1988**, *27*, 1624−1654. (b) Mohrig, J. R.; Lee, P. K.; Stein, K. A.; Mitton, M. J.; Rosenberg, R. E. *J. Org. Chem.* **1995**, *60*, 3529−3532.

Table 2. *cis*/*trans*-Ratio of the Ester 17 after Protonation of the Lithium Enolate 16 by Various Acids at RT in THF and THF/DMF (4:1)

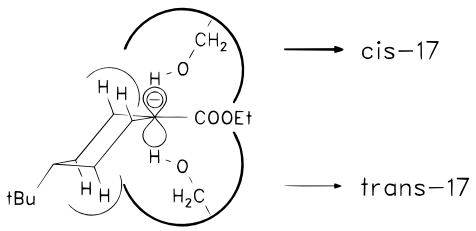
	cis-17/*trans*-17	
acid	THF	THF/DMF (4:1)
7 (X = CH_2OH)	94:6	97:3
triphenylmethanol	81:19	81:19
6 (X = SH)	64:36	
tert-butyl alcohol	58:42	
4 (X = COOH)		54:46
14b (R = Me)	51:49	50:50
benzyl alcohol	51:49	

Also, the di-*tert*-butylphenol **14b** was unselective, even at low temperature (−70 °C, **14b**: *cis*-**17**/*trans*-**17** 53:47). But the use of alcohols that are less acidic proton sources was successful in the diastereoselective protonation of **16**. The best result was obtained with the *m*-terphenyl methanol **7** that formed the *cis*-product in an excess of ≥94:<6.



As Table 2 shows, good selectivities have only been found for acids that are sterically shielded *and* have a relatively low acidity. Steric shielding alone is not sufficient for a *cis*-selective protonation of **16**. In the thiol **6** the proton is more shielded than in the methanol **7** because the distance between the aryl ring and the proton is one atom longer in the alcohol **7**. But **7** gives the larger *cis*/*trans*-ratio. When the alcohol **7**, the thiol **6**, and the acid **4** are compared with one another there is a clear trend: the more acidic the *m*-terphenyl the more unselective is the protonation.

Table 2 also compares different alcohols. The *cis*-selectivity increases from the nonshielded benzyl alcohol via *tert*-butyl alcohol and triphenylmethanol to the *m*-terphenyl alcohol **7**. The contrathermodynamic *cis*-selectivity of the protonation by **7** can be understood if the transition states leading to *trans*- and *cis*-**17** are looked at. As for the *cis*-selective protonation of a cyclic nitronate ion,[6] the smallest substituent in the product, the proton, is a very large pseudosubstituent in the transition state when it is still partly bound to the alcohol. In the pseudoequatorial attack leading to *cis*-**17**, the interaction with adjacent hydrogen atoms of the cyclohexane ring is smaller. Therefore, this pathway dominates.



For the protonation of other anions like the allyl anion **11** or the nitronate anions by sterically shielded acids, no acidity dependence has been observed. A possible

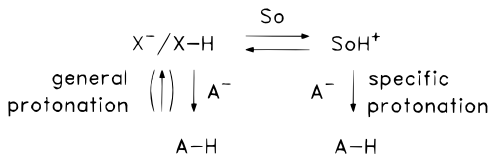


Figure 1. General and specific protonation of an anion A^-. Direct proton transfer from the acid of the buffer (XH) to the anion A^- leads to reagent-controlled general protonation, while dissociation of the acid and proton transfer via the protonated solvent $So{\cdot}H^+$ gives a specific protonation that is not controllable by the nature of the reagent.

explanation is given in Figure 1. In all protonations the two pathways, the general and the specific protonation,[2] have to be looked at. Only a general protonation will lead to a reagent-controlled protonation.

In the solution of the proton source, the protons may be bound to the protonating agent (XH) or to the solvent ($So{\cdot}H^+$). The equilibrium depends on the acidity of the buffer acid *and* on the basicity of the solvent. If other bases, e.g., cosolvents (So′), are present in solution they also may act as proton shuttles, and one more species capable of protonating the anion A^- is present ($So'{\cdot}H^+$). Furthermore, the rate of reaction between the anion and the protonated solvent will depend on the basicity of the anion. These relations may explain the experimental findings.

