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Trityl radicals with a combination of the orthogonal functional groups ethyne and carboxyl: Synthesis without a statistical step and EPR characterization

Henrik Hintz,[†] Agathe Vanas,[§] Daniel Klose,[§] Gunnar Jeschke,[§] and Adelheid Godt[†,*]

[†]Faculty of Chemistry and Center for Molecular Materials (CM2); Bielefeld University, Universitätsstraße 25, 33615 Bielefeld, Germany.

[§]ETH Zurich, Lab. Phys. Chem., Vladimir-Prelog-Weg 2, 8093 Zurich, Switzerland.

ABSTRACT: Finland trityl radical (FTR) shows very attractive EPR spectroscopical properties for a manifold of applications. For most of its applications only one chemically reactive functional group is needed. The presence of three equally reactive carboxyl groups leads to FTR modifications through reactions which give statistical mixtures of onefold, twofold and threefold modified, and unmodified FTR. To avoid the side effects of such a statistical reaction - limited yields and separation challenges - we took a route to FTR-type trityl radicals with scaffold assembly by addition of an aryllithium with one type of substituent to a diarylketone with another type of substituent. This gave the two FTR-type trityl radicals **1** and **2** which carry a combination of the chemically orthogonal groups, carboxyl and triisopropylsilylethynyl. Standard column chromatography was sufficient for product isolation on all stages, whereby polar tagging helped. The EPR spectroscopical properties of the trityl radicals **1** and **2** in ethanol were determined in X and W band. Their g anisotropy and T_1 and T_2 relaxation times make them as good a spin label as the benchmark FTR. The paper discloses also details on the synthesis of building blocks used for FTR preparation and an improved access to the bare FTR scaffold.

Introduction

Persistent radicals are used as analytical tools and nitroxyl radicals have long been the first choice. Concomitant with more recent developments in the area of analytical techniques which rely on unpaired electron spins, persistent radicals with spectroscopical properties other than those of the nitroxides gained importance.[1] This brought the carbon-centered triarylmethyl radicals (trityl radicals, often simply called trityls) into focus.[2] The parent trityl radical, the triphenylmethyl radical (Chart 1), was prepared by Gomberg in 1900.[3]

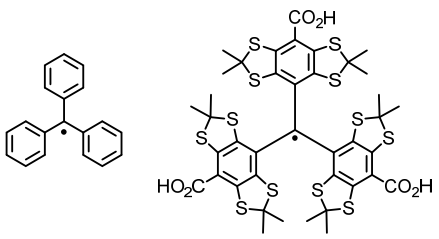


Chart 1. Gomberg's trityl radical (left) and Finland trityl radical (FTR; right).

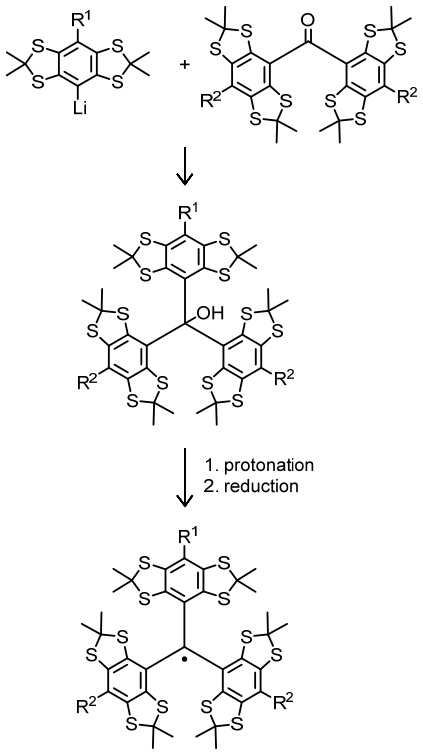
To meet the requirements for applications of trityl radicals in magnetic resonance imaging (MRI), requirements such as water solubility, stability in biological media, toxicological harmlessness, and a single and narrow electron paramagnetic resonance (EPR) line, Nycomed Innovation AB developed a family of tri(tetrathiaaryl)methyl (TAM) radicals whereof Finland trityl radical (FTR, Chart 1),[4,5] disclosed in 1996, is the most prominent one.

FTR is equipped with three carboxyl groups leading to good water solubility when deprotonated.[6] The bulky thioketal groups sterically shield the central carbon atom which carries most of the unpaired electron density and thus are made responsible for the chemical inertness of FTR.[7,8] FTR is remarkably resistant against reduction allowing EPR measurements in biological media and even in living cells.[9–12] Very importantly, FTR contains, in contrast to many other trityl radicals, no hydrogen atoms at the benzene rings. This way, strong broadening of the EPR signal due to coupling with hydrogen nuclear spins is avoided and FTR shows a single, very narrow EPR line[13] which makes techniques relying on signal broadening highly sensitive. Furthermore, FTR has long relaxation times in fluid

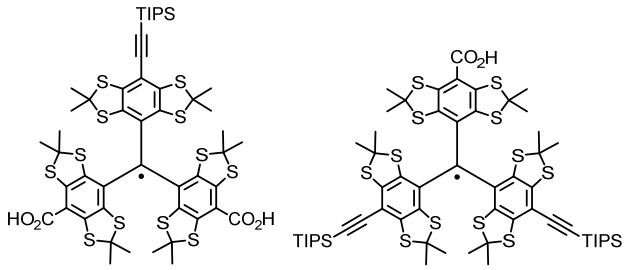
solutions.[14] Due to these favorable properties, FTR and variations thereof found widespread application: MRI,[4,5,15–17] EPR imaging,[16,18,19] EPR oximetry and pH measurement,[6,8,9,20–23] specific detection of the superoxide,[24–26] dynamic nuclear polarization,[27–30] and in a study on molecular diffusion in porous media.[31] More recently, FTR was recognized as a spin label for molecular structure elucidation[32,33] via distance determination with pulsed EPR techniques[34–42] and this application was investigated using non-biological model compounds[36,43,44] as well as oligonucleotides[45–50] and proteins.[12,33,51,52]

FTR is equipped with three carboxyl groups of equal reactivity, of which, in most applications, only one should react. Without any measures taken, the reaction of FTR with less than 3 equivalents of a reaction partner will result in a statistical mixture of unmodified FTR and onefold, twofold and threefold modified FTR. We call such a reaction a statistical reaction because of its close similarity with a statistical copolymerization. This approach was taken in the step of binding FTR to a target compound[45,47–50,53–58] as well as in reactions to obtain FTR derivatives which provide one selectively addressable functional group for binding to a target molecule.[8,12,21,33,43,52,56,59,60] To minimize the probability of multiple reactions of one FTR molecule in the former method, one may apply a large excess of FTR derivative as has been done in conjugation of FTR with an oligonucleotide using a 10-fold excess of the acid chloride of FTR.[49] The latter approach includes statistical ester[8,12,43] or amide formation[33,56] of FTR, statistical ester hydrolysis of the triester of Finland trityl alcohol, the precursor of FTR,[59,60] and statistical reduction of the alkoxycarbonyl group of the ester of the Finland trityl alcohol to a hydroxymethyl group.[21] Statistical ester formation and ester hydrolysis were used to protect two of the three carboxyl groups as alkoxycarbonyl groups.[8,12,43,59,60] Furthermore, the attachment of one functional group that can be selectively addressed in the presence of the residual two carboxyl groups, such as methanethiosulfonate, pyridin-2-yldisulfanyl, and propargyl and allyl moieties was achieved via a statistical ester or amide formation.[12,33,52] Because statistical reactions give product mixtures of starting trityl compound and its onefold, twofold and threefold modifications, yields will be medium to low and product isolation can become quite challenging. The only published access free of a statistical reaction to trityl radicals with the same scaffold as FTR (in the following called FTR-type trityl radicals) and with two types of functional groups is the nucleophilic substitution of one of the three carboxyl groups for a C, N, P or S nucleophile via oxidation of FTR to the corresponding trityl cation, addition of the nucleophile giving a quinone methide, loss of carbon dioxide and finally an oxidation step.[61–64] Similarly, FTR-type trityl radicals with one functional group were prepared via a trityl cation having the FTR scaffold but being void of carboxyl groups, the latter being formed through treatment of the corresponding trityl alcohol with an acid.[59,64]

Here we present an access to FTR-type trityl radicals in which statistical reactions are circumvented through assembly of a trityl alcohol by addition of an aryllithium with one type of substituent to a diarylketone with another type of substituent (Scheme 1). Trityl alcohols are the precursors of trityl radicals, into which they are converted through subsequent addition of a strong acid and a reducing agent. The addition of an organolithium or organomagnesium compound to a ketone is a common access to tertiary alcohols $R_2R'COH$ with $R \neq R'$. In this way, Rajca et al. assembled the scaffold of di- and tetraradicals consisting of triphenylmethyl units.[65,66] However, there is no report on its application to the synthesis of FTR-type trityl alcohol with at least two different substituents, that we are aware of.



Scheme 1. Assembly of FTR-type trityl radicals having two different types of substituents through addition of an aryllithium to a diarylketone and subsequent conversion of the product, trityl alcohol, into the trityl radical.



trityl[CO_2H/CO_2H/CCTIPS] (**1**) trityl[CO_2H/CCTIPS/CCTIPS] (**2**)

Chart 2. The trityl radicals 1 and 2. TIPS = triisopropylsilyl.

Using this method, the trityl radicals trityl[CO_2H/CO_2H/CCTIPS] (**1**) and trityl[CO_2H/CCTIPS/CCTIPS] (**2**) ("trityl" stands for the FTR scaffold, the substituents at the positions of the carboxyl groups of FTR are defined in brackets; Chart 2) were synthesized. Their chemically orthogonal functional groups, the carboxyl group and the triisopropylsilyl (TIPS) substituted ethyne moiety, hold the potential to selectively attach the trityl radicals to a molecule of interest via the functional group of which only one is present, e. g. to attach trityl[CO_2H/CCTIPS/CCTIPS] (**2**) via an ester or amide bond formation or trityl[CO_2H/CO_2H/CCTIPS] (**1**), after removal of the TIPS group, through a 1,3-dipolar azide-alkyne cycloaddition. The other two functional groups can be used for any other purpose, for example to gain water solubility of the compounds, which is of importance when it comes to application in studies on biomolecules. All steps in the syntheses of the trityl radicals **1** and **2** can be performed with gram amounts and standard column chromatography provides pure compounds. The EPR spectroscopical properties of the trityl radicals **1** and **2** in X and W band make them as attractive as FTR for applications.

The paper is organized as follows. First the matter of the functional groups is addressed and then details of the individual synthetic steps are presented. Finally the EPR spectroscopical data of the trityl radicals **1** and **2** including a comparison with the data of FTR are presented.

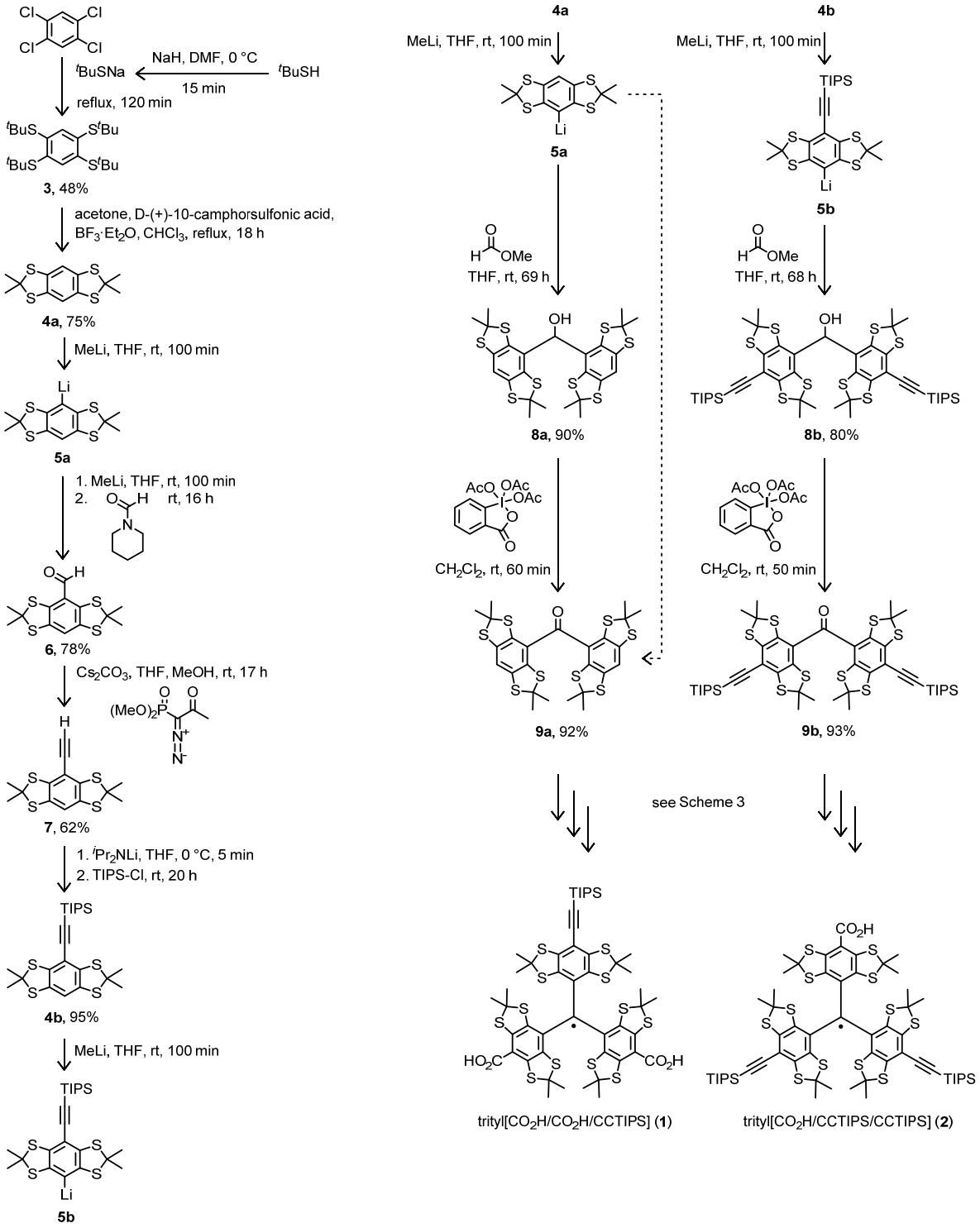
Results and discussion

Crucial for the success was the decision on the type of the functional groups and on when to install them. At least one of the functional groups needed to be already installed in one of the building blocks, the aryllithium compound or the diarylketone. This functional group has to tolerate organolithium compounds in the addition step as well as strong acidic and mild reductive conditions during radical formation. The TIPS protected ethyne group was expected to fulfill these requirements. The other functional group could, in principle, be already present in one of the building blocks or could be installed after scaffold assembly via modification of the trityl alcohol or the trityl radical. To meet the goal of orthogonal reactivity of the functional groups the carboxyl group was chosen as the second functional group. Due to its incompatibility with organolithium compounds it was introduced after scaffold assembly at the stage of the trityl alcohol via lithiation. It was attached in the form of a *tert*-butoxycarbonyl group. In doing so, the isolation of the target compounds was simply achieved through standard column chromatography because of lower polarity of the *tert*-butyl ester as compared to the carboxylic acid. The *tert*-butoxycarbonyl group was converted into the desired carboxyl group concomitant with the generation of the conversion of trityl alcohol into trityl radical.

