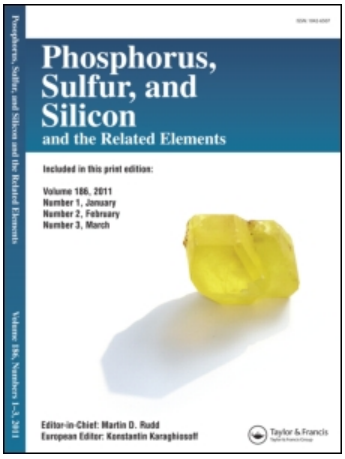


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

SYNTHESIS OF HYDROLYTICALLY STABLE *tert*-BUTYLDIMETHYLSILYL ETHERS OF HYDROXYANTHRAQUINONES

Maria N. Bakola-christianopoulou[a]; Katerina K. Apazidou[a]
[a] Department of Chemical Engineering, School of Engineering, Aristotle University of Thessaloniki, Thessaloniki, Greece

To cite this Article Bakola-christianopoulou, Maria N. and Apazidou, Katerina K.(1996) 'SYNTHESIS OF HYDROLYTICALLY STABLE *tert*-BUTYLDIMETHYLSILYL ETHERS OF HYDROXYANTHRAQUINONES', Phosphorus, Sulfur, and Silicon and the Related Elements, 113: 1, 245 — 253
To link to this Article: DOI: 10.1080/10426509608046395
URL: http://dx.doi.org/10.1080/10426509608046395

Phosphorus, Sulfur, and Silicon, 1996, Vol. 113, pp. 245–253
Reprints available directly from the publisher
Photocopying permitted by license only

SYNTHESIS OF HYDROLYTICALLY STABLE *tert*-BUTYLDIMETHYLSILYL ETHERS OF HYDROXYANTHRAQUINONES

MARIA N. BAKOLA-CHRISTIANOPOULOU† and KATERINA K. APAZIDOU
Department of Chemical Engineering, School of Engineering, Aristotle University of Thessaloniki, P.O. Box 68, Gr-540 06 Thessaloniki, Greece

(Received November 15, 1995; in final form January 29, 1996)

A series of hydrolytically stable hydroxyanthraquinone *tert*-butyldimethylsilyl ethers was synthesized by hydroxyl group silylation, under optimized reaction conditions. *Tert*-butyldimethylsilylchloride and N-methyl-N-*tert*-butyldimethylsilyl-1,1,1-trifluoroacetamide were each used as the silylating agent in two different silylating procedures. The products were studied by several chromatographic and spectroscopic techniques (TLC, GC, MS, IR, UV-Vis, ^{1}H NMR). Some helpful notifications for the advantageous use of each procedure, in regard to the requirements of the application field, were also made.

Key words: Hydroxyanthraquinones, *tert*-butyldimethylsilyl ethers, N-methyl-N-*tert*-butyldimethylsilyl-1,1,1-trifluoroacetamide, *tert*-butyldimethylsilylchloride, *tert*-butyldimethylsilylation of hydroxyl groups.

INTRODUCTION

Tert-butyldimethylsilyl (TBDMS) ethers of hydroxynaphthoquinones as well as the ones achieved by the reductive silylation of hydroxynaphthoquinones were found to be particularly stable over a long period of time, thus allowing their isolation and characterization by several chromatographic and spectroscopic methods[1] in contrast to their trimethylsilyl (TMS) analogues.[2,3] Furthermore, due to their enhanced hydrolytic stability,[4] they could be submitted to pharmacological studies as lipophilic derivatives[5] of biologically active hydroxynaphthoquinones.[6]

Within our interest in silylation reaction of quinones[7,8] and in regard to the potent biological activity of hydroxyanthraquinone derivatives,[9] we herein report on the synthesis and characterization by several spectroscopic techniques of the TBDMS ethers of hydroxyanthraquinones **1–6**, by silylation of their hydroxyl groups (Table I). Two different silylating agents, the *tert*-butyldimethylsilylchloride (TBDMSCl)[4] and N-methyl-N-*tert*-butyldimethylsilyl-1,1,1-trifluoroacetamide (MTBSTFA)[10] were employed in two different silylating procedures (A and B) each one with its own advantages of simplicity, efficacy, clarity and shortness. Some helpful notifications for the advantageous use of each procedure were also made.

