Polycyclic Hydroxyquinones. 28.[1] Synthesis and Diels-Alder Reactions of *N,N,O*-Triacyl Derivatives of 10-Amino-9-hydroxy-1,4-anthraquinones. An Efficient, Regiospecific Synthesis of (±)-5-Iminodaunomycinone, (±)-4-Demethoxy-5-iminodaunomycinone, and (±)-Daunomycinone

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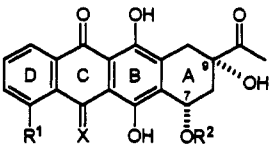
The development of a general strategy for the construction of anthracyclinones based on a Diels-Alder reaction of substituted derivatives of 10-amino-9-hydroxy-1,4-anthraquinone is described. The key stages are (i) formation of *N,O,O*-triacyl derivatives of 1,4-dihydroxy-9,10-anthraquinone monoimines in a tautomer specific fashion, (ii) transacylation into *N,N,O*-triacyl derivatives of the corresponding 10-amino-9-hydroxy-1,4-anthraquinone, and (iii) Diels-Alder reaction with an appropriately substituted 1,3-diene regiocontrolled by steric factors. This strategy has been applied to the total synthesis of (±)-5-iminodaunomycinone (**4**) and (±)-4-demethoxy-5-iminodaunomycinone (**3**) and to a novel and short synthesis of (±)-daunomycinone (**5**).

Introduction

The efficacy of daunomycin (**1**) and related derivatives in the treatment of a variety of human cancers has stimulated continuing interest in the synthesis of this class of antitumor anthracyclines.[2] However, these compounds display various side effects, the most serious being a cumulative dose-dependent cardiotoxicity. 5-Iminodaunomycin (**2**), a quinone-modified analog developed by Acton et al.,[3] has attracted attention because it shows significantly less cardiotoxicity than daunomycin while retaining the antitumor efficacy.[4] The lower cardiotoxicity has been credited to the poor redox capability of **2** for catalytic production of reactive oxygen species.[5]



1, X = O, R^1 = OMe, R^2 = daunosaminyl
2, X = NH, R^1 = OMe, R^2 = daunosaminyl
3, X = NH, R^1 = H, R^2 = H
4, X = NH, R^1 = OMe, R^2 = H
5, X = O, R^1 = OMe, R^2 = H

In retrosynthetic analyses, numerous disconnections to the corresponding aglycones, the anthracyclinones, have been proposed. One of the most simple strategies is based on the formation of the A-ring by a Diels-Alder reaction with an appropriately substituted 1,4-anthraquinone as a BCD-ring synthon. However, there are some limitations to obtaining the expected Diels-Alder adducts directly. A major difficulty is the fact that the appropriate synthon, the 9,10-dihydroxy-1,4-anthraquinone, exists entirely in the 1,4-dihydroxy-9,10-anthraquinonoid tautomeric form (quinizarin), and it does not react as a dienophile under the usual conditions. In an effort to overcome this difficulty, the use of quinizarin boroacetates[6] or fixed derivatives of the 1,4-anthraquinonoid form[7] have been proposed; however, a synthesis of natural anthracyclinones by this method has not yet been reported. To solve the above-mentioned problem, many authors have also used 1,4,9,10-anthradiquinones as dienophiles, but this route has the disadvantage that cycloadditions with electron-rich dienes occur preferentially at the internal double bond of the diquinone;[8] the protection of the 4a,9a double bond as its epoxide has been employed as a viable alternative.[9]

Our present BCD → ABCD approach to the construction of the tetracyclic system of 5-iminodaunomycinone (**4**) and derivatives (Scheme I) is based on our previous studies on tautomerism in quinone imines and employs as the key step a regiocontrolled Diels-Alder reaction between an appropriate 1,3-disubstituted buta-1,3-diene and fixed derivatives of the 1,4-anthraquinonoid tautomer (**B**) of 1,4-dihydroxy-9,10-anthraquinone imines **6** and **7**.

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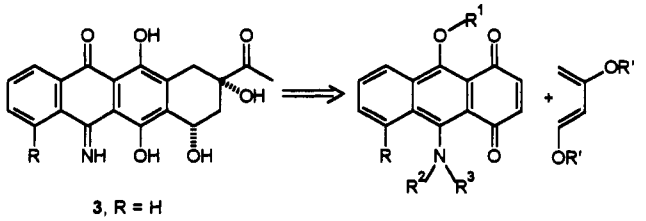
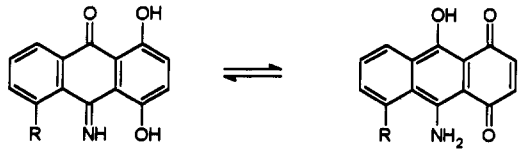
Scheme I



3, R = H
4, R = OMe

In preceding papers[1,10] we have shown that 1,4-dihydroxy-9,10-anthraquinone monoimines **6A** and **7A**, readily obtained by ammonolysis of the corresponding quinizarin, exist in equilibrium with significant amounts of 1,4-anthraquinonoid tautomers **6B** and **7B**. These behave as

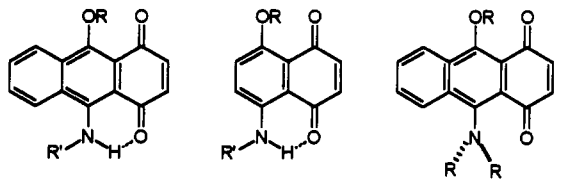


A B

6, R = H
7, R = OMe

dienophiles and can be captured in cycloaddition reactions with simple 1,3-dienes to afford linear tetracyclic systems such as those in anthracyclinones. However, initial attempts to effect Diels–Alder reactions of compounds like **6** with appropriate 1,3-disubstituted dienes afforded only complex and inseparable mixtures, as indicated by the ^{1}H NMR spectra of the reaction mixtures, which showed the presence of signals attributable to both regioisomeric adducts. Therefore, for the construction of anthracyclinone type compounds, appropriate regiocontrol of the cycloaddition reaction was necessary.