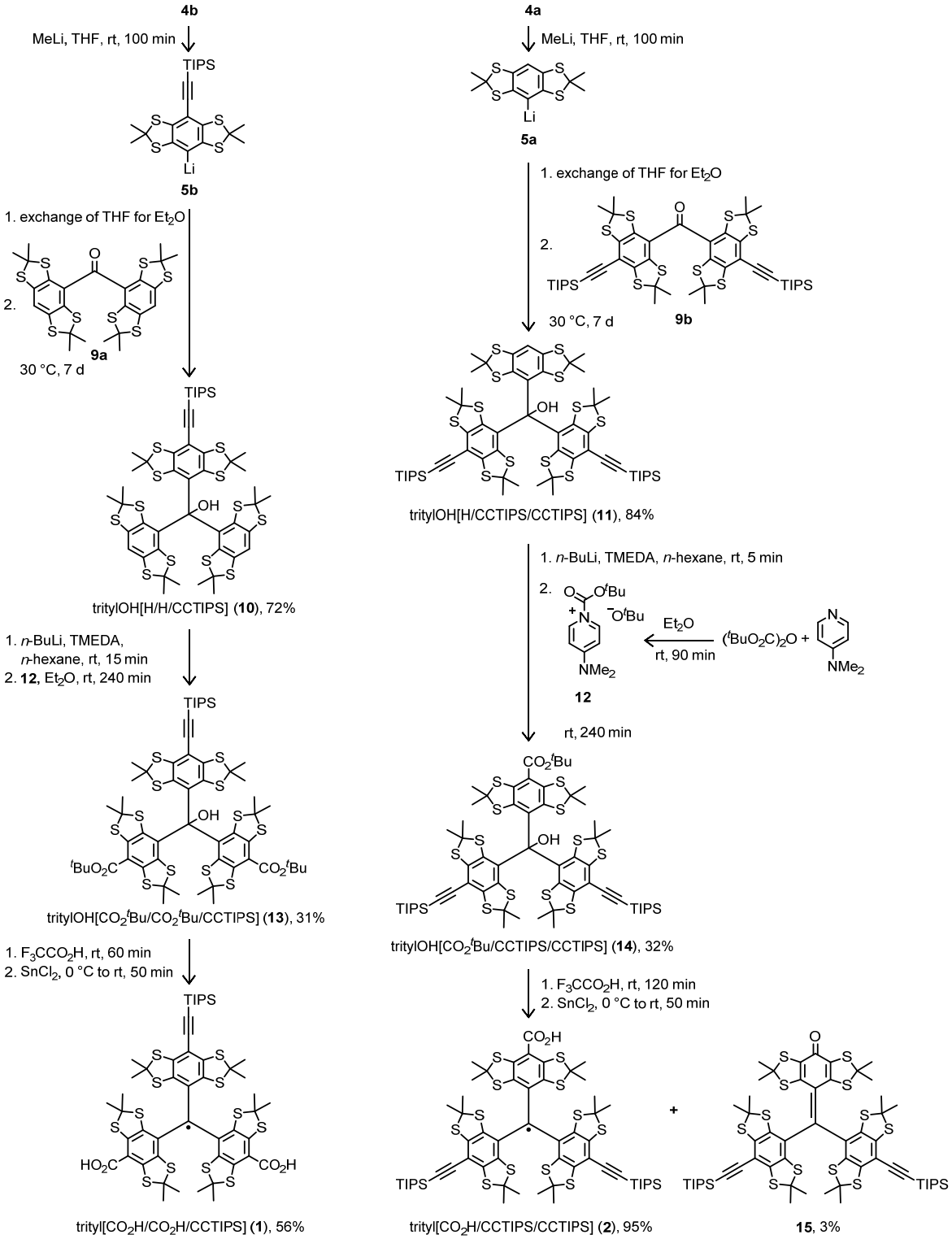
The overall synthetic routes are displayed in Schemes 2 and 3. A look on them reveals unsubstituted tetrathiobenzene **4a** and TIPS-ethyne substituted tetrathiobenzene **4b** as the basic building blocks, their deprotonation at the benzene ring to obtain lithiated tetrathiobenzenes **5a** and **5b** as a central step, diarylketones **9a** and **9b** as key synthetic intermediates, and the reaction of diarylketones **9** with lithiated tetrathiobenzenes **5** as pivotal for the assembly of the trityl scaffold.

Tetrathiobenzenes 4 and their deprotonation

Tetrathiobenzene **4a** was synthesized starting from 1,2,4,5-tetrachlorobenzene (Scheme 2). Nucleophilic aromatic substitution on 1,2,4,5-tetrachlorobenzene with sodium *tert*-butylthiolate following essentially the procedure of Reddy et al. gave tetrathioether **3**.[67] Only sodium was replaced with sodium hydride for the deprotonation of *tert*-butylthiol, a change leading in our hands to a product of higher purity. We observed that a longer reaction time lowered the yield. Heating to reflux for 2 h gave a yield of 48%, the extension of the reaction time to 6 h reduced the yield to 37%, after 15 h only 14% product were obtained, and after 63 h no product was isolated. During heating a slight but steady gas evolution was noticed. Hence, we assume that tetrathioether **3** degrades by thermally induced cleavage of the *tert*-butylthio group whereby isobutene is released. Tetrathioether **3** was converted into tetrathiobenzene **4a** following a procedure of Rogozhnikova et al.[61]

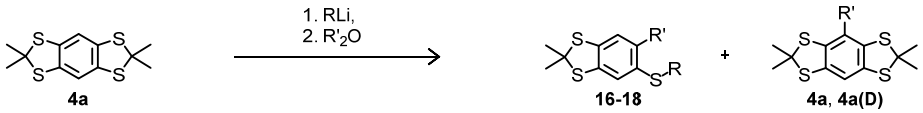


Scheme 2. Syntheses and deprotonation of the tetrathiobenzenes 4 and formation of diarylketones 9. Dashed arrow: Attempts to synthesize diarylketone 9a by addition of phosgene, methyl chloroformate, or dimethylcarbonate to lithiated tetrathiobenzene 5a gave diarylketone 9a only in low yields and in mixture with other products. Lithiated tetrathiobenzenes 5 were not isolated. Methyllithium was applied as a solution in diethylether, lithiumdiisopropylamide as a solution in tetrahydrofuran/*n*-heptane/ethylbenzene. TIPS = triisopropylsilyl, rt = room temperature.



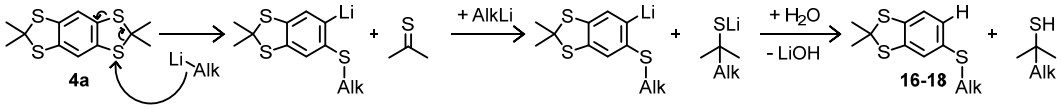
Scheme 3. Assembly of trityl[CO2H/CO2H/CCTIPS] (1) and trityl[CO2H/CCTIPS/CCTIPS] (2). Lithiated tetrathiobenzenes 5 and reagent 12 were not isolated. Methyllithium was applied as a solution in diethylether and butyllithium was applied as a solution in hexanes. TMEDA = tetramethylethylenediamine, rt = room temperature.

Table 1. Molecular ratio of the products from treatment of tetrathiobenzene 4a with *n*-BuLi, *s*-BuLi, or *t*-BuLi determined by ^{1}H NMR spectroscopy.



lithiation condition	R'$_2$O	trithiobenzene	R	R'	molecular ratio of trithiobenzenes **16-18** and tetrathiobenzene **4a**		
1.0 eq. *n*-BuLi[b], Et_2O, rt, 30 min	H_2O	**16**	*n*-Bu	H	17	:	83
1.2 eq. *n*-BuLi[b], Et_2O, 0 °C, 30 min	D_2O	**16, 16(D)**	*n*-Bu	H, D	3	:	97[a]
1.0 eq. *s*-BuLi[c], Et_2O, rt, 30 min	H_2O	**17**	*s*-Bu	H	26	:	74
1.0 eq. *t*-BuLi[d], Et_2O, -20 °C, 30 min	H_2O	**18**	*t*-Bu	H	43	:	57

[a]Protonated and deuterated compounds were not differentiated; [b]solution in hexanes; [c]solution in n-hexane/cyclohexane; [d]solution in heptane



Scheme 4. Proposed mechanism for the formation of trithiobenzenes 16-18 in the reaction of tetrathiobenzene 4a with alkyllithium in diethyl ether.

To use tetrathiobenzene **4a** for diarylketone and trityl alcohol formation as well as to generate TIPS-ethyne substituted tetrathiobenzene **4b**, it had to be lithiated. Commonly, the lithiation is carried out with *n*-butyllithium in diethylether at room temperature.[6,12,61,67,68] Doing so we found that, within 30 min, 17% of tetrathiobenzene **4a** was transformed into trithiobenzene **16** (Table 1). To an even larger extent the corresponding trithiobenzenes **17** and **18** were formed when *sec*-butyllithium or *tert*-butyllithium were applied (Table 1). Based on experimental data that are discussed in the Supporting Information we suggest in Scheme 4 that a nucleophilic attack of alkyllithium at a sulfur atom results in the fragmentation of the thioketal moiety giving trithiobenzene and thioacetone. The cleavage of a C-S bond via nucleophilic addition of *n*-butyllithium to a sulfur atom has been reported for 2,2-diaryl-1,3-dithiolanes and 2,2,-diaryl-1,3-dithianes[69] and for 2,2-dialkyl-2-arylthioacetonitriles.[70] Of the two possible carbanions the more stable was formed. 2-Alkyl-2-aryl-1,3-dithianes and 2,2-dialkyl-1,3-dithianes as well as the corresponding dithiolanes gave unidentified tarry substances if they reacted at all.[69] Therefore, in case of tetrathiobenzene **4a** alkyl-S bond cleavage and thioacetone formation are likely to occur concerted because this leads to a good arylcarbanion and avoids a less favorable sulfanylalkylcarbanion as an intermediate.

Staying with *n*-butyllithium but lowering the temperature to 0 °C still gave 3% of trithiobenzene **16** and, in addition, a degree of only 21% for lithiation of tetrathiobenzene **4a** was achieved as revealed by workup with deuterium oxide. Surprisingly, tetrathiobenzene **4a** can be lithiated with methyllithium in tetrahydrofuran at room temperature within maximum 100 min without fragmentation. Under these conditions the degree of lithiation was 99% as determined by workup with deuterium oxide. When tetrahydrofuran was exchanged for diethyl ether no reaction took place.

The conditions found for the clean and quantitative deprotonation of tetrathiobenzene **4a** were the entry to implement the TIPS-ethyne moiety. Addition of *N*-formylpiperidine to lithiated tetrathiobenzene **5a** gave aldehyde **6**, which was converted into acetylene **7** through a Seyferth-Gilbert homologation[71,72] with the Bestmann-Ohira reagent.[73,74] Acetylene **7** was deprotonated with lithium diisopropylamide. Reaction of TIPS-chloride with the obtained lithium acetylide provided TIPS-ethyne substituted tetrathiobenzene **4b**. Likewise tetrathiobenzene **4a**, TIPS-ethyne substituted tetrathiobenzene **4b** could be efficiently and cleanly lithiated with methyllithium in tetrahydrofuran.