RESULTS AND DISCUSSION

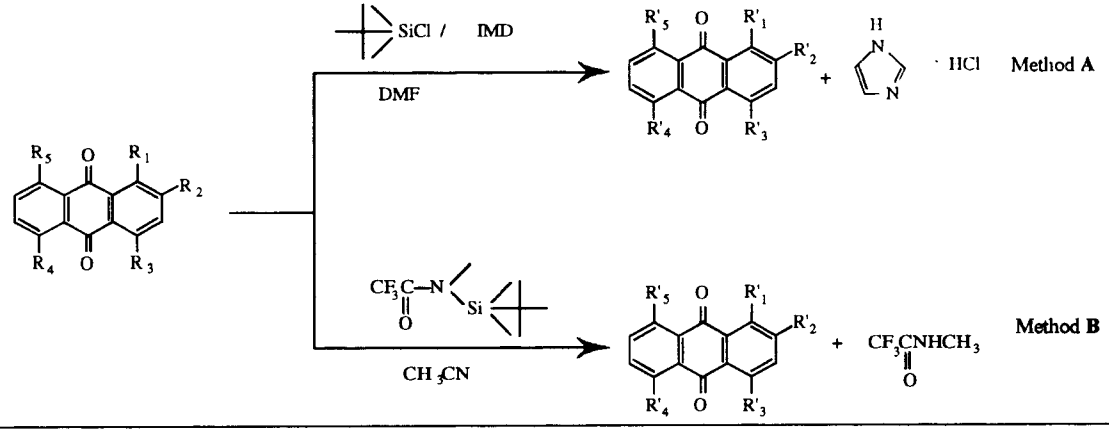
Reaction Conditions Optimization

The TBDMS ethers of six different hydroxyanthraquinones (Table I) namely: 1-hydroxy-9,10-anthracenedione (**1**), 1,4-dihydroxy-9,10-anthracenedione (**2**), 1,5-di-

†Author to whom all correspondence should be addressed.

TABLE I

Reaction conditions for the *tert*-butyldimethylsilylation of hydroxyanthraquinones **1–6**



							Reaction Conditions										
	Substrate						temp.	time	silyl.agent/		Product						
No	R_1	R_2	R_3	R_4	R_5	method	(°C)	(min)	quin (mmol)	No	R'_1	R'_2	R'_3	R'_4	R'_5
1	OH	H	H	H	H	**A**	25	60	3	**1a**	$OSi(CH_3)_2C(CH_3)_3$	H	H	H	H
						B	60	15	20						
2	OH	H	OH	H	H	**A**	25	60	4.5	**2a**	$OSi(CH_3)_2C(CH_3)_3$	H	$OSi(CH_3)_2C(CH_3)_3$	H	H
						B	80	20	20						
3	OH	H	H	OH	H	**A**	25	40	4.5	**3a**	$OSi(CH_3)_2C(CH_3)_3$	H	H	$OSi(CH_3)_2C(CH_3)_3$	H
						B	60	20	20						
4	OH	H	H	H	OH	**A**	25	75	3	**4a**	$OSi(CH_3)_2C(CH_3)_3$	H	H	H	$OSi(CH_3)_2C(CH_3)_3$
						B	80	20	20						
5	OH	OH	H	H	H	**A**	25	45	3	**5a**	$OSi(CH_3)_2C(CH_3)_3$	$OSi(CH_3)_2C(CH_3)_3$	H	H	H
						B	70	15	20						
6	H	CH_2OH	H	H	H	**A**	25	210	1.5	**6a**	H	$CH_2OSi(CH_3)_2C(CH_3)_3$	H	H	H
						B	60	30	5						

hydroxy-9,10-anthracenedione (**3**), 1,8-dihydroxy-9,10-anthracenedione (**4**), 1,2-dihydroxy-9,10-anthracenedione (**5**), 2-hydroxymethyl-9,10-anthracenedione (**6**), were synthesized in high to quantitative yields. The scheme for the silylation reaction, along with the structures of **1–6** and of their silyl ethers **1a–6a**, are presented in Table I.