To estimate the reaction rates for the general and the specific protonation the rate constants as well as the concentrations of XH and $So{\cdot}H^+$ have to be known. If the protonating acid becomes more acidic the equilibrium will be shifted from XH to $So{\cdot}H^+$, increasing the rate for the specific protonation (see Table 2: **7**, **6**, **4**). The XH/$So{\cdot}H^+$ equilibrium will also shift toward $So{\cdot}H^+$ (and $So'{\cdot}H^+$) if the basicity of the solvent/cosolvent increases [diethyl ether/HMPT (Table 1) vs THF/diisopropyl amine (Table 2)]. Therefore, the allyl anions **11** can be selectively protonated by *m*-terphenyls with varying acidity, while the selective protonation of **16** is restricted to the alcohol **7**.

In order to understand the results of the nitronate ion protonation[6] the basicity of the anions have to be compared. Nitro compounds are much more acidic than allyls and esters. Therefore, a larger concentration of $So{\cdot}H^+$ would be necessary to protonate a nitronate ion with the same rate as the ions **11** and **16**.

As a result of these investigations the following requirements for selective reagent-controlled protonations have to be met: (i) the solvent and all cosolvents should be as slightly basic as possible, (ii) the acidity of XH should be as low as possible, but it must be guaranteed that the conjugate base of the buffer will not be able to deprotonate the product AH.[27] Otherwise, a thermodynamically controlled protonation instead of a kinetically and reagent-controlled protonation would occur.

m-Terphenyls seem to do this task because their acidity can be varied widely while keeping the shielding comparable. Substitution with *tert*-butyl groups[14,28] increases the solubility of *m*-terphenyls even in very unpolar solvents.

Experimental Section

For general remarks see ref 29.

(27) Reference 3d and references cited therein.
(28) Kühl, C. Diploma Thesis, Universität Kiel, 1995.
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2,2″,6,6″-Tetramethyl-*m*-terphenyl-2′-carbaldehyde (10). Under nitrogen, 8.7 mL (20.0 mmol) of a 2.3 M solution of *n*-butyllithium in *n*-hexane was added to a solution of 8.28 g (20.0 mmol) of *m*-terphenyl iodide **2** in 50 mL of dry cyclohexane. A colorless precipitate formed. After the mixture was stirred at rt for 15 h, 7.0 mL (6.7 g, 100 mmol) of dry DMF was added to the suspension at 0 °C within 5 min under nitrogen. During stirring at rt for an additional 3 h, the mixture became more viscous. After hydrolysis with 50 mL of water, the mixture was extracted with diethyl ether (100 mL total). The organic layer was washed with water (50 mL twice). After evaporation of the solvent, the remaining slightly yellow material was recrystallized from *n*-hexane yielding 3.82 g of **10** as thin colorless needles, mp 145 −146 °C (*n*-hexane, dec). IR (KBr): ν 1695 (C=O), 1570 (arom). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.98 (s, 12 H), 7.10 (d, J = 8.0 Hz, 4 H), 7.15−7.30 (m, 4 H), 7.66 (t, J = 8.0 Hz, 1 H), 9.61 (s, 1 H). MS (EI, 70 eV): *m*/*z* 314 (5), 299 (12), 296 (100), 281 (46), 266 (14), 165 (28). Anal. Calcd for $C_{23}H_{22}O$ (314.44): C, 87.86; H, 7.05. Found: C, 87.86; H, 7.04.