A possible strategy was the use of partially blocked derivatives such as **8** as BCD synthons. We expected that the presence of a sole hydrogen bond would establish the correct regiocontrol in the cycloaddition with polarized dienes, as we previously reported for model derivatives of type **9**.[11]



8 9 10

Alternatively, we could use fixed derivatives of the 1,4-anthraquinonoid tautomer **6B**, such as **10**, in which the presence of steric interactions between the bulky R groups and the 1- and/or 3-substituents of the diene could control the orientation of both partners in the Diels–Alder reaction.

We have developed and now report herein in full detail[12] the total synthesis of (±)-5-iminodaunomycinone (**4**) and (±)-4-demethoxy-5-iminodaunomycinone (**3**) from the appropriate 1,4-dihydroxy-9,10-anthraquinone imines, which are readily available from the corresponding quinizarins. The proposed stages of our approach to **3** and **4** are (a) preparation of *N,N,O*-substituted derivatives of **6** and **7**, (b) regiospecific Diels–Alder reaction with a suitable 1,3-disubstituted diene, and (c) transformation of the Diels–Alder adducts into anthracyclinones **3** and **4** by removal of the protecting groups and subsequent A-ring functionalization.

Results and Discussion

In order to obtain partially blocked derivatives of type **8**, the methylation of quinone monoimine **6** was studied under a variety of standard alkylating conditions. Unfortunately, the alkylation of **6** was not as simple as expected, and all attempts resulted either in complex reaction mixtures or in decomposition of the starting material.

In a previous paper,[1] we showed that acetylation of **6** affords *N*-monoacetyl derivative **8** (R = H, R′ = Ac), the tautomeric equilibrium of which completely favors 1,4-anthraquinonoid form **B**. However, all efforts to obtain di- or triacetylated derivatives from **8** were unsuccessful. Similarly, attempts to effect the *O*-methylation of *N*-acetyl derivative **8** (R = H, R′ = Ac) resulted only in decomposition of the starting quinone imine.

Then, with the aim of preparing triacyl derivatives of type **10**, we decided to examine other acylating agents, especially those that could effect the acylation under mild conditions and could be removed in the last steps of the synthesis without cleavage of labile substituents such as the trimethylsilyloxy groups. As appropriate reagents we selected di-*tert*-butyl dicarbonate, 2,2,2-trichloroethyl chloroformate, and ethyl chloroformate. These reagents fulfill these requirements[13] and introduce bulky protecting groups suitable for our purposes.

Tautomer-Specific Formation of *N,O,O*-Triacyl Derivatives of 6A and 7A. The introduction of a *tert*-butoxycarbonyl (Boc) protecting group was initially explored, and it was found that the outcome of the reaction was highly dependent on the reaction conditions. Thus, when the reaction of quinone monoimine **6** was effected with di-*tert*-butyl dicarbonate and DMAP in dichloromethane at room temperature for 5 min, the desired *N,O,O*-tris(*tert*-butoxycarbonyl) derivative **11** was produced exclusively in 75% yield (Table I). In a similar manner, quinone monoimine **7** was converted into **12**. These results indicate that, under the above conditions, quinone imines **6** and **7** are converted into the corresponding *N,O,O*-triacyl derivatives in a tautomer specific form.[14]

The structures of *N,O,O*-triacyl derivatives **11** and **12** were confirmed by their elemental analyses and spectral data. Thus, their ^{1}H NMR spectra show the typical signals of the *O*-Boc and *N*-Boc groups, which appear in a 2:1 ratio. Moreover, in derivatives **11** and **12**, the H-2 and H-3 protons resonate as AB systems with chemical shift values of δ 7.39, 7.28 and δ 7.34, 7.21, respectively, in accord with those expected for aromatic protons.

When the acylation of **6** was allowed to continue for prolonged reaction times at room temperature, no *N,O,O*-

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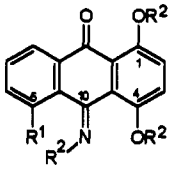
(14) This is a tautomer-specific reaction as defined previously by us. See: Cano, P.; Echavarren, A.; Prados, P.; Fariña, F. *J. Org. Chem.* **1983**, *48*, 5373 (footnote 13).

Table I. Preparation of the *N,O,O*-Triacyl Derivatives 11–16

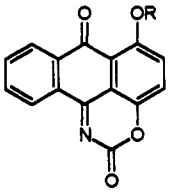


11-16

substrate	base	reagent	R^1	R^2	*N,O,O*-derivative	yield (%)
6	DMAP[a]	Boc_2O	H	Boc[b]	11[c]	75
7	DMAP[a]	Boc_2O	OMe	Boc[b]	12[c]	69
6	Et_3N	ClTroc	H	Troc[d]	13[c]	91
7	Et_3N	ClTroc	OMe	Troc[d]	14[c]	92
6	Et_3N	$ClCO_2Et$	H	CO_2Et	15[c]	83
7	K_2CO_3	$ClCO_2Et$	OMe	CO_2Et	16[e]	65

[a] DMAP = 4-(dimethylamino)pyridine. [b] Boc = *tert*-butoxycarbonyl. [c] In dichloromethane at rt. [d] Troc = 2,2,2-trichloroethoxycarbonyl. [e] In acetone at reflux.

triacyl derivative 11 was obtained; instead, heterocyclic derivative 17 was produced in 90% yield. A shortening of the reaction time (1.75 h) led to a mixture of heterocycle 18 (50% yield) and *N,O,O*-triacyl derivative 11 (26% yield). These results suggest that heterocycles 17 and 18 arise from a prior hydrolysis of compound 11.