The enhanced use of TBDMSCl in numerous syntheses and patents,[11] since its introduction by Corey,[4] as a potent silylating mixture with imidazole (IMD) and dimethylformamide (DMF), prompted us to investigate its efficiency in the silylation of hydroxyanthraquinones, in parallel with that of MTBSTFA which was successfully used in the *tert*-butyldimethylsilylation of a number of hydroxynapthoquinones.[1]

In order to determine the optimal reaction conditions, the relative efficiencies for all hydroxyanthraquinones were studied as a function of reaction temperature, reaction time and amounts of silylating agent (TBDMSCl in method A or MTBSTFA in method B). Concerning method A, 2 moles of IMD were used for each mole of TBDMSCl in all silylation reactions, as it was initially proposed by Corey in the introduction of this classical silylation method for hydroxyl groups.

Table I presents the optimum reaction conditions and yields determined for each hydroxyanthraquinone in each silylating procedure. The observed differences, especially among the four isomers **2–5**, in excess of silylating agent and increase of temperature and reaction time were expected[2] and can be rationalized on the basis of steric effects as the result of the different position of the hydroxyl groups in the molecule and mainly of some strong intramolecular hydrogen bonding.

Although MTBSTFA is characterized by a sufficiently high solvent action,[10] **1–6** were slightly soluble in it. Therefore, acetonitrile was used as the reaction solvent in method B, since MTBSTFA is a readily soluble liquid in most aprotic organic solvents.[10]

Silylation Reaction

Although the *in situ* formed *tert*-butyldimethylsilylimidazole (TBDMSIM) in method A is a weak silylating agent,[12] useful only for the silylation of non-hindered hydroxyl groups, silylation of hydroxyanthraquinones **1–6** with TBDMSCl/IMD/DMF was complete under relatively mild conditions. Enhanced reactivity of the above mentioned silylating mixture is rationalized by the formation of a conjugate acid[4] from the interaction of the *in situ* formed TBDMSIM and HCl (Figure 1)

Silylation of **1–6** with MTBSTFA + 1% TBDMSCl assumed to proceed via a

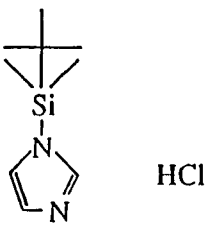
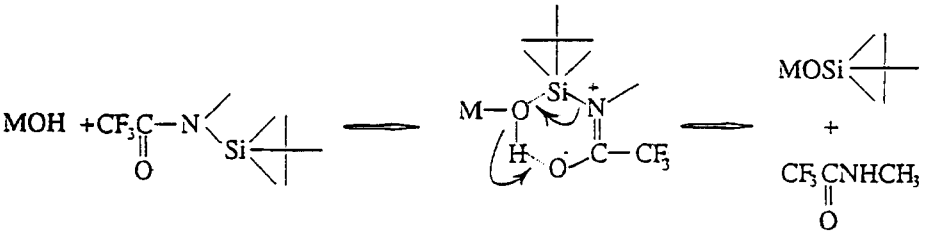


FIGURE 1 Conjugate acid of TBDMSIM with HCl.



SCHEME I Proposed mechanism for the silylation reaction of **1a–6a** with MTBSTFA.

TABLE II
Ions atributed to the chelate structure formed in the mass spectra of **1a–5a**

TBDMS ether	*Fragment*	*m/z*	*rel. int. (%)*
1a	[M-*t*-Bu]$^+$	281	100
2a	[M-2x*t*-Bu]$^{+\bullet}$	354	100
3a	[M-2x*t*-Bu]$^{+\bullet}$	354	100
4a	[M-*t*-Bu]$^+$	411	100
5a	[M-*t*-Bu]$^+$	411	100

mechanism similar to that proposed for the silylation reaction of hydroxynaphthoquinones with the same silylating mixture[1] (Scheme I).

Spectral Data

All synthesized TBDMS ethers were each subjected to combine gas chromatography/mass spectrometry (GC/MS), ultraviolet-visible spectrometry (UV-Vis), infrared spectrometry (IR) and proton nuclear magnetic resonance (^{1}H NMR), in order to confirm their structure.

Each **1a–6a** displayed a single well-shaped chromatographic peak without any significant peak tailing. The retention times (t_R) in the GC trace followed the corresponding retention factors (R_f) in their thin layer chromatographic (TLC) analysis.