2,2″,6,6″-Tetramethyl-*m*-terphenyl-2′-methanol (7). (a) By Reaction of 3 with Gaseous Formaldehyde. Under nitrogen, 3.0 mL (7.5 mmol) of a 2.5 M solution of *n*-butyllithium in *n*-hexane was added to a solution of 2.80 g (7.00 mmol) of **2** in 20 mL of dry cyclohexane. A yellow color appeared quickly, and a colorless solid precipitated. After 15 h of stirring at rt, the solvents were evaporated under nitrogen with reduced pressure and the residue was dried in vacuo. The lithium salt **3** was dissolved at −50 °C in 20 mL of dry diethyl ether and stirred for 10 min. In a second flask ca. 5 g (ca. 0.17 mol) of dry paraformaldehyde (previously dried for several days in a vacuum desiccator over P_4O_{10}) was heated to 180 °C, and the developing formaldehyde was transported by a slight nitrogen flow into the solution of **3**, which was vigorously stirred at −50 °C. After complete depolymerization of the paraformaldehyde, the turbid reaction mixture was hydrolyzed by addition of 50 mL of ice−water and stirred at rt for 30 min. The mixture was filtered and extracted with diethyl ether (100 mL total), and the organic layer was washed with water (twice 50 mL) and dried with $CaCl_2$. After evaporation of the solvents, a slightly yellow oil remained from which colorless needles crystallized at −18 °C. Recrystallization from *n*-hexane gave 1.30 g (59%) of fine colorless crystals, mp 161−162 °C (*n*-hexane).

(b) By Reduction of 10 with $LiAlH_4$. A 1.50 g (4.78 mmol) portion of **10** dissolved in 30 mL of dry diethyl ether was added within 1.5 h to a refluxing suspension of 181 mg (4.77 mmol) of lithium aluminum hydride in 25 mL of dry diethyl ether. After being refluxed for 2 h, the mixture was carefully hydrolyzed. Aluminum hydroxide was dissolved by addition of 30 mL of 10% H_2SO_4 solution. The organic layer was washed with 100 mL of water, and the water layer was extracted twice with diethyl ether (100 mL total). The combined organic layer was dried with $CaCl_2$. After evaporation of the solvent 1.5 g of crude product yielded 1.35 g (89%) of **7**as colorless crystals by recrystallization from *n*-hexane, mp 159−160 °C (*n*-hexane). IR (KBr): ν 3522 (OH), 1579 (arom). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.95 (s, 12 H), 3.77 (s, 2 H), 3.98 (s, 1 H), 6.98 (d, J = 8 Hz, 2 H), 7.06−7.18 (m, 6 H), 7.45 (t, J = 8 Hz, 1 H). ^{1}H-NMR (250 MHz, $CDCl_3$): δ 2.06 (s, 12 H), 4.04 (s, 2 H), 7.10 (d, J = 8 Hz, 2 H), 7.20−7.30 (m, 6 H), 7.46 (t, J = 8 Hz, 1 H). MS (EI, 70 eV): *m*/z 316 (M^+, 5), 298 (100), 283 (59), 268 (22), 253 (21). Anal. Calcd for $C_{23}H_{24}O$ (316.46): C, 87.30; H, 7.64. Found: C, 87.19; H, 7.63.

(c) By Reduction of 4 with $LiAlH_4$. Under nitrogen 40 mL of dry THF was added to 277 mg (0.839 mmol) of **4** and 159 mg (4.19 mmol) of $LiAlH_4$. The mixture was refluxed. After being refluxed for 5 d the mixture was hydrolyzed with 50 g of ice, extracted with 100 mL of dichloromethane, and dried with $MgSO_4$. Evaporation gave a solid that was recrystallized from *n*-hexane to give 204 mg (77%) of colorless crystals.

2,2″,6,6″-Tetramethyl-*m*-terphenyl-2′-sulfonyl Chloride (9). Under nitrogen 4.4 mL (10.0 mmol) of a 2.2 M solution of *n*-butyllithium in *n*-hexane was added to a solution