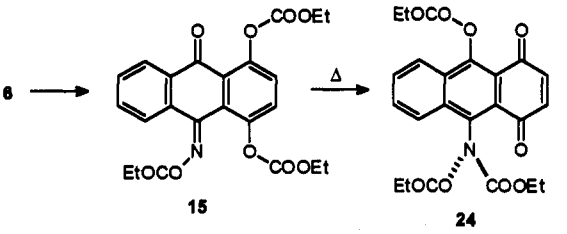
17, R = H
18, R = Boc
19, R = Troc

The introduction of the 2,2,2-trichloroethoxycarbonyl (Troc) protecting group was initially attempted with 2,2,2-trichloroethoxycarbonyl chloride and 2,6-dimethylpyridine in dichloromethane at low temperature for 30 min. Under these conditions, only undesired heterocycle 17 was obtained in 98% yield. In contrast, when triethylamine was used as a base (Table I), we could obtain in good yields expected triacyl derivatives 13 (91%) and 14 (92%) starting from 6 and 7, respectively.[15]

N,O,O-Tris(ethoxycarbonyl) derivative 15 could also be obtained in 83% yield from 6 under conditions similar to those used to introduce the Troc protecting group (Table I). Surprisingly, when the reaction of quinone monoimine 6 with ethyl chloroformate was effected in refluxing acetone with potassium carbonate as a base, a 45% yield of *N,N,O*-tris(ethoxycarbonyl) derivative 24 was produced. THe 1,4-anthraquinonoid structure of 24 was confirmed from its spectral data. Thus, in the ^1H NMR spectrum of 24, the typical signals of OCO_2Et and NCO_2Et appear in a 1:2 ratio, in contrast with those of the *O*-acyl and *N*-acyl groups in derivatives 11–16. Moreover, the H-2 and H-3 protons of 24 resonate as a singlet at δ 6.94, a value expected for quinonoid protons, whereas the ^1H NMR spectrum of *N,O,O*-triacyl derivative 15 shows an AB system (δ 7.50 and 7.41 ppm) and a coupling constant J = 8.8 Hz, as expected for aromatic protons.

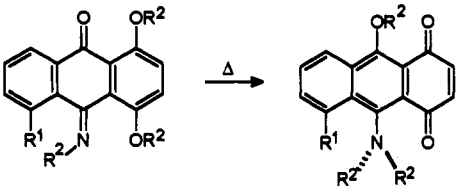
(15) Attempts at acylation of 3 by refluxing for 3 h in acetone with 2,2,2-trichloroethoxycarbonyl chloride and K_2CO_3 afforded 1,4-bis[(2,2,2-trichloroethoxycarbonyl)oxy]-9,10-anthraquinone (15%) and heterocyclic derivative 19 (75%).

Scheme II



15 24

Table II. Transacylation into *N,N,O*-Triacyl Derivatives 20–25



11-16 20-25

N,O,O-derivative	time (h)[a]	R^1	R^2	*N,N,O*-derivative	yield (%)
11	16	H	Boc	20	95
12	24	OMe	Boc	21	95
13	2	H	Troc	22	96
14	2	OMe	Troc	23	98
15	5	H	CO_2Et	24	93
16	10	OMe	CO_2Et	25	90

[a] In toluene at reflux.

In contrast, when 5-MeO-substituted quinone monoimine 7 was acylated with ethyl chloroformate and potassium carbonate in acetone under reflux for 8 h, *N,O,O*-triacyl derivative 16 was obtained in 65% yield. The different behavior of 6 and 7 is presumably due to the steric effects of the 5-methoxy group in 7.

Transacylation into *N,N,O*-Triacyl Derivatives of 6B and 7B. The above results, which indicate the direct formation of *N,N,O*-tris(ethoxycarbonyl) derivative 24 in the reaction of 6 with ethyl chloroformate, can be rationalized in terms of a kinetically controlled formation of *N,O,O*-triacyl derivative 15 and a subsequent transacylation to *N,N,O*-triacyl derivative 24 (Scheme II), which is the product of themrodynamic control. In fact, when *N,O,O*-triacyl derivative 15 was heated in refluxing toluene for 5 h, a solid compound identical with *N,N,O*-triacyl derivative 24 was obtained in 93% yield. This type of intramolecular acyl migration is in accord with our previous results[16] on transacylation in naphthazarin diacetates, although the present case is the first example in which NCOR groups are involved in such a process. In order to determine the scope of this intramolecular transacylation, *N,O,O*-triacyl derivatives 11–14 and 16 were heated in refluxing toluene, and *N,N,O*-tris(alkoxycarbonyl) derivatives 20–25 were obtained as stable solids in excellent yields. The results are shown in Table II.

Regioselective Diels–Alder Reactions. *N,N,O*-Triacyl derivatives 20–25 possess the 1,4-anthraquinonoid structure required for the dienophiles in Diels–Alder reactions. Moreover, in their Diels–Alder reactions with a 1,3-disubstituted diene with bulky groups, only one of the two possible *endo* transition states is free of severe

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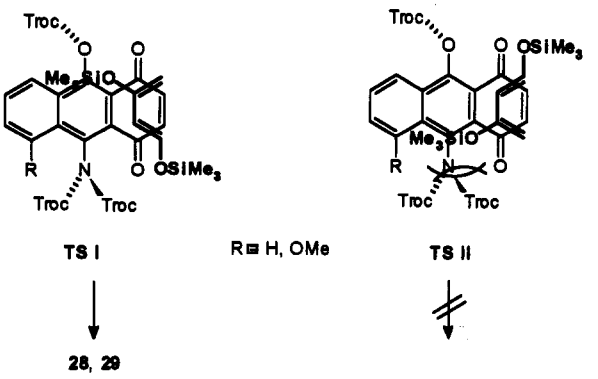
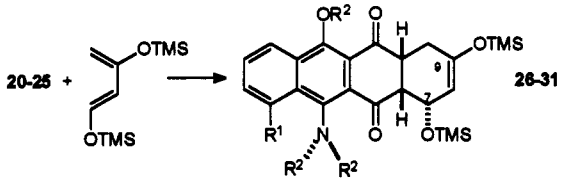


Figure 1. Transition states for the cycloaddition of 1,3-bis-[(trimethylsilyl)oxy]buta-1,3-diene and quinones **22** and **23**.