The mass spectra of **1a–6a** shared two unique figures with those of their TMS analogues,[2] besides the presence of the typical in TBDMS ethers [M-57]$^+$ ion, attributed to the loss of a *tert*-butyl group from the molecular ion. Thus, the stability of the oxygen-silicon bond led to the formation of stable chelate structures (Table II) and of doubly charged ions (Table III), with regard to the *peri* or *ortho* position of the silyl moiety. Ions attributed to the chelate structure usually appeared as the base peaks in the mass spectra of **1a–6a**.

Additionally, the fragmentation pattern proposed[2] for each individual TMS ether of **1–6** was confirmed by the mass spectrum of its TBDMS analogue. Moreover, a weak [M-15]$^+$ ion representing the loss of a methyl radical from a TBDMS group is usually displayed [e.g., for **4a** m/z 453 (12%) and **5a** m/z 453 (5%)].

TABLE III

Doubly charged ions of silylethers **2a** and **3a**

Silyl ether	*m/z, relative intensities %*					
	$[M\text{-}2x\,t\text{-}Bu]^{2+}$	$[M\text{-}2x\,t\text{-}Bu]^{+}$	$[M\text{-}2x\,t\text{-}Bu\text{-}2Me]^{2+}$	$[M\text{-}2x\,t\text{-}Bu\text{-}2Me]^{+}$	$[M\text{-}2x\,t\text{-}Bu\text{-}4Me]^{2+}$	$[M\text{-}2x\,t\text{-}Bu\text{-}4Me]^{+}$
2a	177 (7)	354 (100)	162 (20)	324 (9)	147 (6)	294 (4)
3a	177 (5)	354 (100)	162 (10)	324 (13)	167 (7)	294 (5)

Furthermore, the absence in the IR spectra of **1a–6a** of an absorption band at ~3450 cm^{-1}, attributed to the resonance of the hydroxylic bond, along with the presence of clear absorption bands at 780 and ~1250 cm^{-1}, at ~830 and ~1050 cm^{-1}, and at ~710 cm^{-1}, attributed to the resonance of the $Si(CH_3)_2$, Si—O—C and Si—C respectively, confirmed silylation of **1–6**. A final validation for the formation of **1a–6a**, was the observed major *tert*-butyl resonance in their ^1H NMR spectra, at 1.25–0.85 ppm and that of a major dimethyl at 0.95–0.6 ppm supported by the absence of an acidic hydroxylic proton resonance.

Silylation Procedures

One drawback to the use of the TBDMSCl/IMD/DMF mixture in silylation reactions by method A, is the prolonged reaction times (0.75–2 hours for the silylation of **1–6**). Additionally, the time consuming work up increases further the length of the whole procedure. However, the relatively small excess of low cost used TBDMSCl as well as the low cost of all used reagents (IMD, DMF), is of particular interest for the industrial production of silyl ethers. Finally, silylation reaction usually proceeds at room temperature thus favoring silylation of heat-sensitive compounds.

On the other hand, the necessity quite often, of moderate to slightly elevated temperatures in silylation reactions with MTBSTFA/TBDMSCl, prohibits the use of this silylating mixture in the silylation of heat-sensitive compounds. Moreover, the large excess of MTBSTFA used limits its use in high scale productions, though from all reactions any unreacted MTBSTFA and a considerable amount (>70%) of the by-product N-methyl-1,1,1-trifluoroacetamide (MTFA) could be recovered and reused, directly or in the synthesis of MTBSTFA,[4] respectively. However, the short reaction times, the simplified protocol for the isolation and purification of the final TBDMS ether and the possibility of simultaneous silylation of all active proton sites besides those of hydroxyl, counter balance the previous disadvantages. Finally, in view of the great importance of the GC/MS technique in the analysis of biological fluids in extremely low quantities, achievement of an almost clean crude product which demands no work up prior to injection on the GC-column, as the one prepared by MTBSTFA, is the principal requirement and advantage.

Conclusively, method A outstands in terms of cost whereas method B distinguishes by enhanced convenience.

