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3,5-Di-tert-butylthiobenzoyltriphenylsilane: a versatile spin trapping agent

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Abstract

3,5-Di-tert-butylthiobenzoyltriphenylsilane (DBTBTPS) has been synthesized and tested as a spin trapping agent for electron spin resonance studies. Upon reaction with a variety of radicals of different nature inside the cavity of the ESR spectrometer, DBTBTPS leads to the observation of rather persistent spectra which in nearly all cases allow the unambiguous identification of the trapped species DBTBTPS is somewhat less stable than thiobenzoyltriphenylsilane (TBTPS), the unsubstituted thiobenzoyltriphenylsilane; yet, as it affords spin adducts whose spectra are characterized by a smaller number of lines, it may prove more useful than TBTPS itself when dealing with radicals leading to species with a large number of magnetically active nuclei interacting with the unpaired electron.

Introduction

Free radicals are usually very reactive species that are characterized by extremely short lifetimes in solution; hence the designation transient that is often associated with them. In principle radicals can be directly detected in solution by means of electron spin resonance spectroscopy; in many instances, however, their observation is not feasible, normally because their lifetimes are too short.

To overcome this, the spin-trapping technique was devised, consisting of adding to the system under examination an unsaturated compound (the trap) that readily undergoes addition by the transient species affording a radical-adduct characterized by a longer lifetime, and which therefore can be easily detected. This technique has been widely exploited over the last two decades, and its use has been well documented [1–3].

The success of the spin-trapping experiment depends heavily on the choice of the trapping agent, which must possess a number of features: it must be stable and easy to handle; it must lead to adducts characterized by a high persistence and by ESR spectra as simple as possible; and it must not undergo side reactions with species other than those to be trapped [1].

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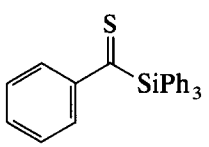
The most popular spin traps belong to two chemical families: nitroso compounds (*e.g.* 2-methyl-2-nitrosopropane, nitrosobenzene, pentamethoxynitrosobenzene) and nitrones (*e.g.* phenyl tert-butyl nitrone, 5,5-dimethyl-1-pyrroline-*N*-oxide) [3]. In both cases the resulting radicals are nitroxides, but whereas in the adducts with the former, the trapped radical is bound directly to the nitroxide nitrogen, in those with the latter, the radical is bound to the carbon atom adjacent to the nitrogen atom. As a consequence, nitroxides from nitroso compounds give spectra containing more information on the nature of the trapped species, and their use is favoured over that of nitrones. On the other hand, aliphatic nitroso-compounds and nitrones, although to a less extent, are sensitive to light; their use in spin-trapping experiments involving UV irradiation can thus be troublesome.

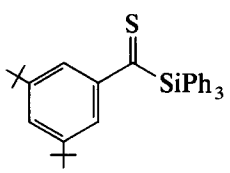
In several cases, spin-trapping agents not belonging to these two families have been exploited: these include sterically hindered *p*-benzoquinones [4,5], nitrile oxides [6,7], azodicarboxylates [8], 1,2,4-triazoline-3,5-dione [9], and some thiocarbonylcompounds [10–14]. In particular, it was shown that TBTPS readily reacts with radicals centred at carbon, silicon, germanium, tin, lead, phosphorus, oxygen, or sulphur, as well as at transition metal atoms such as manganese or rhenium, to give rather persistent spin adducts characterized by intense and well resolved ESR spectra [15]. Actually this compound has only two drawbacks which prevent it from being the ideal diamagnetic spin trap: first, it is not soluble in water, which prevents its use in biological systems (with the possible exception of lipids), and secondly, because in its spin adducts the unpaired electron is coupled with all the ring protons, rather complicated ESR spectra are often observed.

The solution to the first drawback poses more than one synthetic problem; moreover, the chances are that after a tedious and time-consuming synthesis, a compound is obtained which lacks the stability required for spin-trapping experiments in biological systems.

This paper presents a solution to the second drawback: the excessive number of lines sometimes observed in the spectra of the spin adducts with TBTPS, and describes the synthesis of 3,5-di-tert-butylthiobenzoyltriphenylsilane (DBTBTPS) as well as its use in spin trapping experiments.