Table III. Diels-Alder Reaction of *N,N,O*-Triacyl Derivatives 20–25



N,N,O-derivative	R^1	R^2	time (h)	adduct	yield (%)
20	H	Boc	12	26[a]	98
21	OMe	Boc	12	27[a]	96
22	H	Troc	24	28[b]	96
23	OMe	Troc	24	29[b]	94
24	H	CO_2Et	40	30[c]	80
25	OMe	CO_2Et	1	31[a]	73

[a] In toluene at reflux. [b] In benzene at reflux. [c] In dichloromethane at reflux.

steric interactions (the transition states of the cycloaddition of quinones **22–23** are shown in Figure 1). We have chosen (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene as a suitable diene because it provides the necessary steric requirements, and its utility as an A-ring forming precursor has been well established.[17] Inspection of models indicated that **TS II** was more sterically congested than **TS I**, and, therefore, the regioisomeric adducts of type **28, 29** would prevail.

The Diels–Alder reactions of *N,N,O*-triacyl derivatives **20–25** were carried out with an excess of the diene in a inert solvent and afforded regio- and stereospecifically a single adduct in excellent yields. The experimental conditions and the results obtained are shown in Table III.

Adducts **26, 27** and **30, 31** were obtained as crystalline solids. In contrast, adducts **28** and **29** could not be isolated in pure state because of the easy hydrolysis of the OTMS group in position 9. The high-field ^1H NMR spectra of the crude reaction mixtures obtained from quinones **22** and **23** and the diene indicated the formation, in each case, of a single regioisomer, adducts **28** and **29**, respectively.

The structures of the adducts were confirmed on the basis of their spectral data. As a representative example, we will discuss the ^1H NMR spectrum ($CDCl_3$) of adduct **26**. The presence in this spectrum of only two sharp singlets at δ −0.21 and 0.55 ppm, attributable to the OTMS groups at the 7- and 9-position, respectively, indicates the absence of regioisomers. Likewise, only three sharp singlets at δ 1.65, 1.39, and 1.33 ppm, assignable to the OBoc and $NBoc_2$ groups, were observed. Moreover, the ^1H NMR spectrum of adduct **26** recorded in benzene-d_6 showed changes in the chemical shifts of the signals, but no splitting of the signals appeared.

Table IV. Diels–Alder Adducts 26–31 from *N,O,O*-Triacyl Derivatives 11–16

N,O,O-derivative	time (h)[a]	adduct	yield (%)
11	12	26	98
12	13	27	94
13	24	28	96
14	24	29	94
15	40	30	75
16	1	31	73

[a] In refluxing toluene.

A coupling constant of 6.5 Hz between protons H-6a and H-10a is in accord with a relative *gauche* disposition, indicating that the A and B rings have a *cis* arrangement. On the other hand, the values of the coupling constants $J_{7,8} = 6.0$, $J_{8,10'} = 1.3$, $J_{6a,7} = 3.4$, $J_{10',10a} = J_{6a,10a} = 6.5$, and $J_{10,10'} = 18.3$ Hz are in good agreement with those of closely related adducts described in the literature.[9b–d] In these cases, after a conformational study of the A ring, a *endo–cis* stereochemistry was proposed. It should be pointed out that the control of the relative stereochemistry between H-6a and H-7a is not important in the synthesis of anthracyclinones because B-ring aromatization is a necessary subsequent step.

It was not possible to determine by NMR if the adducts had the desired or the undesired regiochemistry. We have tentatively assigned to them the regiochemistries shown in structures **26–31** on the assumption that the cycloaddition proceeds through an *endo* transition state of type **TS I** (Figure 1) that minimizes the nonbonding interactions. Inspection of models clearly indicated that the reverse orientation (**TS II**, Figure 1) was less favored because of steric interactions between the 3-$OSiMe_3$ substituent of the diene and the bulky *N*-protecting groups of the quinone.[18] This assignment has been conclusively proved in the last steps of the synthesis by the chemical correlation between adduct **29** and natural daunomycinone.

Interestingly, a one-pot procedure was developed wherein *N,O,O*-triacyl derivatives **11–16** were directly converted to adducts **26–31** by being heated in an inert solvent with an excess of (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene. This one-pot transformation, which comprises the transacylation and cycloaddition reactions, proceeded in excellent yields. The experimental conditions and results are summarized in Table IV.

Indeed, the above-mentioned possibility of using *N,O,O*-triacyl derivatives as starting materials instead of the corresponding *N,N,O*-derivatives reduces by one the total number of operations required for the synthesis of anthracyclinones **3** and **4**.

Removal of the Protecting Groups on the Diels–Alder Adducts. After achieving an effective preparation of Diels–Alder adducts **26–31**, the experimental conditions to remove the protecting groups on the A and C rings had

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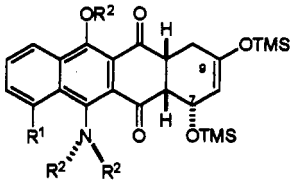
(18) Such an explanation is also consistent with the low regioselectivity (1.5:1) obtained in the Diels–Alder reaction of *N,N,O*-triacyl derivative **24** with (*E*)-1-[(trimethylsilyl)oxy]buta-1,3-diene, in which the absence of the 3-$OSiMe_3$ group eliminates the barrier to approach by the diene.

to be carefully chosen because of the easy aromatization of the hydroaromatic A ring in the tetracyclic structures.[17c]

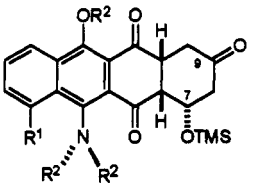
Our first attempts to remove the trimethylsilyl groups were effected on adduct **30**. Thus, treatment of **30** with hydrochloric acid in THF yielded selectively ketone **32** in 85% yield. The remaining trimethylsilyl group of **32** was then removed by using a mixture of hydrochloric acid and 30% hydrogen peroxide[17c] to give **33** in 83% yield. Hydroxy ketone **33** could also be directly obtained from **30** in 72% yield by using the latter conditions over a period of 5 h.

In contrast, it was not possible to find appropriate conditions for the chemoselective deprotection of the silyl enol ether of adduct **26**, and all attempts resulted only in mixtures of **34** and **35**. Moreover, attempts to obtain **35** gave only complex mixtures, probably because of extensive cleavage of the Boc groups on the C ring and easy aromatization of the A ring under the reaction conditions.