EXPERIMENTAL

General

All reactions were carried out under nitrogen. Melting points were determined in a heated oil bath and are uncorrected. Infrared spectra were recorded on a Jasco IR-Report-100 spectrometer. Ultraviolet-Visible spectra were obtained using a Shimadju, model 160A UV-Vis spectrometer. Proton Nuclear Magnetic Resonance spectra were measured with a Perkin Elmer 240 B, 80MHz spectrometer. All NMR spectra were recorded in deuteriochloroform solution using tetramethylsilane as internal reference, while decimal shifts are reported in δ values.

Analytical thin layer chromatography (TLC) was performed on precoated Merck sheets with a 0.2 mm layer of silica gel containing a 254 nm fluoresce indicator. Combined gas chromatographic/mass spectrometric analysis was performed on a Hewlett Packard, model 5890, gas chromatograph equipped with a 25 mm × 0.2 mm I.D., OV-1 capillary column and coupled with a VG, model TS-250, high resolution mass spectrometer at 70 eV. GC analyses were run over 80–280°C with a heating rate of 25°C/min and 280°C injector temperature.

The hydroxyanthraquinones employed were purchased from Fluka Chemical Co. and were of analytical reagent grade. The silylating agent, MTBSTFA containing 1% TBDMSCl was also obtained from Fluka Chemical Co, and was normally stored in the cold and dark under nitrogen. TBDMSCl was obtained from Aldrich Co. and was also stored in cold under nitrogen. All solvents were freshly dried by distillation over anhydrous sodium sulphate.

Method A. General Procedure for the Silylation of **1–6**

Preparation of 1-tert-butyldimethylsiloxy-9,10-anthracenedione (**1a**): In an oven-dried, nitrogen filled round-bottom flask of 100 ml, equipped with a magnetic stir bar, **1** (224 mg, 1 mmol) was treated with TBDMSCl (451 mg, 3 mmol) and imidazole (IMD) (409.5 mg, 6 mmol) in DMF (3 ml). The mixture was stirred in room temperature (~25°C) for 1 h. The progress of the reaction was monitored by TLC at regular intervals by following disappearance of the hydroxyanthraquinone. Soon after the completion of the reaction, the crude product was poured into water (50 ml) and extracted with ethyl ether (50 ml). The etherial layer was then successively washed with 1 M HCl (50 ml), with saturated aqueous $NaHCO_3$ solution (50 ml), dried over Na_2SO_4, filtered and then evaporated under vacuum to dryness to yield 256.9 mg (76%) of **1a**.

Preparation of 1,4-bis(tert-butyldimethylsiloxy)-9,10-anthracenedione (**2a**): Following the general silylation procedure described above, **2** (240 mg, 1 mmol) was treated with TBDMSCl (451.5 mg, 3 mmol) and IMD (409.5 mg, 6 mmol) in dry DMF (3 ml) for 1 h, to give 346.3 mg (74%) of **2a**.

Preparation of 1,5-bis(tert-butyldimethylsiloxy)-9,10-anthracenedione (**3a**): Following the general silylation procedure described above, **3** (240 mg, 1 mmol) was treated with TBDMSCl (677.5 mg, 4.5 mmol) and IMD (614.5 mg, 9 mmol) in dry DMF (3 ml) for 40 min, to give 351.2 mg (75%) of **3a**.

Preparation of 1,8-bis(tert-butyldimethylsiloxy)-9,10-anthracenedione (**4a**): Following the general silylation procedure described above, **4** (240 mg, 1 mmol) was treated with TBDMSCl (451.5 mg, 3 mmol) and IMD (409.5 mg, 6 mmol) in dry DMF (3 ml) for 1.25 h, to give 341.8 mg (73%) of **4a**.

Preparation of 1,2-bis(tert-butyldimethylsiloxy)-9,10-anthracenedione (**5a**): Following the general silylation procedure described above, **5** (240 mg, 1 mmol) was treated with TBDMSCl (451.5 mg, 3 mmol) and IMD (409.5 mg, 6 mmol) in dry DMF (3 ml) for 45 min, to give 347.7 mg (74%) of **5a**.

Preparation of 2-tert-butyldimethylsiloxymethyl-9,10-anthracenedione (**6a**): Following the general silylation procedure described above, **6** (238 mg, 1 mmol) was treated with TBDMSCl (225.8 mg, 1.5 mmol) and IMD (204.5 mg, 3 mmol) in dry DMF (3 ml) for 3.5 h, to give 271.2 mg (77%) of **6a**.