(TBTPS)



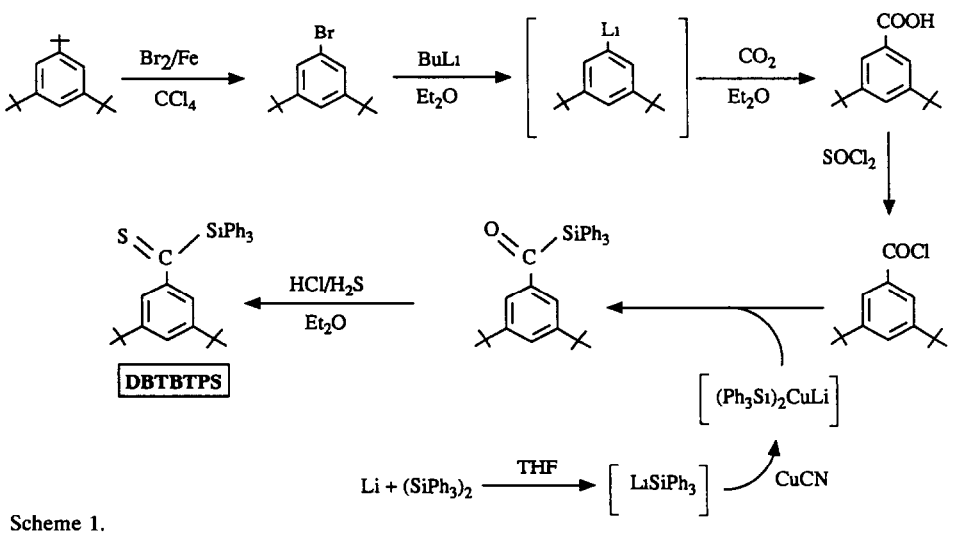
(DBTBTPS)

Results and discussion

One way to eliminate undesired hyperfine splittings from aromatic ring protons in organic radicals is to substitute tertiary alkyl groups, typically tert-butyl groups, for these hydrogens. Of course, due to the bulk of the tert-butyl group, it would be impossible to substitute adjacent hydrogen atoms, and therefore the choice is restricted either to the two *ortho* or to the two *meta* positions, the substitutions of only the *para* hydrogen being expected to lead to the removal of a doublet

coupling of approx. 4 G, and therefore to less of a simplification of the spectrum than that resulting from the substitution of two equivalent hydrogen atoms. Substitution at the *ortho* position was disregarded, as it was thought that the proximity of two large groups would hamper the introduction of the thiocarbonylic function. The only remaining possibility was then *meta* substitution.

One of the most popular methods for the preparation of thioketones is the conversion of the carbonyl into a thiocarbonyl function by the combined action of hydrogen chloride and hydrogen sulphide [16]; our problem thus reduced to the preparation of 3,5-di-tert-butylphenyl(triphenylsilyl)ketone. Reported syntheses of α-silylketones proceed through two general routes. One involves the lithiation of a suitable 1,3-dithiane, substitution of lithium with a trialkylsilyl group by action of the corresponding silyl chloride, and conversion of the resulting compound to the silyl ketone by treatment with mercury chloride–mercury oxide in aqueous methanol [17]. The unsubstituted thiobenzoyltriphenylsilane was first obtained following this route [18]. A second route to α-silyl ketones involves the preparation of a *gem*-dibromo compound from an appropriate benzylsilane, which is then converted to the α-silyl ketone by reaction with silver acetate in aqueous ethanol [19]. Our approach to DBTBTPS is based on the recent report [20] that α-silyl ketones can be obtained by reaction of a carboxylic acid chloride with a silyl lithium cuprate generated *in situ*, and is outlined in Scheme 1. 1,3,5-Tri-tert-butyl benzene is treated with bromine in the presence of iron in carbon tetrachloride to afford the *ipso* substitution product 3,5-di-tert-butylbromobenzene. This bromide is then lithiated in tetrahydrofuran (THF) and subsequently converted to the corresponding acid by reaction with CO_2 and to the acyl chloride with thionyl chloride. Reaction of this last derivative with *in situ* generated lithium triphenylsilane in the presence of cuprous cyanide leads to di-tert-butylbenzoyltriphenyl-



Scheme 1.