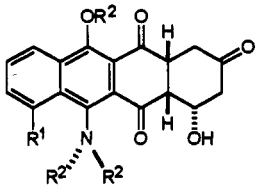
Because adducts **28** and **29** could not be isolated, their crude reaction mixtures were subjected to a mild selective hydrolysis with 3 N hydrochloric acid in THF at 0 °C for 5 min to give excellent yields of tetracyclic ketones **36** (95%) and **37** (92%). It is remarkable, however, that the use of a slight excess of acid or longer reaction times afforded fully aromatized naphthacenedione **38**.



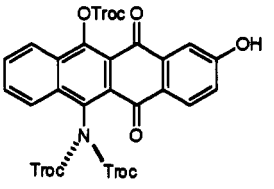
26, R^1 = H, R^2 = Boc
28, R^1 = H, R^2 = Troc
29, R^1 ≡ OMe, R^2 = Troc
30, R^1 = H, R^2 = CO_2Et



32, R^1 = H, R^2 ≡ CO_2Et
34, R^1 = H, R^2 = Boc
36, R^1 = H, R^2 = Troc
37, R^1 = OMe, R^2 = Troc



33, R^1 = H, R^2 = CO_2Et
35, R^1 = H, R^2 = Boc



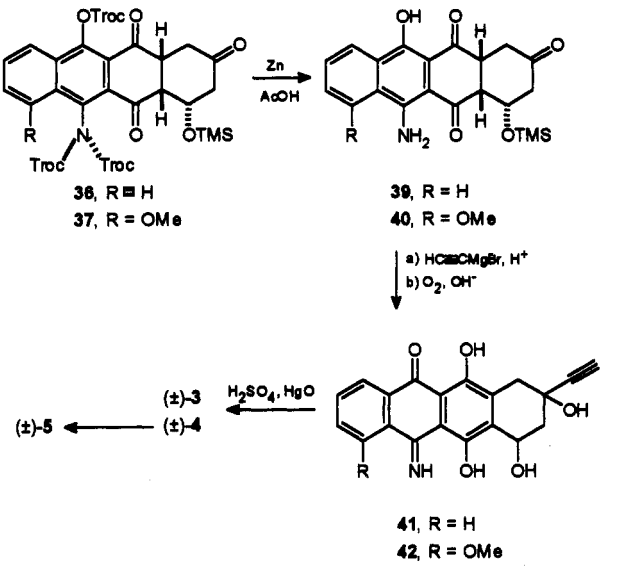
38

We have also found that *N,O,O*-tris(Troc) derivatives **13** and **14** can be efficiently converted into ketones **36** (91%) and **37** (92%), respectively, in a single operation, by heating **13** and **14** in toluene in the presence of the diene and subsequent mild acidic hydrolysis.

Numerous reagents and conditions have been attempted to remove the alkoxycarbonyl groups from adducts **26**–**31**.[13] However, in our hands, only removal of the Troc protecting groups of **36** and **37** was readily accomplished. Thus, treatment of **36** and **37** with Zn in acetic acid in the presence of a buffer[19] yielded the corresponding deprotected products **39** (71%) and **40** (73%), respectively.

A-Ring Functionalization. The next steps in the synthesis were directed to obtaining the correct A-ring functionality (Scheme III). Thus, treatment of **39** and **40** with excess of ethynylmagnesium bromide and subsequent acidic workup and oxidation (O_2, aqueous 5% KOH) of the crude product afforded **41** (80%) and **42** (79%), respectively. It should be pointed out that **41** appeared as a 5:2 mixture of the C-7 epimers, whereas **42** was obtained as a single epimer.

Scheme III



Finally, hydration of the ethynyl side chains in **41** and **42** afforded (±)-4-demethoxy-5-iminodaunomycinone (**3**, 72%) and (±)-5-iminodaunomycinone (**4**, 70%), respectively. During the hydration of **41**, epimerization at C-7, caused by the acidic conditions employed, was observed, in agreement with literature precedent.[20]

Our synthetic (±)-**4** was converted by acidic hydrolysis in 75% yield into a product identical to the previously reported (±)-daunomycinone. Moreover, the ^1H NMR spectrum of the crude reaction mixture contained no signals attributable to the (±)-isodaunomycinone.[17b,c] As an additional proof, when a sample of authentic (+)-daunomycinone derived from the hydrolysis of natural (+)-daunomycin (**1**) was treated with methanolic ammonia, a violet product that was identical by direct comparison of spectral properties with our synthetic (±)-**4** was obtained. All these facts corroborate the tentative regiochemical assignment of Diels–Alder adduct **29**.

In summary, we describe herein the first total synthesis of (±)-5-iminodaunomycinone (**4**), which was obtained in only five laboratory operations by the sequence **7** → **14** → **37** → **40** → **42** → (±)-**4** in a 34% overall yield. Similarly, the total synthesis of (±)-4-demethoxy-5-iminodaunomycinone (**3**) has been effected in only five laboratory operations by the sequence **6** → **13** → **36** → **39** → **41** → (±)-**3** in 31% overall yield. Our approach also allows a short and efficient synthesis of (±)-daunomycinone (**5**) by acidic hydrolysis of (±)-5-iminodaunomycinone. The synthetic methodology described herein may also be relevant for the construction of novel unnatural anthracyclinones. In fact, the amino group that is present in the intermediates leading to **3** and **4** could serve for the introduction of other different groups or, *via* deamination, for the synthesis of related deoxyanthracyclinones.