Method B. General Procedure for the Silylation of **1–6** *with MTBSTFA + 1% TBDMSCl*

Preparation of 1-tert-butyldimethylsiloxy-9,10-anthracenedione (**1a**): In an oven-dried, nitrogen filled apparatus, consisting of a 50 ml round-bottom flask, fitted with a water condenser and a dry nitrogen inlet and equipped with a magnetic stir bar, **1** (112 mg, 0.5 mmol) in 5 ml of dry acetonitrile was treated with 2.24 ml, (10 mmol) of the silylating mixture MTBSTFA + 1% TBDMSCl. The mixture was heated at 60°C and stirred for 15 min, during which time dry nitrogen was bubbled through the solution. The progress of the reaction was monitored by removing aliquots periodically and analyzing them by TLC by following the disappearance of **1**. Soon after the completion of the reaction, the mixture was evaporated to dryness under vacuum to remove acetonitrile and excess MTBSTFA and the residue was taken up in hexane. After the hexane solution had cooled enough (−4°C, 2–3 h) it was filtered to remove the white crystalline precipitate which is MTFA. Evaporation to dryness under vacuum of the filtrate afforded 317.8 mg (94%) of the pure silyl ether of **1**, **1a**. (**2a** and **6a** were further purified by sublimation to obtain crystalline solid.)

Preparation of 1,4-bis(tert-butyldimethylsiloxy)-9,10-anthracenedione (**2a**): **2** (120 mg, 0.5 mmol) was treated with MTBSTFA + 1% TBDMSCl (2.24 ml, 10 mmol) in dry acetonitrile (5 ml) as described above for 20 min at 80°C, to give 435.6 mg (93%) of **2a**.

Preparation of 1,5-bis(tert-butyldimethylsiloxy)-9,10-anthracenedione (**3a**): **3** (120 mg, 0.5 mmol) was treated with MTBSTFA + 1% TBDMSCl (2.24 ml, 10 mmol) in dry acetonitrile (5 ml) as described above for 20 min, at 60°C to give 438.2 mg (94%) of **3a**.

Preparation of 1,8-bis(tert-butyldimethylsiloxy)-9,10-anthracenedione (**4a**): **4** (120 mg, 0.5 mmol) was treated with MTBSTFA + 1% TBDMSCl (2.24 ml, 10 mmol) in dry acetonitrile (5 ml) as described above for 20 min at 80°C, to give 435.8 mg (93%) of **4a**.

Preparation of 1,2-bis(tert-butyldimethylsiloxy)-9,10-anthracenedione (**5a**): **5** (120 mg, 0.5 mmol) was treated with MTBSTFA + 1% TBDMSCl (2.24 ml, 10 mmol) in dry acetonitrile (5 ml) as described above for 15 min at 70°C, to give 430.6 mg (92%) of **5a**.

Preparation of 2-tert-butyldimethylsiloxymethyl-9,10-anthracenedione (**6a**): **6** (119 mg, 0.5 mmol) was treated with MTBSTFA + 1% TBDMSCl (0.56 ml, 2.5 mmol) in dry acetonitrile (5 ml) as described above for 30 min at 60°C, to give 341.8 mg (97%) of **6a**.

Spectral Data of the Synthesized Silyl Ethers **1a–6a**

1a: yellow, viscous oil, chromatographically homogeneous; TLC (SiO_2, chloroform-ethyl ether, 90:10), R_f 0.76; UV-Vis ($CHCl_3$) λ_{max} 253, 334, 371 nm; IR (NaCl, film) ν_{max} 3070, 2950, 2930, 2890, 2850, 1665, 1595, 1560, 1460, 1420, 1270, 1040, 830, 780, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9 (s, 6H), 0.97 (s, 9H), 7.8–7.42 (m, 3H), 8.01–7.82 (m, 1H), 8.34–8.07 (m, 2H); MS m/z (relative intensity) 284 (5), 283 (23), 282 (95), 281 [(M-*t*-Bu)$^+$, 100], 263 (7), 253 (20), 252 (5), 235 (7), 224 (5), 223 (7), 151 (10), 126 (7), 73 (5), 57 (5). Anal. Calcd. for $C_{20}H_{22}O_3Si$: C, 70.97; H, 6.55. Found: C, 70.58; H, 6.38.