Table 1

ESR spectral parameters [a] for some radical adducts with DBTBTPS in benzene at room temperature

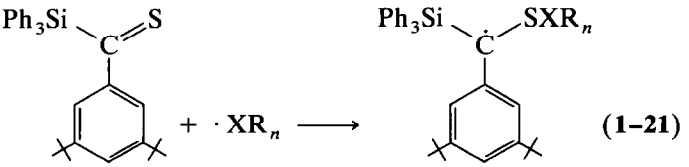
Radical	XR_n	a_o	a_p	a_{other}	g
1	Me	3 18	3 83	1 74(3H)	2.0043_2
2	Et	3.16	3.34	0.95(2H), 047(3H), 9.23(^{29}Si) 24.2(^{13}C)	2.0043_4
3	^{t}Bu	3.08	3.50	0.42(9H)	2.0038_9
4	$PhCH_2$	3.11	3.18	0.73(2H), 9.15(^{29}Si), 25.0(^{13}C)	$2\ 0042_1$
5	Ph	3.45	3.86	0.39(5H), 9.43(^{29}Si), 24.4(^{13}C)	2.0039_7
6	Btz [b]	3 83	4.40	0 35(1N)	2.0038_9
7	$SiPh_3$	3 79	4.28	10.47($^{29}Si_\alpha$), 14.16($^{29}Si_\beta$), 26.7(^{13}C)	$2\ 0038_6$
8	$GePh_3$	3.64	4.08	10.35(^{29}Si), 7.20(^{73}Ge)	2.0038_5
9	$SnMe_3$	3 52	3.76	0.21(9H), 113.6(^{119}Sn)	2.0043_8
10	$SnBu_3$	3 57	3 65	10.66(^{29}Si), 91.8(^{119}Sn), 25.7(^{13}C)	2.0045_7
11	$PbPh_3$	3.52	3 62	267.9(^{207}Pb)	1.9974_9
12	PPh_2	3.80	4.10	20.4(^{31}P)	2.0036_2
13	$P(O)Ph_2$	4.03	4.74	37.9(^{31}P)	2.0033_1
14	$P(S)Ph_2$	3.97	4 62	53.8(^{31}P)	2.0040_3
15	$P(S)Et_2$	4.21	4.52	45.7(^{31}P), 9 91(^{29}Si)	2.0038_0
16	O^{t}Bu	3.49	3.85	0.27(9H), 8.87(^{29}Si), 24.7(^{13}C)	2.0036_5
17	SPh	3.43	3.86	8.10(^{29}Si), 24.4(^{13}C)	2.0037_5
18	SBtz [b]	3.54	4.04	0.66(1N)	$2\ 0034_2$
19	SePh	3.50	3 66		2.0068_0
20	$Mn(CO)_5$	2.45	2.45	6.32(^{55}Mn)	2.0074_5
21	$Re(CO)_5$	2.51	2.51	55.1($^{185/187}$Re)	2.0105_0

[a] Coupling constants in Gauss = 10^{-4} Tesla. [b] Btz = Benzo-1,3-thiazol-2-yl.

silane, from which DBTBTPS is eventually obtained by reaction with hydrogen sulphide in acidic medium.

3,5-Di-tert-butylthiobenzoyltriphenylsilane is a turquoise crystalline compound, which readily undergoes desulphuration in the presence of oxygen, but which can be safely stored under argon for long periods.

In the presence of free radicals, DBTBTPS undergoes thiophilic attack at the thiocarbonylic function, leading to the formation of rather persistent spin adducts which can be characterized by means of ESR spectroscopy. The spectral parameters for the observed radical adducts are given in Table 1.



(1–21)

(X = C, Si, Ge, Sn, Pb, P, O, S, Se, Mn, or Re)