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Experimental Section

Melting points are uncorrected. Microanalyses were performed with a Heraeus analyzer. UV-Visible spectra λ values are in nm. IR frequencies are in cm^{-1}. NMR chemical shifts are reported in ppm (δ) downfield from Me_4Si. Merck silica gel 60 (70–230 mesh), 60 (230–400 mesh), and DC-Alufolien 60 F_{254} were used for conventional, flash column chromatography, and analytical TLC, respectively. Quinone monoimines **6,7** were prepared according to the method previously reported.[1]

Acylations with Di-*tert*-butyl Dicarbonate. Method A. To a stirred suspension of 1,4-dihydroxy-9,10-anthraquinone monoimine (**6**) (100 mg, 0.42 mmol) in CH_2Cl_2 (8 mL) under Ar at 0 °C were added DMAP (153 mg, 1.25 mmol) and di-*tert*-butyl dicarbonate (274 mg, 1.25 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was stirred at rt for 5 min. Celite was added, the solvent was removed, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate, 2:1) to afford 460 mg (75%) of *N,O,O*-triacyl derivative **11**.

***N,O,O*-Tris(*tert*-butoxycarbonyl)-1,4-dihydroxy-9,10-anthraquinone Monoimine (11)**: mp 212–214 °C; UV ($CHCl_3$) 250, 297, 400 (log ε 4.38, 3.85, 2.79); IR (KBr) 2985, 1765, 1715, 1670, 1650, 1595, 1270, 1250, 1225, 1145; ^1H NMR ($CDCl_3$) δ 8.06 (m, 1H), 7.91 (m, 1H), 7.58–7.51 (m, 2H), 7.39, 7.28 (AB syst, 2H, J = 9.4 Hz), 1.58 (s, 9H), 1.52 (s, 9H), 1.39 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 184.0, 150.6, 150.1, 149.2, 147.5, 139.7, 139.6, 134.7, 131.1, 130.6, 130.2, 124.5, 124.0, 123.3, 119.5, 109.9, 84.6, 83.1, 27.8; MS *m/z* 466, 439, 344, 265, 239, 57 (100). Anal. Calcd for $C_{29}H_{33}NO_9$: C, 64.55; H, 6.16; N, 2.59. Found: C, 64.28; H, 5.89; N, 2.63.

***N,O,O*-Tris(*tert*-butoxycarbonyl)-1,4-dihydroxy-5-methoxy-9,10-anthraquinone 10-Imine (12).** By means of the above procedure, quinone monoimine **7** was converted into **12** (69%): purified by column chromatography (*n*-hexane/ethyl acetate, 1:1); mp 173.5–175.5 °C; UV ($CHCl_3$) 255, 345 (log ε 4.32, 3.58); IR (KBr) 2980, 1770, 1735, 1685, 1640, 1595, 1280, 1240, 1150; ^1H NMR ($CDCl_3$) δ 7.58 (dd, 1H, J = 7.6, 1.0 Hz), 7.45 (t, 1H, J = 7.6 Hz), 7.34, 7.21 (AB syst, 2H, J = 8.6 Hz), 7.03 (dd, 1H, J = 7.6, 1.0 Hz), 3.75 (s, 3H), 1.56 (s, 9H), 1.54 (s, 9H), 1.29 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 182.3, 158.5, 156.7, 156.4, 154.3, 151.2, 147.2, 145.2, 134.9, 132.7, 132.6, 126.4, 124.6, 119.1, 115.9, 114.9, 114.3, 84.1, 81.2, 55.4, 27.9, 27.7, 27.6; MS *m/z* 496, 269, 240, 84, 57 (100). Anal. Calcd for $C_{30}H_{35}NO_{10}$: C, 63.26; H, 6.19; N, 2.46. Found: C, 63.00; H, 6.28; N, 2.15.

Method B. To a stirred suspension of 1,4-dihydroxy-9,10-anthraquinone monoimine (**6**) (250 mg, 1.05 mmol) in CH_2Cl_2 (20 mL) under Ar at 0 °C were added DMAP (383 mg, 3.1 mmol) and di-*tert*-butyl dicarbonate (707 mg, 3.25 mmol) in CH_2Cl_2 (10 mL). After 4.5 h at rt, Celite was added, the solvent was removed, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate, 3:1) to afford 195 mg (90%) of **17**.

6-Hydroxyanthra[9,1-*d,e*]-1,3-oxazine-2,7-dione (17): mp 246–250 °C; UV ($CHCl_3$) 250, 285, 297, 347 (log ε 5.09, 4.90, 4.87, 4.64); IR (KBr) 1785, 1775, 1760, 1670, 1640, 1590, 1210; ^1H NMR ($CDCl_3$) δ 12.39 (s, 1H), 8.77 (m, 1H), 8.39 (m, 1H), 7.85 (m, 2H), 7.55, 7.44 (AB syst, 2H, J = 9.3 Hz); ^{13}C NMR ($CDCl_3$) δ 179.9, 166.8, 153.7, 150.8, 145.4, 135.4, 135.1, 134.8, 133.3, 132.3, 127.6, 126.1, 123.9, 119.3, 113.2; MS *m/z* 267 (M^+ + 2) (30), 240, 57 (100).

Method C. By means of procedure A, the reaction mixture was stirred at rt for 1.75 h. The crude residue was purified by column chromatography (*n*-hexane/ethyl acetate, 2:1) to afford 77 mg (50%) of heterocycle **18** and 56 mg (26%) of *N,O,O*-triacyl derivative **11**.

***O*-(*tert*-Butoxycarbonyl)-6-hydroxyanthra[9,1-*d,e*]-1,3-oxazine-2,7-dione (18)**: mp 184.5–185.5 °C; UV (CH_3OH) 290, 300, 350, 390 (log ε 3.99, 3.98, 4.66, 3.54); IR (Nujol) 1775, 1760, 1675, 1595, 1460, 1375, 1150, 775; ^1H NMR ($CDCl_3$) δ 8.83 (m, 1H), 8.44 (m, 1H), 7.92 (m, 2H), 7.66 (s, 2H), 1.64 (s, 9H); MS *m/z* 367 (M^+ + 2) (1), 291, 265 (100), 57, 41, 39.

Acylation with 2,2,2-Trichloroethyl Chloroformate. Method A. To a stirred suspension of 1,4-dihydroxy-9,10-anthraquinone monoimine (**6**) (750 mg, 3.13 mmol) in CH_2Cl_2 (150 mL) under Ar at 0 °C were added triethylamine (1.42 mL, 10.04 mmol) and 2,2,2-trichloroethyl chloroformate (1.35 mL, 10.03 mmol). The reaction mixture was stirred at rt for 5 min. Celite was added, the solvent was removed, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate, 3:1) to afford 2.18 g (91%) of **13**.