2a: yellow solid m.p. 119–120°C; TLC (SiO_2, chloroform-ethyl ether, 90:10), R_f 0.81; UV-Vis ($CHCl_3$) λ_{max} 251, 316, 412 nm; IR (KBr) ν_{max} 3070, 2950, 2930, 2880, 2850, 1670, 1630, 1590, 1550, 1460, 1230, 980, 830, 780, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.62 (s, 12H), 0.85 (s, 18H), 7.21–6.91 (m, 2H), 7.75–7.43 (m, 2H), 8.33–7.89 (m, 2H); MS m/z (relative intensity) 356 (11), 355 (30), 354 [(M-2x*t*-Bu)$^{+\cdot}$, 100], 324 (13), 294 (5), 177 (5), 162 (10), 147 (7). Anal. Calcd. for $C_{26}H_{36}O_4Si_2$: C, 66.62; H, 7.74. Found: C, 66.34; H, 7.23.

3a: yellow, chromatographically homogeneous, viscous oil; TLC (SiO_2, chloroform-ethyl ether, 90:10), R_f 0.82; UV-Vis ($CHCl_3$) λ_{max} 230, 255, 435 nm; IR (NaCl, film) ν_{max} 3070, 2950, 2930, 2890, 2860, 1670, 1580, 1460, 1430, 1255, 1060, 830, 780, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.63 (s, 12H), 1.06 (s, 18H), 7.4–6.95 (m, 2H), 8.15–7.44 (m, 4H); MS m/z (relative intensity) 356 (9), 355 (29), 354 [(M-2x*t*-Bu)$^{+\cdot}$, 100], 324 (9), 294 (4), 177 (7), 162 (20), 147 (6), 57 (4), 42 (36). Anal. Calcd. for $C_{26}H_{36}O_4Si_2$: C, 66.62; H, 7.74. Found: C, 66.35; H, 7.21.

4a: pale yellow, chromatographically homogeneous, viscous oil; TLC (SiO_2, chloroform-ethyl ether, 90:10), R_f 0.83; UV-Vis ($CHCl_3$) λ_{max} 251, 331, 375 nm; IR (NaCl, film) ν_{max} 3070, 2950, 2930, 2890, 2860, 1670, 1590, 1460, 1430, 1255, 1020, 835, 780, 670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (s, 12H), 1.04 (s, 18H), 7.27–7.07 (m, 2H), 7.63–7.43 (m, 2H), 7.99–7.74 (m, 2H); MS m/z (relative intensity) 454 (5), 453 [(M-Me)$^+$, 12], 414 (8), 413 (38), 412 (93), 411 (100), 355 (6), 341 (6), 340 (15), 339 (37), 298 (20), 297 (76), 281 (5), 177 (6), 75 (9), 74 (6), 73 (87), 57 (12). Anal. Calcd. for $C_{26}H_{36}O_4Si_3$: C, 66.62; H, 7.74. Found: C, 66.28; H, 7.32.

5a: pale yellow, chromatographically homogeneous, viscous oil; TLC (SiO_2, chloroform-ethyl ether, 90:10) R_f 0.89; UV-Vis ($CHCl_3$) λ_{max} 252, 322, 390 nm; IR (NaCl, film) ν_{max} 3075, 2950, 2930, 2850, 1670, 1590, 1560, 1470, 1410, 1255, 1040, 830, 780, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (s, 12H), 0.96 (s, 9H), 1.05 (s, 9H), 7.25–7.03 (m, 2H), 8.34–7.56 (m, 4H); MS m/z (relative intensity) 453 [(M-Me)$^+$, 5], 414 (7), 413 (22), 412 (55), 411 (100), 355 (8), 341 (9), 340 (27), 339 (43), 297 (10), 282 (7), 281 (8), 165 (5), 75 (13), 74 (7), 73 (64), 58 (7), 57 (30), 56 (20), 42 (20). Anal. Calcd. for $C_{26}H_{36}O_4Si_2$: C, 66.62; H, 7.74. Found: C, 66.46; H, 7.43.