The structural information that one may derive from the ESR spectrum of a radical is related to the *g*-factor of the spectrum itself, as well as to its hyperfine spectral pattern. The larger the number of coupled nuclei, the more detailed are the inferences one may draw. On the other hand, a large number of coupled nuclei may lead to a very complicated spectral pattern, too difficult to interpret: what is actually needed is a maximum of information with the lowest possible number of interacting nuclei. The data collected in Table 1 for radicals **1–21** are straightfor-

ward and need little comment. They indicate that although the ESR spectra of these adducts are much simpler than those of the corresponding adducts of TBTPS [15], they generally provide the same structural information. In all cases, the spectra consist basically of a doublet of triplets due to coupling of the unpaired electron with the two *ortho* and the *para* protons. In most instances, additional splittings due to magnetically active nuclei (H, N, P, Mn, or Re) of the trapped radical may also be observed, as well as satellite lines due to other active nuclei present in low natural abundance (Si, Ge, Sn, or Pb). ^{13}C satellites for the α-carbon atom are also detected in several cases: assuming that the radical centre is completely planar, the measured splitting (25–27 G) indicates that nearly 65% of the spin density resides on this carbon atom. This is substantially in line with that found with structurally related ketyl and thioketyl radicals [21,22], as is the ^{29}Si hyperfine splitting (9–11 G) due to the silicon atom bound to the radical centre [22].

It is worthwhile noting that alkyl radicals lead to adducts with spectra which always exhibit splitting characteristics of the particular alkyl, and thus provide a sort of fingerprint of the trapped species. In the case of phosphorus-centred radicals, it is readily possible to discriminate between $R_2P^{\cdot}$, $R_2(O)P^{\cdot}$, and $R_2(S)P^{\cdot}$ species simply on the basis of the value of the ^{31}P hyperfine splitting, which is typically approx. 20 G for phosphinyl, 35–40 G for phosphonyl, and ≥ 50 G for thiophosphonyl adducts. As to Group 14 radicals, ^{29}Si, ^{73}Ge, $^{117/119}Sn$ and ^{207}Pb satellite lines can be easily observed by recording the spectra at high gain.

The photoreaction of DBTBTPS with phenyl disulphide leads to the detection of the phenyl and the phenylthiyl radical adducts, although the former is present in smaller amount (approx. 8%). Two radical adducts are also observed simultaneously from reaction of benzo-1,3-thiazol-2-yl disulphide under similar conditions (see Fig. 1). These species show coupling of the unpaired electron with a nitrogen atom (0.34 or 0.66 G), both indicating the presence of the heterocyclic moiety; by analogy with what was observed with phenyl disulphide, and considering the different g-values of the two radicals, we tentatively assign the spectrum centred at lower field and characterized by the smaller nitrogen splitting to the benzo-1,3-thiazol-2-yl adduct of the thioketone (approx. 26%), and the one characterized by the smaller g-factor to the benzo-1,3-thiazol-2-ylthiyl (approx. 74%). Although these appear to us the most sensible assignments, we note that the values of the two nitrogen splittings are rather large for atoms so far away from the radical centre (in δ and γ positions, respectively), this being presumably a consequence of particularly favourable conformations of the adducts.

As to the advantage of using DBTBTPS instead of TBTPS in spin trapping experiments, Fig. 2 which shows the spectra of the methyl adducts of the two traps is self-explanatory. In both cases, the splitting from the three equivalent protons of the methyl radical is observed, but the former scavenger leads to spectra whose interpretation is much easier due to the reduced number of lines, although the information about the trapped radical is totally retained.

Although similar information might also have been readily obtained using nitrosocompounds, DBTBTPS is particularly suitable when dealing with species that fail to give stable nitroxides. This is the case for radicals centred at Group 14 elements (Si, Ge, Sn, and Pb), which generally react with nitrosoalkanes to give unstable oxyaminyls, but whose adducts with DBTBTPS have lifetimes of hours.