*Diarylketones **9***

Diarylketones **9** were prepared from lithiated tetrathiobenzenes **5** in two steps (Scheme 2). In this way we took advantage of easy chromatographical separation of compounds through polar tagging.[75,76] First, lithiated tetrathiobenzenes **5** were converted in tetrahydrofuran into diarylmethanols **8** employing methyl formate. Their hydroxyl groups acted as polar tags making them easily separable by standard column chromatography from much less polar starting material and other, unidentified compounds even on multigram scales such as 4 g of product. The second

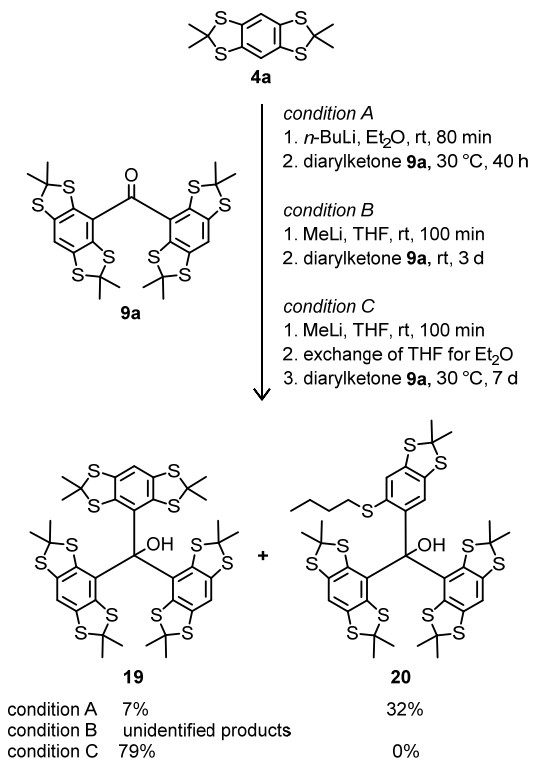
step, the oxidation of diarylmethanols **8** to obtain diarylketones **9**, was performed with Dess-Martin periodinane,[77] which was chosen as the reagent because it does not harm the thioketal moiety.[78] Also in this step, the distinct difference in polarity between the rather nonpolar product and the significantly more polar, unidentified side products helped in isolation: Filtration of a solution of the crude product through a short plug of silica gel was sufficient to isolate diarylketones **9**. They were obtained in yields of 83% and 74%, respectively, over two steps.

Being aware of the report on the synthesis of diarylketone **9a** in a single step from lithiated tetrathiobenzene **5a** and methyl chloroformate in diethyl ether,[68] we investigated this advantageously looking route by adding methyl chloroformate, phosgene or dimethylcarbonate to lithiated tetrathiobenzene **5a** in tetrahydrofuran. Tetrahydrofuran was chosen because we had found it to be the solvent of choice for the preparation of lithiated tetrathiobenzene **5a**. In case of methyl chloroformate and phosgene most of tetrathiobenzene **4a** went into unidentified compounds. Only traces of diarylketone **9a** were detected. With dimethylcarbonate diarylketone **9a** was obtained, however only in a yield of about 40%. The residual tetrathiobenzene **4a** and the reaction intermediate methoxycarbonylated tetrathiobenzene point to an incomplete conversion. Trityl alcohol was not detected. Also this reaction was accompanied by the formation of unidentified compounds, albeit only in small amounts. It looks like that the lithium chloride, that forms when chloroformate or phosgene are used, changes the reactivity of the lithiated tetrathiobenzene **5a** in an unfavorable manner. Probably the form in which lithiated tetrathiobenzene **5a** is present in diethylether is changed by lithium chloride. Impact of lithium chloride on the reaction of lithiumamides is known.[79]

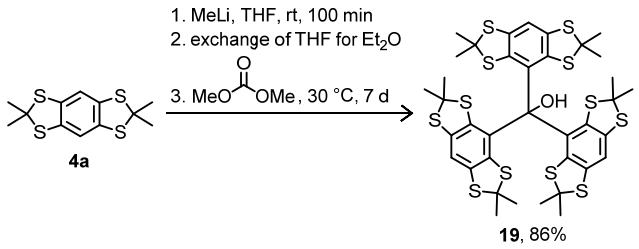
Assembly of the trityl scaffold

The assembly of the trityl alcohols, tritylOH[H/H/CCTIPS] **10** and tritylOH[H/CCTIPS/CCTIPS] **11** was elaborated with the preparation of tritylOH[H/H/H] **19** (Scheme 5) which is a synthetic intermediate in the synthesis of FTR. As reported,[68] tetrathiobenzene **4a** was lithiated with *n*-butyllithium in diethyl ether, then diarylketone **9a** was added and the reaction mixture was stirred at 30 °C for 40 h. Considering the above mentioned formation of trithiobenzene **16** in the reaction of tetrathiobenzene **4a** with butyllithium in diethyl ether, it came as no surprise, that trityl alcohol **20**, which shows trithiobenzene **16** as a substituent, was found as one of the products (32% isolated yield; For details see Supporting Information). TritylOH[H/H/H] **19** was obtained in a yield of only 7%. The above named literature reports a yield of 96% and does not mention any side-product.[68] Having found methyllithium in tetrahydrofuran to be the reagent of choice for the lithiation of tetrathiobenzene **4a**, the overall reaction sequence was pursued in tetrahydrofuran. No trityl alcohol was produced at room temperature within 3 days. Instead, diarylketone **9a** was converted into unidentified compounds. Obviously, the addition step proceeded too slowly. The reactivity of tetrahydrofuran towards carbanions made it suspect of being the origin for the side products, that became visible probably due to the very long reaction time of three days. Therefore, tetrahydrofuran was considered as an inappropriate solvent for the addition step and we strove to replace it for diethyl ether because diethyl ether is the standard solvent for trityl assembly[61,68] and the above mentioned experiment which had been run in diethyl ether had given at least some addition product. However, lithiation of tetrathiobenzene **4a** does not work well in diethylether. Therefore, the lithiation step was performed in tetrahydrofuran, then tetrahydrofuran was removed and lithiated tetrathiobenzene **5a** was suspended in diethyl ether. Finally, diarylketone **9a** was added (Scheme 5). After stirring the reaction mixture at 30 °C for seven days, tritylOH[H/H/H] **19** was obtained in 79% yield. This procedure was directly transferable to the syntheses of tritylOH[H/H/CCTIPS] **10** and tritylOH[H/CCTIPS/CCTIPS] **11** giving yields of 84% und 72%, respectively (Scheme 3). In all of these reactions some of the diarylketone **9** were found unchanged, which means that none of these reactions went to completion although lithiated tetrathiobenzene **5a** had been used in excess. Longer reaction time may improve the conversion. On the other hand, the conversion may be limited by competing protonation of the lithiated tetrathiobenzene **5a** by the solvent.

Having found suitable conditions for lithiation of tetrathiobenzenes and for the addition of lithiated tetrathiobenzene **5** to diarylketone **9**, we tested their application to a one-pot synthesis of tritylOH[H/H/H] **19** which is the precursor of FTR (Scheme 6). Lithiated tetrathiobenzene **5a** was prepared from tetrathiobenzene **4a** and methyllithium in tetrahydrofuran, then the solvent was exchanged for diethylether and dimethyl carbonate was added. The suspension was stirred at 30 °C for seven days. This gave tritylOH[H/H/H] **19** in gram amounts with 86% yield. The highest yield reported in literature so far is 73%.[12]



Scheme 5. Exploring the synthesis of tritylOH[H/H/H] (19). Methyllithium was applied as a solution in diethylether and butyllithium was applied as a solution in hexanes. rt = room temperature.



Scheme 6. One-pot synthesis of tritylOH[H/H/H] (19). Methyllithium was applied as a solution in diethylether.

*Trityl radicals **1** and **2***

The last modification on the stage of the trityl alcohols was the mounting of the carboxyl groups. As mentioned above, for the reason of most simple product isolation the carboxyl group should be introduced in form of a *tert*-butoxycarbonyl group. For this step, trityl alcohols **10** and **11** needed to be lithiated. Lithiation conditions were worked out using the parent trityl alcohol, tritylOH[H/H/H] **19** (see Supporting Information for the applied conditions and the results). Surprisingly, methyllithium in tetrahydrofuran, the best conditions to deprotonate tetrathiobenzenes **4**, failed. The reaction with 10 equivalents of methyllithium for 100 min at room temperature followed by workup with deuterium oxide resulted in only 11% of deuteration at the benzene rings. Luckily, the reported conditions *n*-butyllithium and tetramethylethylenediamine in *n*-hexane at room temperature[61] were very effective resulting in a deuteration degree of the benzene rings of 94%, and, remarkably, caused not the above described fragmentation of the thioketal moiety. This thioketal fragmentation was not found under any of the conditions tested during the search for quantitative lithiation, including *n*-butyllithium and *sec*-butyllithium in diethylether (For details see Supporting Information). Obviously, the fragmentation tendencies of the thioketal moieties of tetrathiobenzene **4a** and trityl alcohols **10, 11** and **19** are distinctly different. However, a very careful reaction time control was necessary because other side reactions occurred with prolonged reaction time (For details see Supporting Information).

The trityl alcohol tritylOH[$CO_2{}^t$Bu/$CO_2{}^t$Bu/$CO_2{}^t$Bu] prepared through the reaction of deprotonated tritylOH[H/H/H] **19** with di-*tert*-butyldicarbonate is reported to be isolated by precipitation.[68] This elegant procedure does not work in case of trityl alcohols **13** and **14** because the TIPS groups drastically improve their solubility in organic solvents and thus prevent their precipitation. Column chromatography was no solution either because the removal of di-*tert*-butyldicarbonate from trityl alcohol **14** was incomplete. Hence, instead of di-*tert*-butyldicarbonate *N*-*tert*-butoxycarbonylpyridinium *tert*-butanolate (**12**), freshly prepared from di-*tert*-butyldicarbonate and 4-*N*,*N*-dimethylaminopyridine, was used. In contrast to di-*tert*-butyldicarbonate this reagent is simply removed during workup by filtration through silica gel and subsequent washing of the eluate with aqueous ammonium chloride solution removes 4-*N*,*N*-dimethylaminopyridine.

Finally, *tert*-butyl esters **13** and **14** were converted into trityl radicals **1** and **2** by protonation with trifluoroacetic acid and reduction of the generated trityl cations with tin(II) chloride following the procedure[61] reported for the preparation of FTR. FTR formation is accompanied by quinone methide formation.[61] The generation of trityl radical **1** went without quinone methide formation, whereas in case of trityl radical **2** a small amount (3% isolated yield) of quinone methide **15** formed. Quite in contrast to the difficulties with chromatographic separation of the two highly polar compounds FTR and accompanying quinone methide,[6] the separation of trityl radical **2** and quinone methide **15** was easy because trityl radical **2** interacts strongly with silica gel due to its carboxyl group and quinone methide **15** is a rather unpolar compound.

As expected, trityl radicals **1** and **2** are not soluble in water, water/glycerol, 0.1 M phosphate buffer at pH 7.4 or 2

M aqueous solution of NaOH, but they are soluble in organic solvents, including ethanol.

Table 2. Fit parameters as determined from the W band cw EPR spectra. For line broadening a Gaussian distribution of the g values with the stated full width at half maximum (FWHM) is assumed.

compound	g			g distribution (Gaussian, FWHM)		
1	2.00339	2.00333	2.00245	$2.8 \cdot 10^{-4}$	$4.6 \cdot 10^{-4}$	$3.1 \cdot 10^{-4}$
	$\pm 1 \cdot 10^{-5}$	$\pm 1 \cdot 10^{-5}$	$\pm 1 \cdot 10^{-5}$	$\pm 2 \cdot 10^{-5}$	$\pm 2 \cdot 10^{-5}$	$\pm 2 \cdot 10^{-5}$
2	2.00335	2.00331	2.00240	$2.0 \cdot 10^{-4}$	$4.6 \cdot 10^{-4}$	$3.1 \cdot 10^{-4}$
	$\pm 1 \cdot 10^{-5}$	$\pm 1 \cdot 10^{-5}$	$\pm 1 \cdot 10^{-5}$	$\pm 2 \cdot 10^{-5}$	$\pm 2 \cdot 10^{-5}$	$\pm 2 \cdot 10^{-5}$
FTR	2.00345	2.00338	2.00254	$2.0 \cdot 10^{-4}$	$4.2 \cdot 10^{-4}$	$3.0 \cdot 10^{-4}$
	$\pm 1 \cdot 10^{-5}$	$\pm 1 \cdot 10^{-5}$	$\pm 1 \cdot 10^{-5}$	$\pm 2 \cdot 10^{-5}$	$\pm 2 \cdot 10^{-5}$	$\pm 2 \cdot 10^{-5}$

EPR spectroscopical properties of trityl radicals 1 and 2

The EPR spectroscopical properties of trityl radicals **1** and **2** dissolved in ethanol were investigated at X and W band frequencies with continuous wave (cw) and pulse EPR techniques (Figures 1, S4-S6). FTR was included in these measurements as the benchmark trityl radical. All pulse EPR experiments were performed at 50 K, representing a temperature typically used in EPR measurements for distance determination, which is envisaged as an important application of the new trityl radicals and derivatives thereof.

Quantitative analysis with cw EPR spectroscopy at X band frequencies, with FTR as the reference, gave 89% and 99% of the expected signal intensity (at an error margin of about ±15% for quantitative EPR) for solutions of the final synthesis products **1** and **2**, respectively (Figure S4), thus proving them to be pure trityl radicals without diamagnetic contamination. The cw EPR spectra of both trityl radicals showed a single very narrow line (Figure S5), suggesting that in applications at ambient temperature the new radicals behave similar to FTR. The g-tensors of these lines were determined through fitting of cw and echo-detected EPR spectra recorded at W band frequencies (94.2 GHz) using a calibrated carbon fiber as an internal g factor standard[80] as shown in Figures 1 and S6. The determined g-anisotropies of trityl radicals **1** and **2** are very similar to the g-anisotropy of FTR (see Table 2 for fitting parameters). This indicates that the singly-occupied molecular orbital is essentially unaffected by the partial exchange of carboxyl groups for TIPS-ethyne substituents.