6a: pale yellow solid m.p. 121–122°C; TLC (SiO_2, chloroform-ethyl ether, 90:10), R_f 0.9; UV-Vis ($CHCl_3$) λ_{max} 255, 331 nm; IR (KBr) ν_{max} 3070, 2960, 2930, 2890, 2860, 1670, 1590, 1470, 1460, 1250, 1090, 840, 780, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (s, 6H), 1.25 (s, 9H), 4.87 (s, 2H), 7.92–7.65 (m, 3H), 8.41–8.17 (m, 4H); MS m/z (relative intensity) 281 (7), 280 (22), 279 [(M-*t*-Bu-CH_4)$^+$, 100], 193 (13), 165 (9), 164 (5), 75 (7), 57 (7). Anal. Calcd. for $C_{21}H_{24}O_3Si$: C, 71.55; H, 6.86. Found: C, 71.22; H, 6.56.

REFERENCES

1. M. N. Bakola-Christianopoulou and K. K. Apazidou, *J. Org. Chem.*, **61**, 1850 (1996).
2. M. N. Bakola-Christianopoulou, V. P. Papageorgiou and K. K. Apazidou, *Phosphorus, Sulfur and Silicon*, **88**, 53 (1994).
3. M. N. Bakola-Christianopoulou, V. P. Papageorgiou and K. K. Apazidou, *J. Chromatogr.*, **645**, 293 (1993).
4. E. J. Corey and A. Venkateswarlu, *J. Am. Chem. Soc.*, **94**, 6190 (1972).
5. (a) A. J. Crowe, *Chem. Ind.* (London), 304 (1983); (b) F. G. A. Stone and R. West, eds., "Advances in Organometallic Chemistry," Academic Press, New York, 1980, Vol. 18, pp. 275–299.
6. F. Arcamone, G. Cassinelli, G. Fautini, A. Grein, P. Orezzi, C. Pol and C. Spalla, *Biotechnol. Bioeng.*, **11**, 1101 (1969); (b) A. J. Lin and A. C. Sartorelli, *J. Org. Chem.*, **38**, 813 (1973); (c) El. H. S.

Khadem, ed., "Anthracycline Antibiotics," Academic Press, New York, 1982; (d) D. E. Williamson and G. W. Eyerett, Jr., *J. Am. Chem. Soc.*, **97,** 2397 (1975); (e) T. Lialiaris, D. Mourelatos, L. Boutis, A. Papageorgiou, M. Christianopoulou, V. Papageorgiou and J. Dozi, *J. Pharm. and Exp. Therap.*, **251,** 368 (1989).

7. M. N. Bakola-Christianopoulou, *J. Organomet. Chem.*, **308,** C24 (1986).
8. M. N. Bakola-Christianopoulou, *J. Mol. Catal.*, **65,** 307 (1991).
9. M. N. Bakola-Christianopoulou, K. J. Sarris and L. B. Ekateriniadou, *Eur. J. Med. Chem.*, **21,** 385 (1986).
10. T. P. Mawhinney and M. A. Madson, *J. Org. Chem.*, **47,** 3336 (1982).
11. (a) S. J. Nelson U.S. US 4,680,419 (Cl. 549-343; C07D309/10), 14 Jul. 1987, Appl. 757,659, 22 Jul. 1985, 13 pp; (b) G. Solladie, S. Forestier and G. Lang, Eur. Pat. Appl. EP 312,412 (Cl. C07C69/608), 19 Apr. 1989, FR Appl. 887/14,298, 16 Oct. 1987, 24 pp; (c) Asahi Chemical Industry Co., Ltd. Jpn. Kokai Tokkyo Koho JP 60 58,992 [85 58,992] (Cl. C07F7/18), 05 Apr. 1985, Appl. 83/167,329, 10 Sep. 1983, 12 pp; (d) N. Shinohara, Y. Inoue, A. Yoko, S. Ueno and H. Kosugi, Ltd. Jpn. Kokai Tokkyo Koho JP 63 57,592 [88 57,592] (Cl. C07F7/12), 12 Mar. 1988, Appl. 86/201,490, 29 Aug. 1986, 3 pp.
12. M. A. Quilliam and J. B. Westmore, *Anal. Chem.*, **50,** 59 (1977).