***N,O,O*-Tris(2,2,2-trichloroethoxycarbonyl)-1,4-dihydroxy-9,10-anthraquinone Monoimine (13)**: mp 104–109 °C; UV (MeOH) 235, 255, 390, (log ε 4.36, 4.27, 3.33); IR (Nujol) 1780, 1740, 1730, 1690, 1650, 1610, 1600, 1280, 1270, 1230, 820, 720; ^1H NMR ($CDCl_3$) δ 8.12 (m, 1H), 7.78 (m, 1H), 7.62 (m, 2H), 7.53, 7.45 (AB syst, 2H, J = 8.9 Hz), 5.02 (s, 2H), 4.99 (s, 2H), 4.93 (s, 2H); MS *m/z* 765 (M^+) (2), 728, 618, 616, 588, 569, 399, 397, 264 (100), 239, 220, 131, 95, 49, 44. Anal. Calcd for $C_{23}H_{12}NO_9Cl_9$: C, 36.09; H, 1.58; N, 1.83. Found: C, 36.29; H, 1.70; N, 1.60.

***N,O,O*-Tris(2,2,2-trichloroethoxycarbonyl)-1,4-dihydroxy-5-methoxy-9,10-anthraquinone 10-Imine (14).** By means of the above procedure, quinone monoimine **7** was converted into **14** (92%). purified by column chromatography (*n*-hexane/ethyl acetate, 4:1); mp 157–160 °C; UV (CH_3OH) 237, 250, 292 (log ε 4.07, 4.15, 3.39); IR (KBr) 1780, 1730, 1670, 1640, 1580, 1280, 1220, 730; ^1H NMR ($CDCl_3$) δ 7.72 (dd, 1H, J = 0.8, 6.9 Hz), 7.61 (dd, 1H, J = 7.6, 6.9 Hz), 7.56, 7.44 (AB syst, 2H, J = 9.0 Hz), 7.17 (d, 1H, J = 7.6 Hz), 5.00 (s, 2H), 4.97 (s, 2H), 4.96 (s, 2H), 3.93 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 181.4, 179.7, 158.6, 158.4, 156.7, 151.8, 151.7, 147.5, 145.9, 134.4, 134.1, 129.8, 127.2, 120.2, 116.7, 115.8, 111.2, 94.3, 94.2, 93.9, 77.7, 77.5, 75.4, 56.2; MS *m/z* 795 (M^+) (6), 619, 428, 269, 131, 95 (100). Anal. Calcd for $C_{24}H_{14}NO_{10}CCl_9$: C, 36.23; H, 1.77; N, 1.76. Found: C, 36.50; H, 1.99; N, 1.53.

Method B. To a stirred suspension of 1,4-dihydroxy-9,10-anthraquinone monoimine (**6**) (50 mg, 0.21 mmol) in 2,2,2-trichloroethyl chloroformate (200 mL, 14.43 mmol) under Ar at −20 °C was added 2,6-dimethylpyridine (0.07 mL, 0.62 mmol). The reaction mixture was stirred for 30 min, CH_2Cl_2 was added, and the organic layer was washed with water and dried ($MgSO_4$). The solvent was removed, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate, 1:1) to afford 55 mg (98%) of heterocycle **17**.

Method C. To a stirred suspension of 1,4-dihydroxy-9,10-anthraquinone monoimine (**6**) (300 mg, 1.25 mmol) in acetone (10 mL) under Ar were added K_2CO_3 (1.04 g, 7.53 mmol) and 2,2,2-trichloroethyl chloroformate (0.678 mL, 5.0 mmol). The reaction mixture was heated under reflux for 3 h. Celite was added, the solvent was removed, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate, 1:2) to afford 111 mg (15%) of 1,4-bis[(2,2,2-trichloroethoxycarbonyl)oxy]-9,-10-anthraquinone and 555 mg (75%) of heterocycle **19**.

1,4-Bis[(2,2,2-trichloroethoxycarbonyl)oxy]-9,10-anthraquinone: mp 204–206 °C; UV ($CHCl_3$) 252, 266 (sh), 333 (log ε 4.53, 4.16, 3.76); IR (KBr) 1780, 1770, 1680, 1600, 1280, 1230, 720; ^1H NMR ($CDCl_3$) δ 8.14 (2H, m), 7.74 (2H, m), 7.57 (2H, s), 4.92 (2H, s); MS *m/z* 594 (M^+ + 4) (0.2), 592 (M^+ + 2) (0.4), 590 (M^+) (0.6), 441, 240 (100). Anal. Calcd for $C_{20}H_{10}O_8Cl_6$: C, 40.64; H, 1.71. Found: C, 40.63; H, 1.72.

***O*-(2,2,2-Trichloroethoxycarbonyl)-6-hydroxyanthra[9,1-*d,e*]-1,3-oxazine-2,7-dione (19)**: mp 200–201.5 °C; UV (CH_3OH) 253, 290, 299, 328, 360 (log ε 4.12, 4.12, 4.11, 3.38, 3.57); IR (Nujol) 1785, 1750, 1680, 1665, 1630, 1590, 1550, 1445, 1375, 1210, 860, 780; ^1H NMR ($CDCl_3$) δ 8.70 (1H, m), 8.28 (1H, m), 7.83 (2H, m), 7.67, 7.63 (AB syst, 2H, J = 9.0 Hz), 4.91 (2H, s); ^{13}C NMR (DMSO-d_6) δ 179.9, 166,8, 153.7, 150.9, 145.4, 135.5, 134.8, 133.4, 132.3, 131.3, 127.6, 126.2, 123.9, 119.4, 113.3, 94.2, 77.0; MS *m/z* 441 (M^+) (2), 404, 292, 265 (100), 236, 208, 180, 130, 95. Anal. Calcd for $C_{18}H_8O_6Cl_3$: C, 49.06; H, 1.83; N, 3.18. Found: C, 48.76; H, 2.10; N, 2.89.