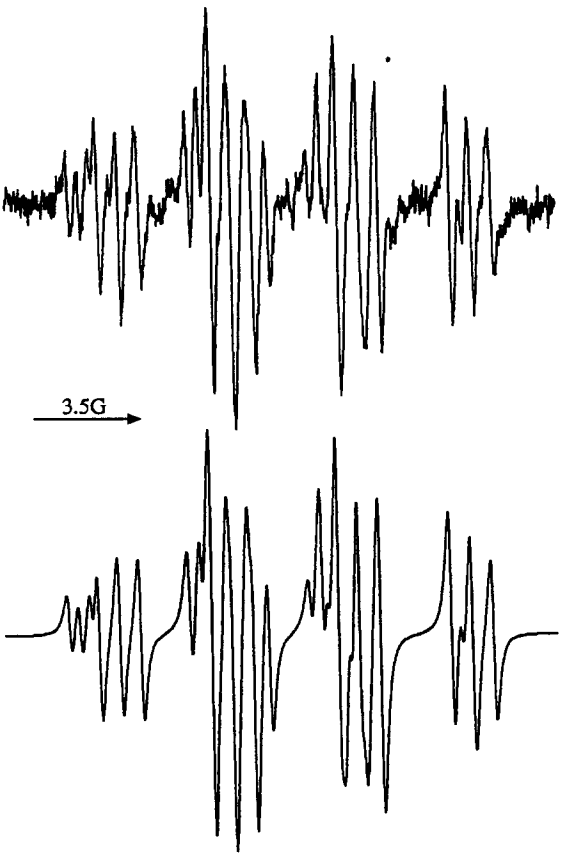


Fig. 1. Room temperature experimental (above) and simulated (below) ESR spectra observed upon UV irradiation of a benzene solution containing DBTBTPS and benzo-1,3-thiazol-2-yl disulphide.

Similar considerations apply to thiyl radicals, which have been previously shown to be readily trapped by thioketones [14,15] and to metal carbonyls such as $[Mn(CO)_5]$ and $[Re(CO)_5]$.

Concluding remarks

3,5-Di-tert-butylthiobenzoyltriphenylsilane is a versatile spin-trapping agent which, like thiobenzoyltriphenylsilane itself, readily scavenges nucleophilic as well as electrophilic radicals. DBTBTPS is particularly useful in those spin-trapping experiments carried out in organic media and involving Group 14 organometallic radicals or radicals centred at sulphur or oxygen. Although less stable than TBTPS, its use is preferred over that of the unsubstituted compound when dealing with radicals leading to adducts characterized by complicated ESR spectra, or in systems where more than one radical species may be present.

Experimental

Materials

3,5-Di-tert-butylbromobenzene was prepared as described in the literature [23] from 1,3,5-tri-tert-butylbenzene, which was purchased from Aldrich and used without further purification.

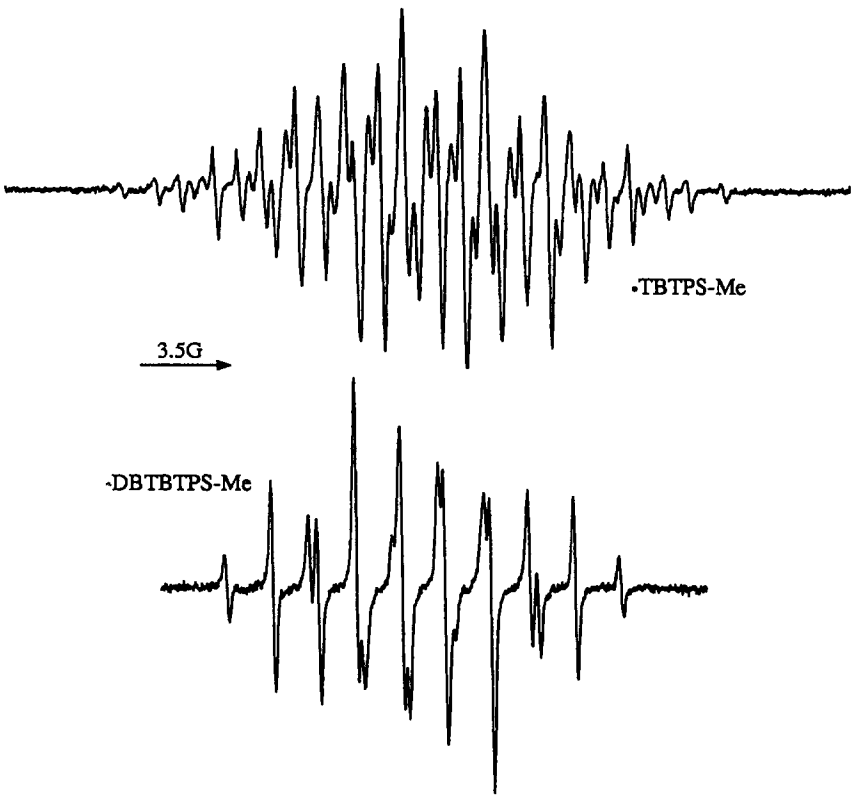


Fig. 2. ESR spectra of the methyl adduct of thiobenzoyltriphenylsilane (above) and of DBTBTPS (below) in benzene at room temperature.