In addition to the line shape, relaxation behavior is of relevance for the usage of radicals as reporters. Since all pulsed dipolar spectroscopy experiments measure the distance via echo modulation by the dipole-dipole coupling frequency, distance resolution and the maximum accessible distance depend on the transverse relaxation time T_2 which determines the lifetime of the echo.[40] The longer T_2, the larger the determinable distances and also the stronger the signal obtained for a given distance.

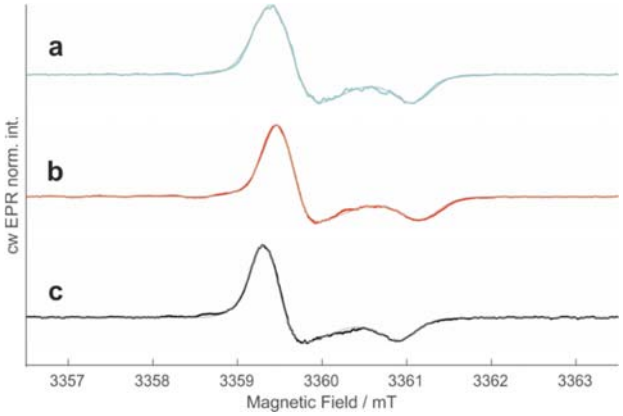


Figure 1. Echo-detected EPR spectra (W band, 94.2 GHz) shown as numerical first derivative of (a) trityl[CO_2H/CO_2H/CCTIPS] **1**, (b) trityl[CO_2H/CCTIPS/CCTIPS] **2**, and (c) FTR in ethanol at 50 K with the respective fits overlaid in grey. For fit parameters see Table 2, for echo-detected EPR absorption spectra of samples containing the carbon fiber as the g factor standard see Figure S6.

Therefore, a longer T_2 is generally desirable. The longitudinal relaxation time T_1 on the other hand describes the return of the system to its unperturbed state thus determining the recycle delay, which one wishes to be short as the required measurement time for a certain signal to noise ratio increases linearly with a longer recycle delay. The T_1 and T_2 relaxation times of trityl radicals **1**, **2**, and FTR were determined at X and W band frequencies by inversion recovery and 2-pulse ESEEM, respectively. At W band frequencies the T_1 and T_2 relaxation times of trityl radical **1** are very similar to that of FTR, while trityl radical **2** shows a longer $T1$ and a slightly shorter $T2$ time (Figure 2 and Table 3). At X band frequencies, interestingly, the T_1 relaxation of trityl radicals **1** and **2** is distinctly slower than that of FTR (Figure 3 and Table 3), which would increase the experimental time required in frozen EtOH solution by a factor

of 2.7 and 2.4 for trityl radicals **1** and **2**, respectively. For all three trityl radicals T_1 relaxation times are larger and T_2 relaxation times are smaller at the higher field for solutions in ethanol at 50 K. For distance measurements on trityl labeled compounds and therefore on samples with specific conditions, especially in respect to the type of solvent, an optimal maximum temperature T with respect to signal to noise ratio can be determined and applied at which T_2 starts to converge to its maximal value and T_1 is still as short as possible. Here we only investigated the relative trends between trityl radicals **1**, **2** and FTR, which are likely to reflect trends rather than absolute values for conditions to be used for distance determination experiments.

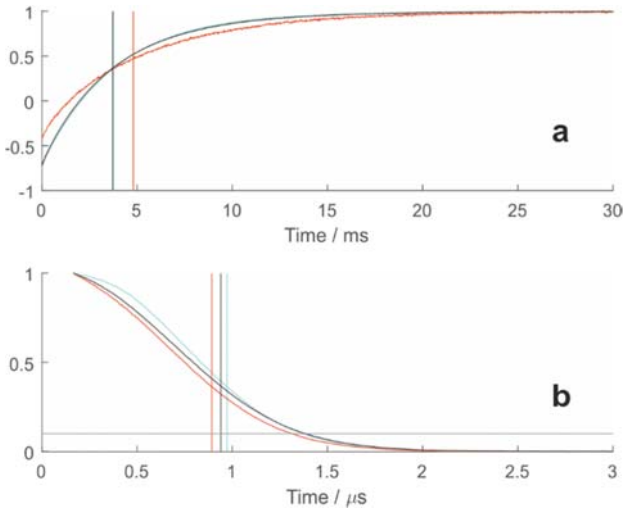


Figure 2. Results of spin relaxation measurements of trityl[CO_2H/CO_2H/CCTIPS] **1** (cyan), trityl[CO_2H/CCTIPS/CCTIPS] **2** (red) and FTR (black) in ethanol at 50 K at W band frequencies (94.2 GHz). Measurements were performed at the spectral maximum. (a) Inversion recovery reflecting the longitudinal relaxation time (T_1). (b) 2-pulse ESEEM signal decay providing insight into the transverse relaxation times (T_2). The grey line indicates a remaining signal level of 10 %. The 1/e-relaxation times are shown as vertical lines and are summarized in Table 3.

The 2-pulse ESEEM signal decay at X band frequencies (Figure 3b) shows nuclear modulations which are attributed to partial excitation of forbidden transitions when the electron spin is coupled to close-by nuclear spins. These nuclear modulations were further analyzed by 3-pulse ESEEM (Figure S7, Figure 3c) and the coupled spins were, based on the observed resonance frequency in the Fourier transformed spectra, unambiguously identified as protons. We found an increased intensity of the proton signal of trityl radicals **1** and **2** as compared to FTR, clearly seen in Figure S7. The coupling constants are too small for the couplings to become resolved beyond the matrix peak in the spectrum (Figure 3c). The increased signal intensity of trityl radicals **1** and **2** may be due to their larger number of protons surrounding the central carbon atom with the unpaired electron. However, comparing trityl radicals **1** and **2** shows a higher ESEEM modulation depth for the less proton carrying trityl radical **1**. Therefore, contribution of solvent protons is assumed. Such nuclear modulation can show up as an unwanted oscillation in pulsed dipolar spectroscopy experiments. However, averaging schemes exist to suppress it. Therefore, such small hyperfine couplings do not interfere when using these trityl radicals as spin labels or spin probes.

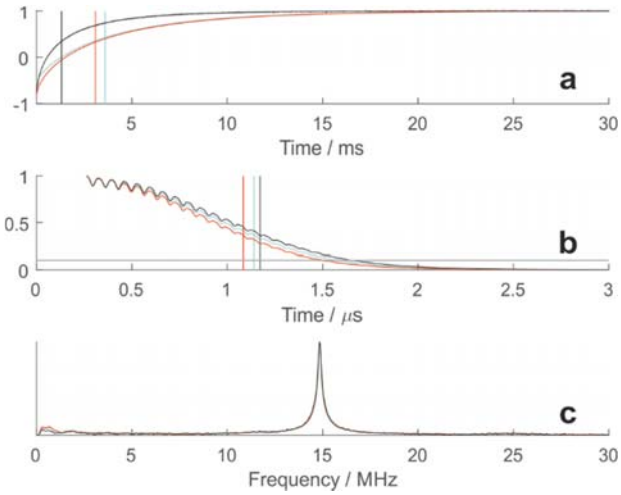


Figure 3. Results of spin relaxation measurements of trityl[CO_2H/CO_2H/CCTIPS] **1** (cyan), trityl[CO_2H/CCTIPS/CCTIPS] **2** (red) and FTR (black) in ethanol at 50 K at X band frequencies (ca. 9.5 GHz). Measurements were performed at the spectral maximum. (a) Inversion recovery reflecting the longitudinal relaxation time (T_1). (b) 2-pulse ESEEM signal decay with strong proton modulations providing insight into transverse relaxation time (T_2). The grey line indicates a remaining signal level of 10%. (c) Fourier transform of the 3-pulse ESEEM time domain data (Figure S7) showing an intense matrix signal at the proton Larmor frequency (14.8 MHz). The 1/e-relaxation times from (a) and (b) are shown as vertical lines and are summarized in Table 3.

Table 3. Relaxation times of trityl radicals as determined with X and W band EPR measurements at 50 K.

compound	X band		W band	
	1/e (T_1) [ms]	1/e (T_2) [μs]	1/e (T_1) [ms]	1/e (T_2) [μs]
1	3.60	1.14	3.76	0.97
2	3.09	1.08	4.80	0.89
FTR	1.31	1.17	3.72	0.94

Conclusions and outlook

FTR-type trityl radicals with two types of substituents at the benzene rings can be obtained without a statistical reaction step through assembly of the trityl scaffold by addi-

tion of an aryllithium with one substituent to a diarylketone with other substituents as was demonstrated with the synthesis of the two FTR-type trityl radicals **1** and **2** showing the TIPS-substituted ethyne and the carboxyl group as substituents. Most reactions were performed on a scale of at least 1 g. Standard column chromatography was sufficient for product isolation. Several findings made during the development of the synthesis of the two trityl radicals **1** and **2** are also of relevance for the synthesis of other FTR-type trityl radicals and even FTR itself because the syntheses have some building blocks and transformations in common. Consequently, we included an improved synthesis of the bare FTR scaffold.

We expect the developed synthesis route to be also applicable to assemble FTR-type trityl radicals with three different functional groups through exchange of methyl formate for (substituted) trithiobenzene carrying a formyl group, e.g. for aldehyde **6**, in the step of diarylmethanol formation. Furthermore, the trityl radicals **1** and **2** may be a starting point for the preparation of metabolically stable[81] and/or thiol compatible[82] trityl radicals and the trityl alcohols **10** and **11** can be used to introduce other functional groups than carboxyl, such as phophonate groups.[20,22]

Relaxation times T_1 and T_2 and g anisotropy prove the trityl radicals **1** and **2** as spectroscopically equally suitable as FTR. Because the trityl radicals **1** and **2** are well accessible and carry functional groups with orthogonal reactivity they may become the starting point of a variety of spin labels. Modifications at the ethyne groups, e. g. attachment of substituents like polyethylene glycol chains to achieve water solubility, are expected to change the spectroscopical properties very little as they will take place far away from the central carbon atom with the unpaired electron. The relaxation times will change upon a solvent change, e. g. to an aqueous solvent for studies on trityl radical labeled biomolecules, however, the impact of a solvent is expected to be similar for the three trityl radicals investigated in this study.

Experimental section

Synthesis

General. All reactions were performed in dried glassware under argon. Argon was passed through anhydrous $CaCl_2$ prior to its use. Unless otherwise stated, degassed solutions were prepared through applying three freeze-pump-thaw cycles. *N*,*N*-Dimethylformamide (DMF) was degassed at room temperature by applying vacuum until the liquid started to boil. Then the flask was ventilated with argon. This procedure was performed three times. Solvents were removed at a bath temperature of ~40 °C and reduced pressure. The products were dried at room temperature at ~0.3 mbar. The pH values of the solutions were determined using pH indicator strips (resolution: 0.5 pH).

Unless otherwise stated, commercial solvents and reagents were used. Source, purity, and batch numbers of the reagents are listed in Table S3. Since all commercial compounds used for syntheses had a purity of > 95%, their molar amount used in the syntheses were calculated with their compound mass and were not corrected by the manufacturer specified purities. THF and Et_2O (both HPLC grade) were dried with sodium/benzophenone prior to their use. The concentrations of organolithium solutions were determined by titration using salicylaldehyde phenylhydrazone as indicator.[83] For the preparation of aqueous solutions, deionized water was used. Solvents used for extraction and chromatography were of technical grade and were distilled prior to their use.

Column chromatography was carried out on silica gel 60 (0.035–0.070 mm) without applying pressure. In the procedures reported below, the size of the column is given as diameter x length. The material was loaded onto the column dissolved in a small quantity of the eluent. Thin layer chromatography (TLC) was performed on silica gel 60 containing fluorescent indicator F254. The solid support for the silica gel layer was aluminum foil. The spots were detected with UV light of λ = 254 nm and 366 nm. For preparative HPLC a Phenomenex Luna® Silica(2) column (particle size: 5 µm, pore size 100 Å, column size 21.2 mm x 250 mm) was used. For analytical HPLC a Phenomenex Luna® Silica(2) column (particle size: 5 µm, pore size 100 Å, column size 4.6 mm x 250 mm) was used. The compositions of solvent mixtures are given in volume ratios.

The ratio of the components in a mixture was determined by ^{1}H NMR spectroscopy and is given as molar ratio. The melting points were determined in open capillaries.

NMR spectra were calibrated using the solvent signal as an internal standard [$CDCl_3$: δ (^{1}H) = 7.25, δ (^{13}C) = 77.0; CD_2Cl_2: δ (1H) = 5.32, δ (^{13}C) = 53.8; C_6D_6: δ (^{1}H) = 7.16, δ (^{13}C) = 128.1]. Signal assignments are supported by DEPT-135, COSY, HMBC, and HMQC experiments.