of 4.14 g (10.0 mmol) of **2** in 30 mL of dry cyclohexane. The mixture turned yellow, and a colorless solid precipitated. After the mixture was stirred for 15 h at room temperature, the solvents were evaporated under nitrogen with reduced pressure and the residue was dried in vacuo. At −50 °C the lithium salt was dissolved in 20 mL of dry diethyl ether and stirred for 10 min. This solution was thoroughly stirred, and 0.93 mL (1.55 g, 11.5 mmol) of freshly distilled sulfuryl chloride (bp 68−69 °C) was added through a septum within 1 min. The solution turned yellow to red. After being stirred for 1 h at −50 °C, the mixture was slowly warmed to rt, stirred for 2 h, poured onto 50 mL of saturated $NaHSO_4$ solution, and extracted with diethyl ether (70 mL total). The organic layer was washed with 50 mL of water and dried with $CaCl_2$. Evaporation of the solvent gave 3.7 g of a slightly red product that was recrystallized from a small amount diethyl ether. Yield: 2.86 g (75%) (55% yield in a 0.1 mol batch). Mp: 215−216 °C (diethyl ether), 231 °C [after chromatography, silica gel/cyclohexane/dichloromethane (1:1)]. IR (KBr): ν 1567 (arom), 1172 (S=O). ^{1}H-NMR (250 MHz, $CDCl_3$): δ 2.08 (s, 12 H), 7.11−7.30 (m, 8 H), 7.77 (t, J = 7.7 Hz, 1 H). MS (EI, 70 eV): *m*/*z* 386, 384 (M^+, 4, 12), 350 (1), 319 (6), 40 (100). Anal. Calcd for $C_{22}H_{21}ClO_2S$ (384.94): C, 68.65; H, 5.50. Found: C, 68.56; H, 5.44.

2,2″,6,6″-Tetramethyl-*m*-terphenyl-2′-sulfinic Acid (5). (a) See ref 13. (b) By Reduction of 9 with $LiAlH_4$. A 322 mg (8.48 mmol) portion of $LiAlH_4$ suspended in 20 mL of diethyl ether was added to a refluxing solution of 1.35 g (3.50 mmol) of **9** in 80 mL of dry diethyl ether. Because TLC after 3 h showed that the reaction was not complete, an additional 188 mg (4.95 mmol) of $LiAlH_4$ was added, and the mixture was refluxed for an additional 12 h. After hydrolysis with 50 mL of water, the mixture was acidified with ca. 100 mL of 2 N HCl. The organic layer was washed twice with 100 mL of water and dried with $CaCl_2$. Concentration to dryness gave a colorless solid that was recrystallized from cyclohexane/ethyl acetate (1:1), yielding 625 mg of **5** as fine colorless needles, mp 173 °C (cyclohexane/ethyl acetate, dec).

2,2″,6,6″-Tetramethyl-*m*-terphenyl-2′-thiol Acetate (8). A 3.0 g (7.8 mmol) portion of **9** was added to a boiling mixture of 20 mL of acetic acid p.a., 3 mL of acetic anhydride, 600 mg (19.4 mmol) of red phosphorus, and 40 mg (0.32 mmol) of iodine. The red mixture was refluxed for 15 h, and then the remaining red phosphorus was filtered off. The solution was mixed with 100 mL of dichloromethane and 100 mL of 10% sodium dithionite solution. The organic layer was washed twice with 100 mL of Na_2CO_3 solution and 100 mL of 10% NaCl solution. After the organic layer was dried with $MgSO_4$, the solvent was evaporated and the remaining brown-green oil was dissolved in *n*-hexane and filtered. Storage at −18 °C gave 2.24 g (80%) of slightly red crystals, mp 130 °C (*n*-hexane). IR (KBr): ν 1705 (C=O). ^{1}H-NMR (250 MHz, $CDCl_3$): δ 1.81 (s, 3 H), 2.02 (s, 12 H), 7.06 (d, J = 7.3 Hz, 4 H), 7.09−7.21 (m, 4 H), 7.55 (t, J = 7.7 Hz, 1 H). MS (EI, 70 eV): *m*/*z* 360 (M^+, 26), 318 (82), 303 (100), 288 (22). Anal. Calcd for $C_{24}H_{24}OS$ (360.53): C, 79.96 H, 6.71. Found: C, 79.93; H, 6.70.

2,2″,6,6″-Tetramethyl-*m*-terphenyl-2′-thiol (6). (a) By Basic Hydrolysis of 8. A 9.23 g (25.6 mmol) portion of **8** was mixed with 140 mL of water/ethanol (1:1) and 1.43 g (25.5 mmol) of KOH and refluxed for 7 h. After extraction with 250 mL of dichloromethane, the organic layer was washed with 50 mL of water and dried with $MgSO_4$. Evaporation of the solvents gave a solid that was recrystallized from a small amount of dry diethyl ether, yielding 6.52 g (80%) of **6**, mp 130 °C (diethyl ether).