3,5-Di-tert-butylbenzoic acid. To a stirred solution of 3,5-di-tert-butylbromobenzene (9.15 g, 34 mmol) in THF (100 ml) cooled to −78°C, 138 ml of a 2.5 *M* ethereal solution of LiBu were added dropwise. After 3 h, when all the bromo-compound had been consumed, anhydrous CO_2 was bubbled through the solution for about 5 min, which was then allowed to warm up to room temperature. After acidification with 1 *N* HCl, the solution was extracted with ether and the ethereal layer was dried over Na_2SO_4. Upon evaporation of the ether, the crude acid was obtained quantitatively and was then crystallized from hexane (m.p. 159°C). ^1H NMR spectrum: δ 1.4 (s, 18H); 7.7 (s, 1H); 8.0 (s, 2H); 10.8 (broad s, 1H, disappears upon addition of D_2O) ppm. Mass spectrum: peaks at m/z 234 (M^+), 233 ($M^+ - H$), 216 ($M^+ - OH$), 57 (t-butyl$^+$).

3,5-Di-tert-butylbenzoyl chloride. The acid (2.57 g, 11 mmol) was heated under reflux in an excess of $SOCl_2$ (5 ml) until the evolution of HCl ceased. After evaporation of the thionyl chloride, the residue was distilled at reduced pressure (b.p.$_{0.1\ mmHg}$ 90°C). ^1H NMR spectrum: δ 1.36 (s, 18H); 7.76 (s, 1H); 7.97 (s, 2H) ppm. Mass spectrum: peaks at m/z 254, 252 (M^+), 237 ($M^+ - Me$), 217 ($M^+ - Cl$), 57 (t-butyl$^+$).

3,5-Di-tert-butylbenzoyltriphenylsilane. To a stirred solution of triphenylsilyl-lithium in THF (obtained as previously described [24] starting from hexaphenyldisi-

lane (2.6 g, 5 mmol) and approx. 10 mg lithium) was added CuCN (0.45 g, 5 mmol), keeping the temperature below 20°C by means of an ice bath. After 30 min the mixture was cooled to −23°C and a solution of the acyl chloride (2.52 g, 10 mmol) in THF (10 ml) was added dropwise. The mixture was then warmed to room temperature and left standing for 1 h. After quenching with 1 *N* HCl, the mixture was extracted with diethyl ether. The organic phase was then dried and evaporated, and after chromatography over silica gel (C_6H_{14}/CH_2Cl_2, 1:1), 3.1 g (6.5 mmol, 65% yield) of pure α-silylketone (m.p. 147–148°C) were obtained. ^{1}H NMR spectrum: δ 1.15 (s, 18H); 7.39 (m, 9H); 7.53 (t, J = 1.1 Hz, 1H); 7.65 (m, 6H), 7.71 (d, J = 1.1 Hz, 2H) ppm. ^{13}C NMR spectrum: δ 230.7 (C=O) ppm. ^{29}Si NMR spectrum: −28.8 (s) ppm. Mass spectrum: peaks at m/z 476 (M^+), 419 (M^+ − t-butyl), 259 (Ph_3Si^+).

3,5-Di-tert-butylthiobenzoyltriphenylsilane. Gaseous HCl and H_2S were bubbled into a stirred solution of α-silylketone (4.8 g, 1 mmol) in distilled diethyl ether (30 ml) kept at −15°C, until an intense pale blue colour was observed. The solution was neutralized with cold 20% NaOH, the organic layer separated, the solvent evaporated, and the residue chromatographed over silica gel (C_6H_{14}/CH_2Cl_2, 1:1) under argon. After crystallization from hexane at −30°C, 0.29 g (0.6 mmol, 60% yield) of pure DBTBTPS (m.p. 140°C) were obtained. ^{1}H NMR spectrum: δ 1.13 (s, 18H); 7.35 (m, 10H); 7.55 (m, 6H); 7.64 (d, J = 1.8 Hz) ppm. ^{13}C NMR spectrum: δ 282.7 (C=S) ppm. ^{29}Si NMR spectrum: δ −21.8 (s) ppm. Mass spectrum: peaks at m/z 492 (M^+), 435 (M^+ − t-butyl), 259 (Ph_3Si^+). UV: λ_{max} = 697 nm, ϵ = 48.

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