ESI MS spectra were recorded using an Esquire 3000 ion trap mass spectrometer (Bruker Daltonik) equipped with a standard ESI source. Unless otherwise stated, accurate ESI mass measurements were performed using a Q-IMS-TOF mass spectrometer Synapt G2Si (Waters, Manchester, UK) in resolution mode, interfaced to a nano-ESI ion source. Nitrogen served as the nebulizer gas and the dry gas for nano-ESI. Nitrogen was generated by a nitrogen generator NGM 11. Helium 5.0 was used as buffer gas in the IMS entry cell, nitrogen 5.0 was used for IMS. ESI samples were introduced by static nano-ESI using in-house pulled glass emitters.

Mass spectra with GC-inlet and electron ionization (EI) where measured on a Triplequad Quattro Micro GC (Waters-Micromass, Manchester, UK) (compounds **7** and **4b**) or on a GC17A with QP5050 Single Quad Mass Spectrometer (Shimadzu GmbH, Germany) (compounds **4a** and **17**). EI mass spectra were also recorded using an Autospec X magnetic sector mass spectrometer with EBE geometry (Vacuum Generators, Manchester, UK) equipped with a standard EI source (compounds **16**, and **17**). Samples were introduced by push rod in aluminium crucibles. Ions were accelerated by 8 kV in EI mode. Accurate mass measurements were performed in the high resolution mode with perfluorokerosene as internal standard.

MALDI TOF mass spectra were recorded with an Ultraflex MALDI-TOF/TOF mass spectrometer (Bruker Daltonik, Bremen, Germany) operated in reflectron mode. Samples were mixed on a polished steel target with 1 µL of a saturated solution of trans-2-[3-(4-tert-butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) in methanol. Ionization was achieved using an LTB nitrogen laser MNL 200 (337 nm beam wavelength, 50 Hz repetition rate).

The monoisotopic masses of the compounds are reported.

Trityl radical 1 (Trityl[CO_2H/CO_2H/CCTIPS]). A solution of tritylOH[CO_2^{t}Bu/CO_2^{t}Bu/CCTIPS] (**13**) (30 mg, 24 µmol) in trifluoroacetic acid (500 µL) was stirred at room temperature for 60 min. The dark green solution was cooled with an ice water bath and $SnCl_2$ (22.5 mg, 74.3 µmol) dissolved in dry THF (600 µL) was added within 1 min. After additional 5 min the ice water bath was removed and the green solution was stirred at room temperature for 45 min. Then CH_2Cl_2 (20 mL) was added and the solution was washed with pH 2.0 buffer (0.5 M H_3PO_4, 0.5 M KH_2PO_4, 2 x 10 mL) and water (10 mL). The organic phase was dried over $MgSO_4 \cdot x\ H_2O$ and filtered. The solvents were removed. The components of the residual brown solid were separated by column chromatography (1.5 cm x 31 cm). Elution with Et_2O/AcOH 1000:1 gave a mixture (4 mg; R_f = 1.00, 0.50) of unidentified compounds as a brown solid and trityl[CO_2H/CO_2H/CCTIPS] (**1**) (15 mg after freeze-drying with benzene, 56%; R_f = 0.15; Mp: 218 – 220 °C) as a brown solid. The ^{1}H NMR spectrum is displayed in Figure S8. MS (ESI), m/z = 566.4 [M - 2H]$^{2-}$, 544.4 [M - 2H - CO_2]$^{2-}$, 522.5 [M - 2H - 2CO_2]$^{2-}$. Accurate MS (ESI): m/z calcd for [M - 2H]$^{2-}$ $C_{50}H_{57}O_4S_{12}Si^{2-}$: 566.5343; found, 566.5334. Anal. Calcd for $C_{50}H_{59}O_4S_{12}Si$: C, 52.83; H, 5.23. Found: C, 53.01; H, 5.47. Analytical HPLC (isocratic run with CH_2Cl_2/EtOH 96:4, flow rate of 1 mL/min): 5.0 min (**1**, relative integral of 98%), 4.5 min (not identified compound, relative integral of 2%). The chromatogram is displayed in Figure S9.

Trityl radical 2 (Trityl[CO_2H/CCTIPS/CCTIPS]). A solution of tritylOH[CO_2^{t}Bu/CCTIPS/CCTIPS] (**14**) (40 mg, 30 µmol) in trifluoroacetic acid (500 µL) was stirred at room temperature for 120 min. The dark green solution was cooled with an ice water bath and $SnCl_2$ (14.1 mg, 74.3 µmol) dissolved in dry THF (280 µL) was added within 1 min. After additional 4 min the ice water bath was removed and the brown solution was stirred at room temperature for 45 min. Then CH_2Cl_2 (20 mL) was added and the solution was washed with pH 2.0 buffer (0.5 M H_3PO_4, 0.5 M KH_2PO_4, 2 x 10 mL) and water (10 mL). The organic phase was dried over $MgSO_4 \cdot x\ H_2O$ and filtered. The solvents were removed. The components of the residual brown solid were separated by column chromatography (3 cm x 20 cm). Elution with CH_2Cl_2 gave a mixture (6 mg; R_f(CH_2Cl_2) = 0.69; R_f(CH_2Cl_2/AcOH 100:1) = 0.74) of unidentified compounds as an orange solid and a mixture (1.5 mg; R_f(CH_2Cl_2) = 0.36, R_f(CH_2Cl_2/AcOH 100:1) = 0.56) of quinone methide **15** (< 3%) and grease as a violet solid. Then, the eluent was changed to CH_2Cl_2/AcOH 100:1 and a mixture (2 mg; R_f(CH_2Cl_2) = 0; R_f(CH_2Cl_2/AcOH 100:1) = 0.29) of unidentified compounds as an orange solid and trityl[CO_2H/CCTIPS/CCTIPS] (**2**) (36 mg after freeze-drying with benzene, 95%; R_f(CH_2Cl_2) = 0; R_f(CH_2Cl_2/AcOH 100:1) = 0.29; Mp: 202 °C, molten compound is black) as a brown solid were obtained. Additional analytical data of trityl[CO_2H/CCTIPS/CCTIPS] (**2**): The ^{1}H NMR spectrum is displayed in Figure S10. MS (ESI): m/z = 1270.1 [M - H]$^-$. Accurate MS (ESI): m/z calcd for [M - H]$^-$ $C_{60}H_{78}O_2S_{12}Si_2^-$: 1270.2194; found, 1270.2222. Anal. Calcd for $C_{60}H_{79}O_2S_{12}Si_2$: C, 56.60; H, 6.25. Found: C, 56.77; H, 6.22. Additional analytical data of quinone methide **15**: For ^{1}H NMR data, see Table S4. MS (ESI): m/z = 1265.2 [M + Na]$^+$. Accurate MS (ESI): m/z calcd for [M + Na]$^+$ $C_{59}H_{78}OS_{12}Si_2Na^+$: 1265.2132; found, 1265.2133. Analytical HPLC (isocratic run with CH_2Cl_2/EtOH 95:5, flow rate of 1 mL/min): 4.1 min. The chromatogram is displayed in Figure S11.

1,2,4,5-Tetrakis(*tert*-butylthio)benzene (Tetrathioether 3). The procedure of Reddy et al.[67] was followed with making modifications. To a suspension of sodium hydride (19.26 g, 802.8 mmol) in dry degassed DMF (320 mL) cooled with an ice water bath was added degassed *tert*-butylthiol (83 mL, 0.76 mol) within 15 min (***Caution!*** *Very exothermic, strong gas evolution, reaction mixture tends to foam*). The released gas was led through a gas bubbler filled with silicone oil, an empty gas washing bottle, and a gas washing bottle filled with saturated aqueous $KMnO_4$ solution (*Please note: gas washing bottles equipped with a porous glass filter disc must not be used. The filter gets clogged during the washing process by precipitated MnO_2 leading to dangerous overpressure in the apparatus*). Then, the ice water bath was removed, 1,2,4,5-tetrachlorobenzene (32.84 g, 152.1 mmol) was added and the brown-grey suspension was stirred under reflux (bath temperature 170 °C) for 120 min. After cooling to room temperature, water (1 mL) was added and the yellow-green suspension was poured onto ice (430 g) and the suspension was filtered. The filter cake was washed with water (2 x 30 mL) and dried over P_4O_{10} at reduced pressure. In this way, an off-white solid (31.73 g) was obtained consisting of tetrathioether **3** (48% yield) and DMF in the molar ratio of 97:3. For ^{1}H NMR and ^{13}C NMR data, see Tables S4 and S6. Data are in agreement with data given in the literature.[67] MS (ESI): m/z = 453.1 [M + Na]$^+$.

Due to the strong odor of *tert*-butylthiol all glassware contaminated with *tert*-butylthiol was put into a bath of aqueous $KMnO_4$ solution for one day. Afterwards, the MnO_2 that stuck to the glassware was removed using an aqueous solution of a mixture of oxalic acid and a small amount of $MnSO_4$.

2,2,6,6-Tetramethylbenzo[1,2-*d*:4,5-*d*']bis([1,3]dithiole) (Tetrathiobenzene 4a). The procedure of Rogozhnikova et al.[61] was followed with making slight modifications. The degassed (applying two freeze-pump-thaw cycles) brownish suspension of a 96.5:3.5 mixture (79.21 g) of tetrathioether **3** (183.9 mmol) and DMF (6.670 mmol), acetone (130 mL, 1.77 mol), D-(+)-10-camphorsulfonic acid (8.59 g, 37.0 mmol) and BF_3 (50 wt.% in diethyl ether, 67 mL, 0.55 mol) in $CHCl_3$ (225 mL) was stirred under reflux (bath temperature 78 °C) for 18 h. After cooling down to room temperature, water (200 mL) was added to the red-brown suspension and the pH was raised to 7.0 by addition

of an aqueous solution of NaOH (2.0 M, 300 mL, 600 mmol). Then, $CHCl_3$ (30 mL) was added and the brown organic phase was separated from the greenish aqueous phase. The aqueous phase was extracted with $CHCl_3$ (3 x 50 mL). The combined organic phases were washed with brine (50 mL) and filtered through silica gel (4 cm x 4 cm, rinsing with $CHCl_3$). All volatiles were removed. The residual yellow solid was mixed with MeOH (250 mL) and the suspension was heated to reflux (bath temperature 85 °C) for 30 min. Filtration gave a yellow filter cake which was washed with a 4:1 mixture of MeOH and *n*-hexane (2 x 40 mL, 6 x 80 mL) and dried at reduced pressure to give tetrathiobenzene **4a** (39.68 g, 75%; Mp: 145 °C) as a colorless solid. For ^{1}H NMR and ^{13}C NMR data, see Tables S4 and S6. NMR data are in agreement with those given in the literature.[61] MS (EI): *m*/*z* (%) 285.9 (45) $[M]^{+\bullet}$, 270.9 (100) $[M - \bullet CH_3]^+$, 127.9 (30).

Triisopropyl((2,2,6,6-tetramethylbenzo[1,2-*d*:4,5-*d*']bis([1,3]dithiole)-4-yl)ethynyl)silane (TIPS-ethyne substituted tetrathiobenzene 4b). To a solution of alkyne **7** (1.00 g, 3.22 mmol) in dry THF (25 ml) cooled with an ice water bath was added a solution of lithium diisopropylamide (1.75 M, 2.2 mL, 3.9 mmol) in THF, *n*-heptane and ethylbenzene. Immediately after the addition of lithium diisopropylamide the color of the solution had changed from slightly brownish to dark red. After 5 min the ice water bath was removed and the solution was stirred for another 15 min at room temperature. Degassed triisopropylsilylchloride (1.0 mL, 4.8 mmol) was added and the brown solution was stirred at room temperature for 20 h. Et_2O (50 mL) was added and the orange solution was extracted with an aqueous solution of HCl (2 M, 30 mL). The organic phase was separated, washed with water (20 mL), dried over $MgSO_4 \cdot x\ H_2O$, and filtered. The solvents were removed. The components of the brownish oil were separated by column chromatography (3 cm x 30 cm). Elution with CH_2Cl_2/pentane 1:8 gave TIPS-ethyne substituted tetrathiobenzene **4b** (1.43 g, 95%; R_f = 0.41, Mp: 74 °C) as a yellow oil changing to a solid within few days of storage at room temperature. For ^{1}H NMR and ^{13}C NMR data, see Tables S4 and S6. MS (EI): *m*/*z* (%) 266.4 (100) $[M]^{+\bullet}$, 451.3 (30) $[M - \bullet CH_3]^+$. Anal. Calcd for $C_{23}H_{34}S_4Si$: C, 59.17; H, 7.34. Found: C, 59.53; H, 7.31.

2,2,6,6-Tetramethylbenzo[1,2-*d*:4,5-*d*']bis([1,3]dithiole)-4-carbaldehyde (Aldehyde 6). To a slightly yellowish solution of tetrathiobenzene **4a** (5.00 g, 17.5 mmol) in dry THF (100 mL) was added a solution of MeLi (1.80 M, 10.2 mL, 18.4 mmol) in Et_2O within 5 min. During addition of MeLi a gas development started. After stirring the solution at room temperature for 100 min *N*-formylpiperidine (9.7 mL, 87 mmol) was added and the orange solution was stirred at room temperature for 16 h. Then, Et_2O (200 mL) was added and the yellow solution was washed with an aqueous solution of HCl (2 M, 50 mL). The organic phase was separated, and the red aqueous phase was extracted with Et_2O (30 mL). The combined organic phases were washed with water (30 mL), dried over $MgSO_4 \cdot x\ H_2O$, and filtered. The solvents were removed. The components of the residual orange solid were separated by column chromatography (7 cm x 20 cm). Elution with CH_2Cl_2/pentane 1:1 gave tetrathiobenzene **4a** (362 mg, 7%; R_f = 0.72) as an off-white solid and aldehyde **6** (4.25 g, 78%; R_f = 0.57; Mp: 145 – 146 °C) as an orange solid. For ^{1}H NMR and ^{13}C NMR data, see Tables S4 and S6. MS (ESI): *m*/*z* = 337.1 $[M + Na]^+$, 651.0 $[2M + Na]^+$. Accurate MS (ESI): *m*/*z* calcd for $[M + Na]^+$ $C_{13}H_{14}OS_4Na^+$: 336.9819; found, 336.9813.