(b) By Reduction of 5 with $LiAlH_4$. A 4.0 g (105 mmol) portion of $LiAlH_4$ was added to a solution of 7.10 g (20.2 mmol) of **5** in 100 mL of dry diethyl ether within 1 h. After being refluxed for 9 h and stirred at rt for 14 h, the mixture was poured carefully onto ice and extracted with 700 mL of diethyl ether. The organic layer was washed with 200 mL of water and dried with $CaCl_2$. Evaporation of the solvents gave a slightly yellow residue that was dissolved in a small amount of dichloromethane/cyclohexane (1:1) and filtered through silica gel (6 × 4 cm). The solvent was evaporated, and the colorless residue was recrystallized from little diethyl ether, giving 2.5 g (39%) of **6**.

(c) By Reduction of 9 with $LiAlH_4$. A 1.5 g (40 mmol) portion of $LiAlH_4$, suspended in 20 mL of diethyl ether, was added to a refluxing solution of 1.35 g (3.50 mmol) of **9** in 80 mL of dry diethyl ether within 1 h. After being refluxed for 2 d, the mixture was carefully hydrolyzed with 50 mL of water and acidified with 2 N HCl. The organic layer was washed twice with 100 mL of water and dried with $CaCl_2$. Evaporation of the solvent gave a colorless solid that was dissolved in a small amount of dichloromethane/cyclohexane (1:1) and filtered through silica gel (6 × 4 cm). After evaporation to dryness the solid was recrystallized from little diethyl ether, yielding 550 mg (49%) of **6** as colorless needles, mp 140 °C (diethyl ether). IR (KBr): ν 2557 (SH), 1575 (arom). ^{1}H-NMR (250 MHz, $CDCl_3$): δ 2.05 (s, 12 H), 2.97 (s, 1 H), 7.04 (d, J = 7.7 Hz, 2 H), 7.08−7.28 (m, 7 H). MS (EI, 70 eV): *m*/*z* 318 (M^+, 6), 303 (100), 288 (24). Anal. Calcd for $C_{22}H_{22}S$ (318.49): C, 82.97; H, 6.96. Found: C, 82.89; H, 6.97.

Deprotonation of 17 and Reprotonation. Under nitrogen, a 2.5 M solution of *n*-butyllithium in *n*-hexane (560 μL, 1.40 mmol) was added dropwise to a solution of diisopropylamine (180 μL, 1.40 mmol) in THF (4 mL) at 0−5 °C. The solution was stirred for 60 min. After addition of ester **17**[30] (100 mg, 472 μmol) in THF (1 mL), stirring was maintained for 60 min. The proton source (71 μmol) was dissolved in the solvents (200 μL) listed in Table 2. At rt the ester enolate solution (300 μL, 24 μmol) was added slowly with stirring, and the solution was stirred for another 14 h. Then a 0.1 M HCl solution (200 μL) was added, and the aqueous layer was extracted two times with 2 mL of diethyl ether. The solvents of the combined organic layers were evaporated, and the residue was dissolved in diethyl ether (200 μL) and analyzed by GC (SE 30, OV 101, or OV 17 capillary columns, no special conditions needed).

Unused ester enolate solution was treated with ethyl iodide (100 μL, 1.2 mmol) in THF to check for completion of deprotonation by GC analysis (less than 4% of ester **17** was detected).

Protonation of 11. **11** was protonated as previously described,[20] but the experiments were carried out on a slightly larger scale (200 μL of the anion solution). At least a 40-fold excess of the acid was used. The degree of deprotonation of **12**/**13** (generally >95%) was checked by alkylation of the resulting **11** with ethyl iodide. The GC analyses were carried out on a 25 m OV17 column connected to 25 m of OV 1701. Synthesis: **11a**,[31] **11b**,[32] **11c**,[33] **11d**.[34]

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