4-Ethynyl-2,2,6,6-tetramethylbenzo[1,2-*d*:4,5-*d*']bis([1,3]dithiole) (Alkyne 7). To a solution of aldehyde **6** (2.00 g, 6.36 mmol) and Cs_2CO_3 (5.17 g, 15.9 mmol) in dry THF (100 mL) and MeOH (100 mL) was added Bestmann–Ohira reagent (1.93 g. 10.1 mmol). The yellow-orange solution showing gas development was stirred at room temperature for 17 h. Et_2O (200 mL) was added and the green solution was extracted with a mixture of aqueous saturated $NaHCO_3$ solution (30 mL) and water (30 mL). The phases were separated. The organic phase was washed with water (50 mL), the aqueous phase was extracted with Et_2O (50 mL). The combined organic phases were dried over $MgSO_4 \cdot x\ H_2O$ and filtered. The solvents were removed. The components of the residue were separated by column chromatography (6.5 cm x 30 cm). Elution with CH_2Cl_2/pentane 1:4 gave five fractions: (1) an unidentified compound (91 mg; R_f = 0.54) as a yellow oil; (2) a mixture of the unidentified compound from fraction (1) with other unidentified compounds (3 mg; R_f = 0.54) as a brown oil; (3) alkyne **7** (1.23 g, 62%; R_f = 0.44; Mp: 144 – 145 °C) as an off-white solid; (4) a mixture of unidentified components (56 mg; R_f = 0.44, 0.29) as a dark brown solid; (5) an unidentified compound in mixture with other unidentified compounds in minor amounts (126 mg; R_f = 0.15) as a greenish oil. Additional analytical data of alkyne **7**: for ^{1}H NMR and ^{13}C NMR data, see Tables S4 and S6. MS (EI): *m*/*z* (%) 310.1 (65) $[M]^{+\bullet}$, 295.1 (100) $[M - \bullet CH_3]^+$, 140.1 (38). Analytical data of the unidentified compound of fraction 1: ^{1}H NMR (500 MHz, CD_2Cl_2): δ 7.52 (dd, 1H, *J* = 5.5 Hz, 0.4 Hz), 7.35 (d, 1H, *J* = 0.4 Hz), 7.13 (d, 1H, *J* = 5.5), 5.09 (q like, 1H, *J* = 5.1 Hz), 4.82 (m, 1H), 1.95 (s, 6H), 1.94 (m, 3H). ^{13}C NMR (125 MHz, CD_2Cl_2): *δ* 143.3, 139.9, 135.2, 134.8, 133.6, 129.1, 125.4, 123.4, 122.9, 112.5, 66.9, 31.6, 22.9. NMR and ESI-MS spectra are displayed in Figures S25-S31. Analytical data of the unidentified compound of fraction 5: ^{1}H NMR (500 MHz, C_6D_6): *δ* 7.51 (d, 1H, *J* = 0.4 Hz), 6.95 (d, 1H, *J* = 5.5), 6.85 (dd, 1H, *J* = 5.5 Hz, 0.4 Hz), 3.21 (s, 3H), 1.65 (s, 6H), 1.35 (s, 6H). ^{13}C NMR (125 MHz, CD_2Cl_2): *δ* 145.2, 135.2, 134.6, 133.0, 128.9, 128.4, 128.2, 128.0, 126.0, 124.7, 123.3, 91.3, 66.5, 50.6, 31.4, 28.2. The NMR spectra show additional signals of comparatively low intensity. They are not reported here. Very likely they belong to other unidentified components. NMR and ESI-MS spectra are displayed in Figures S37-S43.

Bis(2,2,6,6-tetramethylbenzo[1,2-*d*:4,5-*d*']bis([1,3]dithiole)-4-yl)methanol (Diarylmethanol 8a). To a slightly yellow solution of tetrathiobenzene **4a** (5.00 g, 17.5 mmol) in dry THF (100 mL) was added a solution of MeLi (1.49 M, 11.1 mL, 16.6 mmol) in Et_2O. During addition of MeLi a gas development started. After 100 min of stirring the solution at room temperature methyl formate (515 µL, 8.32 mmol) was added and the turbid yellow solution was stirred for 69 h at room temperature. Then, Et_2O (200 mL) was added and the turbid brownish solution was washed with water (2 x 50 mL). The organic phase was separated,

and the combined aqueous phases were extracted with Et_2O (2 x 25 mL).The combined organic phases were dried over $MgSO_4 \cdot x\ H_2O$, and filtered. The solvents were removed. The components of the residual yellow solid were separated by column chromatography (7 cm x 27 cm). Elution with CH_2Cl_2/pentane 4:1 gave tetrathiobenzene **4a** (362 mg; R_f = 0.76) as a yellowish solid, a mixture of unidentified compounds (105 mg; R_f = 0.67) as an orange oil, and a yellowish solid (4.59 g; R_f = 0.48; Mp: 210 °C) consisting of diarylmethanol **8a** (90% yield) and CH_2Cl_2 in the molar ratio of 89:11. For ^{1}H NMR and ^{13}C NMR data, see Tables S4 and S6. MS (ESI): m/z = 622.9 $[M + Na]^+$.

Bis(2,2,6,6-tetramethyl-8-((triisopropylsilyl)ethynyl)benzo[1,2-*d*:4,5-*d*']bis([1,3]dithiole)-4-yl)methanol (Diarylmethanol 8b). To a slightly yellowish solution of a 85:15 mixture (3.61 g) of TIPS-ethyne substituted tetrathiobenzene **4b** (7.52 mmol) and *n*-pentane (1.31 mmol) in dry THF (50 mL) was added a solution of MeLi (1.56 M, 4.6 mL, 7.1 mmol) in Et_2O. During addition of MeLi a gas development started. After 100 min of stirring the solution at room temperature a solution of methyl formate in THF (2.2 mL of the solution of 220 µL methyl formate in 1980 µL THF; This corresponds to 3.6 mmol of methyl formate) was added and the green solution was stirred for 68 h at room temperature. Then, Et_2O (100 mL) was added and the solution was washed with water (50 mL). The brownish organic phase was washed with water (50 mL), dried over $MgSO_4 \cdot x\ H_2O$, and filtered. The solvents were removed. The components of the residual yellow solid were separated by column chromatography (4 cm x 30 cm). Elution with CH_2Cl_2/pentane 1:1 gave four fractions: (1) TIPS-ethyne substituted tetrathiobenzene **4b** (422 mg; R_f = 0.78) as a yellow oil; (2) a mixture of TIPS-ethyne substituted tetrathiobenzene **4b** and unidentified compounds (37 mg; R_f = 0.78, 0.67, 0.56) as a red oil; (3) a mixture of diarylmethanol **8b** with traces of unidentified compounds (50 mg; R_f = 0.56, 0.41) as a yellow oil; (4) diarylmethanol **8b** (2.76 g, 80%; R_f = 0.41; Mp: 125 – 127 °C) as a yellow solid. For ^{1}H NMR and ^{13}C NMR data, see Tables S4 and S7. MS (ESI): m/z = 983.0 $[M + Na]^+$.

Bis(2,2,6,6-tetramethylbenzo[1,2-*d*:4,5-*d*']bis([1,3]dithiole)-4-yl)methanone (Diarylketone 9a). To a solution of a 89:11 mixture (4.52 g) of the diarylmethanol **8a** (7.38 mmol) and CH_2Cl_2 (0.91 mmol) in dry CH_2Cl_2 (100 mL) was added Dess–Martin periodinane (3.98 g, 9.38 mmol). After stirring the solution at room temperature for 60 min Et_2O (200 mL) was added. The orange solution was washed with an aqueous solution of NaOH (2.0 M, 100 mL, 200 mmol) and water (2 x 50 mL). The organic phase was separated, dried over $MgSO_4 \cdot x\ H_2O$, and filtered. The solvents were removed. The components of the residual orange solid were separated by filtration through silica gel (4 cm x 7 cm). Elution with CH_2Cl_2/pentane 1:1 gave an orange solid (4.14 g; R_f = 0.64) consisting of diarylketone **9a** (92% yield) and CH_2Cl_2 in the molar ratio of 88:12. For the synthesis of tritylOH[H/H/CCTIPS] (**10**) part of the material was dissolved in Et_2O and then all volatiles were removed giving diarylketone **9a** containing some Et_2O. For analytical purposes solvent-free diarylketone **9a** (Mp: 215 – 216 °C) was obtained by crystallization from *n*-hexane. The melting point measured by us differs drastically from the melting point reported in the literature (120-127 °C).[68] For ^{1}H NMR and ^{13}C NMR data, see Tables S4 and S6. Data are in agreement with data given in the literature.[68] MS (ESI): m/z = 620.9 $[M + Na]^+$. Accurate MS (ESI): m/z calcd for $[M + Na]^+$ $C_{25}H_{26}OS_8Na^+$: 620.9642; found, 620.9636. Anal. Calcd for $C_{25}H_{26}OS_8$: C, 50.13; H, 4.38. Found: C, 50.38; H, 4.32.

Bis(2,2,6,6-tetramethyl-8-((triisopropylsilyl)ethynyl)benzo[1,2-*d*:4,5-*d*']bis([1,3]dithiole)-4-yl)methanone (Diarylketone 9b). To a yellow solution of diarylmethanol **8b** (2.60 g, 2.70 mmol) in dry CH_2Cl_2 (50 mL) was added Dess–Martin periodinane (1.44 g, 3.39 mmol). After stirring the solution at room temperature for 50 min Et_2O (100 mL) was added. The red solution was washed with an aqueous solution of NaOH (2.0 M, 20 mL) and water (2 x 30 mL). The organic phase was separated, dried over $MgSO_4 \cdot x\ H_2O$, and filtered. The solvents were removed. The components of the residual orange solid were separated by filtration through silica gel (5 cm x 8 cm). Elution with CH_2Cl_2/pentane 3:7 gave an orange solid (2.59 g; R_f = 0.40) consisting of diarylketone **9b** (93% yield) and CH_2Cl_2 in the molar ratio of 55:45. Solvent-free diarylketone **9b** (Mp: 222 – 223 °C) was obtained for analytical purposes by dissolving the material in Et_2O and then removing all volatiles. For ^{1}H NMR and ^{13}C NMR data, see Tables S4 and S7. MS (ESI): m/z = 981.0 $[M + Na]^+$. Accurate MS (ESI): m/z calcd for $[M + Na]^+$ $C_{47}H_{66}OS_8Si_2Na^+$: 981.2310; found, 981.2301. Anal. Calcd for $C_{47}H_{66}OS_8Si_2$: C, 58.82; H, 6.93. Found: C, 58.88; H, 6.92.

(2,2,6,6-Tetramethyl-8-((triisopropylsilyl)ethynyl)benzo[1,2-*d*:4,5-*d*']bis([1,3]dithiole)-4-yl)bis(2,2,6,6-tetramethylbenzo[1,2-*d*:4,5-*d*']bis([1,3]dithiole)-4-yl)methanol (TritylOH[H/H/CCTIPS] (10)). To a yellowish solution of a 90:10 mixture (2.00 g) of TIPS-ethyne substituted tetrathiobenzene **4b** (4.21 mmol) and *n*-pentane (0.47 mmol) in dry THF (25 mL) was added a solution of MeLi (1.44 M, 2.7 mL, 3.9 mmol) in Et_2O. After stirring the solution at room temperature for 100 min the solvent was removed and the remaining brown oil was dissolved in dry Et_2O (50 mL). A 98:2 mixture (2.05 g) of diarylketone **9a** (3.41 mmol) and Et_2O (0.08 mmol) was added and the suspension, a green solution with a yellow solid, was stirred at 30 °C for 7 d. After cooling to room temperature water (50 mL) and CH_2Cl_2 (100 mL) were added to the suspension consisting of a colorless solid in a green solution. The aqueous phase was separated and extracted with CH_2Cl_2 (2 x 20 mL). The combined organic phases were dried over $MgSO_4 \cdot x\ H_2O$ and filtered. The solvents were removed. The components of the remaining orange solid were separated by column chromatography (7 cm x 28 cm). Elution with CH_2Cl_2/pentane 2:3 gave three fractions: (1) a mixture (673 mg, R_f (CH_2Cl_2/pentane 2:3) = 0.85, 0.83) of TIPS-ethyne substituted tetrathiobenzene **4b** with unidentified compounds as a yellow oil; (2) a mixture (95 mg, R_f (CH_2Cl_2/pentane 2:3) = 0.68) of grease and unidentified compounds as a yellow oil; (3) tritylOH[H/H/CCTIPS] (**10**) (2.63 g, 72%; R_f (CH_2Cl_2/pentane 2:3) = 0.55; Mp: turned black above 200

°C, no melting) as a yellow solid. Then, the eluent was changed to CH_2Cl_2 and a mixture (165 mg; R_f (CH_2Cl_2/pentane 2:3) = 0.55, 0.33) of tritylOH[H/H/CCTIPS] (**10**) and unidentified compounds was obtained as a yellow oil. As the fifth fraction a mixture (697 mg; R_f (CH_2Cl_2/pentane 2:3) = 0.33, 0.15) of diarylketone **9a** and unidentified compounds was obtained as an orange oil. For ^{1}H NMR and ^{13}C NMR data, see Tables S4 and S7. MS (ESI): m/z = 1062.9 [M - H]$^-$, 1068.8 [M + Li - 2H]$^-$, 1086.8 [M + Na - 2H]$^-$, 1100.8 [M + K - 2H]$^-$. Accurate MS (ESI): m/z calcd for [M - H]$^-$ $C_{48}H_{59}OS_{12}Si^-$: 1063.0989; found, 1063.0979.

Bis(2,2,6,6-tetramethyl-8-((triisopropylsilyl)ethynyl)benzo[1,2-*d*:4,5-*d*']bis([1,3]dithiole)-4-yl)(2,2,6,6-tetramethylbenzo[1,2-*d*:4,5-*d*']bis([1,3]dithiole)-4-yl)methanol (TritylOH[H/CCTIPS/CCTIPS] (11)). To a slightly yellowish solution of tetrathiobenzene **4a** (657 mg, 2.29 mmol) in dry THF (25 mL) was added a solution of MeLi (1.67 M, 1.3 mL, 2.2 mmol) in Et_2O. After stirring the solution at room temperature for 100 min the solvent was removed and the remaining colorless solid was suspended in dry Et_2O (50 mL). Diarylketone **9b** (992 mg, 1.03 mmol) was added and the suspension, a red solution with a colorless solid, was stirred at 30 °C for 7 d. After cooling to room temperature water (50 mL) and Et_2O (30 mL) were added to the brown solution. The aqueous phase was separated and extracted with Et_2O (2 x 30 mL). The combined organic phases were dried over $MgSO_4 \cdot x\ H_2O$ and filtered. The solvents were removed. The components of the remaining orange solid were separated by column chromatography (6 cm x 38 cm). Elution with CH_2Cl_2/pentane 1:4 gave tetrathiobenzene **4a** (213 mg; R_f (CH_2Cl_2/pentane 1:4) = 0.53; R_f (CH_2Cl_2/pentane 3:7) = 0.61) as a colorless solid. Then, the eluent was changed to CH_2Cl_2/pentane 3:7 and a mixture (27 mg, R_f (CH_2Cl_2/pentane 1:4) = 0.38; R_f (CH_2Cl_2/pentane 3:7) = 0.47) of tetrathiobenzene **4a**, grease, and unidentified compounds was obtained as a yellow oil. As the third fraction tritylOH[H/CCTIPS/CCTIPS] (**11**) (1.08 g, 84%; R_f (CH_2Cl_2/pentane 1:4) = 0.23; R_f (CH_2Cl_2/pentane 3:7) = 0.47; Mp: 197 °C, turned black) was obtained as a yellow solid. As the fourth fraction a mixture (16 mg, R_f (CH_2Cl_2/pentane 1:4) = 0.18; R_f (CH_2Cl_2/pentane 3:7 = 0.34) of diarylketone **9b**, pentane and unidentified compounds was obtained. For ^{1}H NMR and ^{13}C NMR data, see Tables S4 and S7. MS (ESI): m/z = 1243.0 [M - H]$^-$, 1249.0 [M + Li - 2H]$^-$, 1265.0 [M + Na - 2H]$^-$, 1281.0 [M + K - 2H]$^-$. Accurate MS (ESI): m/z calcd for [M - H]$^-$ $C_{59}H_{79}OS_{12}Si_2^-$: 1243.2323; found, 1243.2329.

Di-*tert*-butyl 8,8'-(hydroxy(2,2,6,6-tetramethyl-8-((triisopropylsilyl)ethynyl)benzo[1,2-*d*:4,5-*d*']bis([1,3]dithiole)-4-yl)methylene)bis(2,2,6,6-tetramethylbenzo[1,2-*d*:4,5-*d*']bis([1,3]dithiole)-4-carboxylate) (TritylOH[$CO_2{}^t$Bu/$CO_2{}^t$Bu/CCTIPS] (13)). To prepare *N*-*tert*-butoxycarbonylpyridinium *tert*-butanolate (**12**) di-*tert*-butyl dicarbonate (840 µL, 3.93 mmol) was added to a colorless solution of 4-*N*,*N*-dimethylaminopyridine (688 mg, 5.63 mmol) in dry Et_2O (50 mL). The slightly yellowish solution was stirred at room temperature for 75 min. In the meantime a solution of *n*-BuLi (1.60 M, 1.75 mL, 2.80 mmol) in hexanes was added to a yellow suspension of tritylOH[H/H/CCTIPS] (**10**) (300 mg, 281 µmol) and *N*,*N*,*N*',*N*'-tetramethylethylenediamine (430 µL, 2.85 mmol) in dry *n*-hexane (10 mL). After stirring the dark yellow solution at room temperature for 15 min it was added to the solution of *N*-*tert*-butoxycarbonylpyridinium *tert*-butanolate (**12**). After stirring the turbid green suspension at room temperature for 240 min, it was filtered through silica gel (3 cm x 2 cm, rinsing with Et_2O). The orange filtrate (170 mL) was washed with a saturated aqueous solution of NH_4Cl (2 x 30 mL), water (30 mL), dried over $MgSO_4 \cdot x\ H_2O$, and filtered. The solvents were removed. The components of the residual yellow oil were separated by column chromatography (3 cm x 44 cm). Elution with CH_2Cl_2/pentane 9:11 gave a mixture (30 mg; R_f (CH_2Cl_2/pentane 9:11) = 0.45; R_f (CH_2Cl_2/pentane 3:2) = 0.71) of tritylOH[H/H/CCTIPS] (**10**) and unidentified compounds as an orange oil and a 31:31:38 mixture (74 mg; R_f (CH_2Cl_2/pentane 9:11) = 0.24, 0.18; R_f (CH_2Cl_2/pentane 3:2) = 0.55, 0.45) of the two diastereomers of tritylOH[H/$CO_2{}^t$Bu/CCTIPS] (**23a**,**b**) (together 21% yield; for structural formula see Chart S1) and *tert*-butyl pentanoate (**24**, This compound is the product of the reaction between *n*-BuLi and the reagent *N*-*tert*-butoxycarbonylpyridinium *tert*-butanolate (**12**)) as an orange solid. Then, the eluent was changed to CH_2Cl_2/pentane 3:2 and a mixture (42 mg; R_f (CH_2Cl_2/pentane 9:11) = 0.18; R_f (CH_2Cl_2/pentane 3:2) = 0.45) of unidentified compounds was obtained as an orange oil and, finally, tritylOH[$CO_2{}^t$Bu/$CO_2{}^t$Bu/CCTIPS] (**13**) (110 mg, 31%; R_f (CH_2Cl_2/pentane 9:11) = 0.09; R_f (CH_2Cl_2/pentane 3:2) = 0.29; Mp: 189-191 °C with gas evolution) was obtained as an orange solid. Additional analytical data of tritylOH[$CO_2{}^t$Bu/$CO_2{}^t$Bu/CCTIPS] (**13**): For ^{1}H NMR and ^{13}C NMR data, see Tables S4 and S7. MS (ESI): m/z = 1287.2 [M + Na]$^+$, 1303.1 [M + K]$^+$. Accurate MS (ESI): m/z calcd for [M + Na]$^+$ $C_{58}H_{76}O_5S_{12}SiNa^+$: 1287.2003; found, 1287.2024. ^{1}H NMR spectroscopical data of the mixture of the two diastereomers); signals assigned to the trityl alcohols **23**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.16 (s, 2H, H_{Ar} of **23a** and **23b**), 6.53 (s, 1H, OH of **23a**), 6.49 (s, 1H, OH of **23b**), 1.9-1.6 (m, 72H, $C(CH_3)_2$ of **23a** and **23b**, overlap with ^{t}Bu), 1.64 (s, 18H, ^{t}Bu of **23a** and **23b**, overlap with $C(CH_3)_2$), 1.15 (s, 42H, ^{i}Pr$_3$Si of **23a** and **23b**). The signals of *tert*-butyl pentanoate (**24**) were identified by comparison with ^{1}H NMR spectroscopical data from independently synthesized material. The synthesis is reported in the Supporting Information.

***Tert*-butyl 8-(hydroxybis(2,2,6,6-tetramethyl-8-((triisopropylsilyl)ethynyl)benzo[1,2-d:4,5-d']bis([1,3]dithiole)-4-yl)methyl)-2,2,6,6-tetramethylbenzo[1,2-*d*:4,5-*d*']bis([1,3]dithiole)-4-carboxylate (TritylOH[$CO_2{}^t$Bu/CCTIPS/CCTIPS] (14)).** To prepare *N*-*tert*-butoxycarbonylpyridinium *tert*-butanolate (**12**) di-*tert*-butyl dicarbonate (240 µL, 1.12 mmol) was added to a colorless solution of 4-*N*,*N*-dimethylaminopyridine (196 mg, 1.61 mmol) in dry Et_2O (30 mL). The colorless solution was stirred at room temperature for 90 min. In the meantime, a solution of *n*-BuLi (1.60 M, 0.53 mL, 0.80 mmol) in hexanes was added to an orange solution of tritylOH[H/CCTIPS/CCTIPS] (**11**) (200 mg, 160 µmol) and

N,N,N′,N′-tetramethylethylenediamine (121 µL, 802 µmol) in dry *n*-hexane (11 mL). After stirring this turbid green solution at room temperature for 5 min it was added to the solution of the *N*-*tert*-butoxycarbonylpyridinium *tert*-butanolate (**12**). After stirring the turbid green suspension at room temperature for 240 min, it was filtered through silica gel (2 cm x 7 cm, rinsing with Et_2O). The yellow filtrate (150 mL) was washed with a saturated aqueous solution of NH_4Cl (2 x 30 mL), water (30 mL), dried over $MgSO_4 \cdot x\ H_2O$, and filtered. The solvents were removed. The components of the residual yellow oil were separated by column chromatography (2 cm x 40 cm). Elution with CH_2Cl_2/pentane 1:2 gave tritylOH[H/CCTIPS/CCTIPS] (**11**) (4 mg, 2%; R_f = 0.61) as an orange oil, a mixture (5 mg; R_f = 0.61, 0.36) of tritylOH[H/CCTIPS/CCTIPS] (**11**), tritylOH[$CO_2{}^t$Bu/CCTIPS/CCTIPS] (**14**) and unidentified compounds as a brown oil, and tritylOH[$CO_2{}^t$Bu/CCTIPS/CCTIPS] (**14**) (70 mg, 32%; R_f = 0.36; Mp: 197-198 °C with gas evolution) as a yellow solid. For ^{1}H NMR and ^{13}C NMR data, see Tables S4 and S7. MS (ESI): *m*/*z* = 1367.1 [M + Na]$^+$. Accurate MS (ESI): *m*/*z* calcd for [M + Na]$^+$ $C_{64}H_{88}O_3S_{12}Si_2Na^+$: 1367.2813; found, 1367.2819.

5-(Butylthio)-2,2-dimethylbenzo[*d*][1,3]dithiole (Trithiobenzene 16). To a colorless solution of tetrathiobenzene **4a** (100 mg, 349 µmol) in dry Et_2O (10 mL) was added a solution of *n*-BuLi (1.60 M, 0.22 mL, 0.35 mmol) in hexanes. After stirring the colorless suspension at room temperature for 30 min, degassed water (300 µL) was added. Et_2O (10 mL) was added and the organic phase was washed with water (3 x 5 mL). The combined organic phases were dried over $MgSO_4\ x\ H_2O$ and filtered. The solvents were removed giving a colorless solid (104 mg) consisting of tetrathiobenzene **4a** and trithiobenzene **16** in the molar ratio of 83:17. Preparative HPLC (three isocratic runs with *n*-hexane, flow rate of 20 mL/min; 3 x 24 mg dissolved in *n*-hexane (1300 µL, 2 x 1250 µL) were injected) gave tetrathiobenzene **4a** (31 mg, 31%) at 15.9 min as a colorless solid and a colorless solid (11 mg) at 17.9 min consisting of tetrathiobenzene **4a** and trithiobenzene **16** in the molar ratio of 45:55. For ^{1}H NMR and ^{13}C NMR data see Tables S5 and S8. MS (EI): *m*/*z* (%) 270.1 (40) [M]$^{+\bullet}$, 255.1 (100) [M - $\bullet CH_3$]$^+$.

5-(*Sec*-butylthio)-2,2-dimethylbenzo[*d*][1,3]dithiole (Trithiobenzene 17). To a colorless solution of tetrathiobenzene **4a** (100 mg, 349 µmol) in dry Et_2O (10 mL) was added a solution of *s*-BuLi (1.40 M, 0.25 mL, 0.35 mmol) in *n*-hexane/cyclohexane 8:92. After stirring the colorless suspension at room temperature for 30 min, degassed water (300 µL) was added. Et_2O (10 mL) was added and the colorless solution was washed with water (3 x 5 mL). The organic phase was dried over $MgSO_4 \cdot x\ H_2O$ and filtered. The solvents were removed giving a colorless solid (107 mg) consisting of tetrathiobenzene **4a** and trithiobenzene **17** in the molar ratio of 74:26. Preparative HPLC (isocratic run with *n*-hexane, flow rate of 20 mL/min; 27 mg dissolved in *n*-hexane (1300 µL) was injected) gave tetrathiobenzene **4a** (18 mg) at 15.0 min as a colorless solid and a colorless solid (4 mg) at 18.2 min consisting of tetrathiobenzene **4a** and trithiobenzene **17** in the molar ratio of 4:96. For ^{1}H NMR and ^{13}C NMR data of trithiobenzene **17**, see Tables S5 and S8. Additional analytical data of trithiobenzene **17**: MS (EI): *m*/*z* (%) 270.0 (45) [M]$^{+\bullet}$, 255.0 (43) [M - $\bullet CH_3$]$^+$, 199.0 (100).

5-(*Tert*-butylthio)-2,2-dimethylbenzo[*d*][1,3]dithiole (Trithiobenzene 18). To a colorless solution of tetrathiobenzene **4a** (100 mg, 349 µmol) in dry Et_2O (10 mL) cooled to -20 °C was added a solution of *t*-BuLi (2.70 M, 0.13 mL, 0.35 mmol) in heptane. After stirring the yellowish turbid solution for 30 min, degassed water (300 µL) was added. After warming it to room temperature, Et_2O (10 mL) was added and the colorless solution was washed with water (3 x 5 mL). The organic phase was dried over $MgSO_4 \cdot x\ H_2O$ and filtered. The solvents were removed giving a colorless solid (106 mg) consisting of tetrathiobenzene **4a** and trithiobenzene **18** in the molar ratio of 57:43. Preparative HPLC (gradient run with CH_2Cl_2/*n*-hexane, 2.0% CH_2Cl_2 at 0 min to 10.0% CH_2Cl_2 at 25 min, flow rate of 20 mL/min; 35 mg dissolved in CH_2Cl_2/*n*-hexane 2:98 (900 µL) was injected) gave tetrathiobenzene **4a** (13 mg) at 9.2 min as a colorless solid and trithiobenzene **18** (4 mg) at 11.1 min as a colorless oil. For ^{1}H NMR and ^{13}C NMR data see Tables S5 and S8. MS (EI): *m*/*z* (%) 270.1 (40) [M]$^{+\bullet}$, 214.0 (100). Accurate MS (EI): *m*/*z* calcd for [M]$^{+\bullet}$ $C_{13}H_{18}S_3^{+\bullet}$: 270.0565; found, 270.0558.

5-(*Tert*-butylthio)-2,2-dimethylbenzo[*d*][1,3]dithiole-6-*d* (Trithiobenzene 18(D)). The synthesis was carried out under the conditions reported for the synthesis of trithiobenzene **18** with the only difference that D_2O instead of H_2O was added to the lithiated species. A colorless solid (95 mg) consisting of tetrathiobenzene **4a**, deuterated tetrathiobenzene **4a(D)**, trithiobenzene **18** and deuterated trithiobenzene **18(D)** in the molar ratio of 30:21:7:42 was obtained. Preparative HPLC (two isocratic runs with CH_2Cl_2/*n*-hexane 2:98, flow rate of 20 mL/min; 2 x 35 mg dissolved in CH_2Cl_2/*n*-hexane 2:98 (2 x 1100 µL) were injected) gave a mixture of tetrathiobenzenes **4a** and **4a(D)** (26 mg) at 12.9 min as a colorless solid and a mixture (17 mg) of tetrathiobenzenes **4a**/**4a(D)**, trithiobenzenes **18**, and deuterated trithiobenzene **18(D)** in the molar ratio of 1:12:87 was obtained at 16.8 min as a colorless solid. For ^{1}H NMR and ^{13}C NMR data, see Tables S5 and S8.

Tris(2,2,6,6-tetramethylbenzo[1,2-*d*:4,5-*d*′]bis([1,3]dithiole)-4-yl)methanol (TritylOH[H/H/H] (19)) synthesized by addition of lithiated tetrathiobenzene 5a to diarylketone 9a. To a slightly yellowish solution of tetrathiobenzene **4a** (335 mg, 1.17 mmol) in dry THF (15 mL) was added a solution of MeLi (1.90 M, 0.55 mL, 1.1 mmol) in Et_2O. After stirring the solution at room temperature for 100 min the solvent was removed and the remaining slightly yellowish solid was suspended in dry Et_2O (20 mL). A 56:44 mixture (350 mg) of diarylketone **9a** (525 µmol) and CH_2Cl_2 (413 µmol) was added and the suspension consisting of a colorless solid in a green solution was stirred at 30 °C for 7 d. After cooling to room temperature, water (30 mL) and CH_2Cl_2 (50 mL) were added to the suspension consisting of a yellowish solid in an orange solution. The aqueous phase was separated and extracted with CH_2Cl_2 (2 x 30 mL). The combined organic phases were dried over $MgSO_4 \cdot x\ H_2O$ and filtered. The solvents were removed. The components of the remaining orange

solid were separated by column chromatography (3 cm x 24 cm). Elution with CH_2Cl_2/pentane 5:6 gave four fractions: (1) tetrathiobenzene **4a** (85 mg; R_f = 0.69) as a slightly yellowish solid; (2) a mixture (3 mg; R_f = 0.69, 0.48) of tetrathiobenzene **4a** and unidentified compounds as a brown solid; (3) tritylOH[H/H/H] (**19**) (293 mg, 63%; R_f = 0.31) as a yellowish solid; (4) a 92:2:6 mixture (76 mg, R_f = 0.31) of tritylOH[H/H/H] (**19**) (16% yield), diarylketone **9a** (0.3% yield) and CH_2Cl_2 as a yellow solid. For ^{1}H NMR and ^{13}C NMR data, see Tables S4 and S7. Data are in agreement with data given in the literature.[61] MS (MALDI): m/z = 884.0 $[M]^+$.

Comment: If we were to repeat this synthesis, we would use diarylketone without CH_2Cl_2. CH_2Cl_2 can be exchanged for Et_2O as described in the procedure for the synthesis of diarylketone **9a**.

Tris(2,2,6,6-tetramethylbenzo[1,2-*d*:4,5-*d*']bis([1,3]dithiole)-4-yl)methanol (TritylOH[H/H/H] (19)) synthesized by addition of lithiated tetrathiobenzene 5a to dimethyl carbonate. To a slightly yellowish solution of tetrathiobenzene **4a** (3.00 g, 10.5 mmol) in dry THF (20 mL) was added a solution of MeLi (1.71 M, 5.5 mL, 9.4 mmol) in Et_2O. After stirring the solution at room temperature for 100 min the solvent was removed and the remaining slightly yellowish solid was suspended in dry Et_2O (60 mL). Dimethyl carbonate (0.22 mL, 2.6 mmol) was added and the yellow suspension was stirred at 30 °C for 7 d. After cooling to room temperature, CH_2Cl_2 (80 mL) and water (40 mL) were added to the suspension consisting of a yellowish solid in an orange solution. The aqueous phase was separated and extracted with CH_2Cl_2 (20 mL). The combined organic phases were dried over $MgSO_4 \cdot x$ H_2O and filtered. The solvents were removed. The components of the remaining orange solid were separated by column chromatography (5 cm x 54 cm). Elution with CH_2Cl_2/pentane 5:6 gave a mixture (550 mg, R_f = 0.63) of tetrathiobenzene **4a** and traces of unidentified compounds as a slightly yellowish solid and a mixture (2.03 g, R_f = 0.30) of tritylOH[H/H/H] (**19**) (86% yield), CH_2Cl_2, and pentane in the molar ratio of 80:19:1.

***Tert*-butyl pentanoate (24).** The procedure of Yamada et al.[84] was followed with slight modifications. To a colorless solution of tert-butanol (10.0 mL, 106 mmol), 4-*N*,*N*-dimethylaminopyridine (4 mg, 0.6 mmol), and pyridine (5.0 mL, 62 mmol) in dry CH2Cl2 (15 mL) cooled with an ice water bath was added pentanoyl chloride (6.0 mL, 50 mmol) within 2 min. After 15 min the ice water bath was removed and the suspension consisting of a colorless solid in a yellow solution was stirred at room temperature for 22 h. Et2O (50 mL) was added and the suspension was washed with water (25 mL), an aqueous solution of HCl (2 M, 25 mL), a saturated aqueous solution of NaHCO3 (25 mL) and water (25 mL). The organic phase was separated, dried over MgSO4 · x H2O, and filtered. The solvents were removed at 500 mbar and 40 °C bath temperature. The components of the residual yellow liquid were separated by distillation at 19 mbar. At 80 °C bath temperature two fractions, both with 56 °C vapor temperature, were collected: (1) a colorless liquid (358 mg) consisting of *tert*-butyl pentanoate (**24**) (4% yield) and tert-butanol in the molar ratio of 94:6; (2) a colorless liquid (5.74 g) consisting of tert-butyl pentanoate (**24**) (71% yield) and *tert*-butanol in the molar ratio of 99:1. A part (437 mg) of fraction 2 was dissolved in pentane (10 mL). The colorless solution was washed with water (5 x 50 mL). The organic phase was separated, dried over MgSO4 · x H2O, and filtered. The solvent was removed at 19 mbar at room temperature giving *tert*-butyl pentanoate (**24**) (433 mg) as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.18 (t, ^3J = 7.5 Hz, 2H, CH_2CO), 1.54 (quint like with shoulders, 2H, CH_2CH_2CO), 1.41 (s, 9H, CMe_3), 1.31 (sext like, 2H, $CH_3C\underline{H}_2$), 0.88 (t, ^3J = 7.5 Hz, 3H, $C\underline{H}_3CH_2$). 13C NMR (125 MHz, $CDCl_3$): δ 173.3 (CO), 79.8 ($\underline{C}Me_3$), 35.3 (CH_2CO), 28.1 ($C\underline{Me}_3$), 27.2 CH_2CH_2CO), 22.2 ($CH_3\underline{C}H_2$), 13.7 ($\underline{C}H_3CH_2$).

EPR spectroscopical experiments

The Finland trityl, which was used for EPR measurements, were synthesized according to published procedures.[61,67] Solutions (200 µM) of the trityl radicals in ethanol were filled into quartz capillaries of 3 mm (Aachener Quartzglas, Aachen, Germany) and 0.9 mm (Wilmad Labglass, Vineland, USA) outer diameter for X and W band EPR experiments, respectively, without prior degassing. When needed, a carbon fiber (Institutes of Textile and Fiber Research, Denkendorf, Germany), used as g-factor standard,[80] was added to the solutions.

Pulse EPR experiments were performed on an Elexsys E680 EPR spectrometer (Bruker Biospin, Rheinstetten, Germany) at X band (approx. 9.5 GHz) using a Bruker MD5 resonator as well as at W band (approx. 94.2 GHz) using a Bruker ENDOR resonator. For both X and W band measurements we used pulse lengths of 16 ns and 32 ns for $\pi/2$ and π pulses, respectively, unless stated otherwise. 2-pulse ESEEM was recorded using the sequence ($\pi/2 - \tau - \pi - \tau$ - echo) by incrementing τ for 1024 points in steps of 8 ns using a two-step phase cycle to cancel receiver offsets. The inversion recovery sequence (π - t - $\pi/2 - \tau - \pi - \tau$ - echo) with the two-step phase cycle was used to determine T_1 by incrementing t in steps of 12 µs for 4096 points or 20 µs for 2048 for X and W band, respectively. Additionally, 3-pulse ESEEM ($\pi/2 - \tau - \pi/2 - T - \pi/2 - \tau$ - echo) was measured at X band by incrementing T in steps of 8 ns for 1024 points using a four-step phase cycle with τ = 144 ns, 164 ns, and 184 ns for τ averaging. 3-pulse ESEEM time domain data were baseline-corrected using a 4th order polynomial function, apodized by a Hamming window, zero-filled to twice the number of points, here 2048, and then Fourier transformed and the magnitude spectrum was calculated.

Continuous wave (cw) EPR measurements were performed on a Bruker Elexsys E500 or Bruker EMX spectrometer using a Bruker SHQ resonator and recorded at a microwave power of 3.17 µW (48 dB attenuation) at 50 K or 200.2 µW (30 dB attenuation) at room temperature, respectively, in order to avoid saturation effects. The cw EPR spectra were recorded using 8192 points and a 100 kHz magnetic field modulation with an amplitude of 0.02 mT for subsequent lock-in amplification with a conversion time and time constant of 40.96 ms and 1.28 ms, respectively. The radical content of the samples was quantified

by double integration of the room temperature spectra and comparison to a solution of FTR with known concentration.

W band cw EPR measurements were carried out in the same setup as W band pulse experiments. Spectra were recorded at 50 K and a nominal microwave power of 0.006 μW (60 dB attenuation) ensuring non-saturated conditions using 1024 points and a 100 kHz magnetic field modulation with an amplitude of 0.1 mT with a conversion time of 81.92 ms and time constant of 1.28 ms. Magnetic field offsets of W band cw EPR spectra were corrected using Mn(II) in CaO (Bruker Biospin) and the carbon fiber as a reference. The spectra were baseline corrected and simulated using the Matlab package EasySpin[85], taking into account g tensor and g distribution.

ASSOCIATED CONTENT

Supporting Information. Results for lithiation of tetrathiobenzene **4a** and trityl alcohols **10**, **11**, and **19**, pictures taken during the synthesis of tritylOH[H/CCTIPS/CCTIPS] (**11**), a chapter on identified byproducts and side products, additional EPR spectra, information on the reagents used, tables with ^{1}H and ^{13}C NMR data, and figures showing the NMR spectra and some MS spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

godt@uni-bielefeld.de.

Author Contributions

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Notes

The authors declare no competing financial interest.

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