Acylations with Ethyl Chloroformate. *N,O,O*-Tris(ethoxycarbonyl)-1,4-dihydroxy-9,10-anthraquinone Monoimine (15). To a stirred suspension of 1,4-dihydroxy-9,-10-anthraquinone monoimine (**6**) (900 mg, 3.76 mmol) in CH_2Cl_2 (200 mL) under Ar at 0 °C were added triethylamine (1.57 mL, 11.28 mmol) and ethyl chloroformate (1.08 mL, 11.28 mmol). The reaction mixture was stirred at rt for 5 min, Celite was added, the solvent was removed, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate, 4:1) to afford 1.42 g (83%) of **15**: mp 185–187 °C; IR (Nujol) 1765, 1705, 1680, 1655, 1595, 1455, 1280, 1220, 870, 790, 765, 760, 700; ^1H NMR ($CDCl_3$) δ 8.17 (m, 1H), 7.88 (m, 1H), 7.66 (m, 2H), 7.50, 7.41 (AB syst, 2H, J = 8.8 Hz), 4.40 (m, 4H), 4.31 (q, 2H, J = 7.1 Hz), 1.45 (m,

6H), 1.30 (t, 3H). Anal. Calcd for $C_{23}H_{21}NO_9$: C, 60.65; H, 4.65; N, 3.07. Found: C, 61.00; H, 4.94; N, 3.37.

N,N,O-Tris(ethoxycarbonyl)-10-amino-9-hydroxy-1,4-anthraquinone (24). To a stirred suspension of 1,4-dihydroxy-9,10-anthraquinone monoimine (6) (1.0 g, 4.2 mmol) in acetone (20 mL) under Ar were added K_2CO_3 (3.5 g, 25.3 mmol) and ethyl chloroformate (1.6 mL, 16.7 mmol). The reaction mixture was heated under reflux for 5 h, Celite was added, the solvent was removed, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate, 4:1) to afford 860 mg (45%) of *N,N,O*-triacyl derivative 24: mp 173–175 °C; UV ($CHCl_3$) 250, 286, 296, 400 (log ϵ 4.08, 4.14, 4.20, 3.64); IR (KBr) 2990, 1810, 1780, 1670, 1625, 1610, 1280, 1230, 1090; ^{1}H NMR ($CDCl_3$) δ 8.34 (m, 1H), 8.12 (m, 1H), 7.81 (m, 2H), 6.94 (s, 2H), 4.48 (q, 2H, J = 7.2 Hz), 4.18 (q, 4H, J = 7.2 Hz), 1.53 (t, 3H), 1.13 (t, 6H); MS *m/z* 455, 410, 366, 322, 294, 265 (100), 239, 211, 127. Anal. Calcd for $C_{23}H_{21}NO_9$: C, 60.65; H, 4.65; N, 3.07. Found: C, 60.65; H, 4.66; N, 2.48.

N,O,O-Tris(ethoxycarbonyl)-1,4-dihydroxy-5-methoxy-9,10-anthraquinone 10-Imine (16). To a stirred suspension of 1,4-dihydroxy-5-methoxy-9,10-anthraquinone 10-imine (7) (1.0 g, 3.7 mmol) in acetone (20 mL) under Ar were added K_2CO_3 (3.8 g, 22.3 mmol) and ethyl chloroformate (1.42 mL, 14.85 mmol). The reaction mixture was heated under reflux for 8 h, Celite was added, the solvent was removed, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate, 1:1) to afford 1.17 g (65%) of 16: mp 175–176.5 °C; IR (KBr) 2980, 1780, 1770, 1715, 1680, 1650, 1595, 1275, 1215; ^{1}H NMR ($CDCl_3$) δ 7.79 (dd, 1H, J = 1.2, 7.7 Hz), 7.66 (dd, 1H, J = 7.7, 8.1 Hz), 7.49, 7.43 (AB syst, 2H, J = 8.8 Hz), 7.29 (dd, 1H, J = 1.2, 8.1 Hz), 4.42 (q, 4H, J = 7.2 Hz), 4.12 (q, 2H, J = 7.2 Hz), 3.98 (s, 3H), 1.47 (t, 6H), 1.26 (t, 3H); MS *m/z* 485 (M^+) (27), 413, 396, 352, 324, 296 (100), 268, 252. Anal. Calcd for $C_{24}H_{23}NO_{10}$: C, 59.38; H, 4.77; N, 2.28. Found: C, 59.42; H, 4.55; N, 2.51.

Transacylation of *N,O,O*-Triacyl Derivatives 11–16 into *N,N,O*-Triacyl Derivatives 20–25. General Procedure. A stirred suspension of the *N,O,O*-triacyl derivative in toluene was refluxed under Ar until the starting material was consumed (disappearance of the *N,O,O*-triacyl derivative was monitored by TLC). The solvent was removed, and the residue was purified by column chromatography.

N,N,O-Tris(*tert*-butoxycarbonyl)-10-amino-9-hydroxy-1,4-anthraquinone (20): from *N,O,O*-triacyl derivative 11 (650 mg, 1.20 mmol) in toluene (20 mL); reaction time 16 h; purified by column chromatography (*n*-hexane/ethyl acetate, 3:1) (617 mg, 95%); mp 202.5–203.5 °C; UV ($CHCl_3$) 285, 322, 404 (log ϵ 4.15, 3.60, 3.58); IR (KBr) 2985, 1770, 1740, 1700, 1670, 1620, 1370, 1270, 1255, 1150, 1135; ^{1}H NMR ($CDCl_3$) δ 8.24 (m, 1H), 8.08 (m, 1H), 7.71 (m, 2H), 6.85 (s, 2H), 1.57 (s, 9H), 1.24 (s, 18H); MS *m/z* 466 (M^+), 439, 339, 265, 239, 57(100), 41, 39. Anal. Calcd for $C_{29}H_{33}NO_9$: C, 64.55; H, 6.16; N, 2.59. Found: C, 64.29; H, 6.28; N, 2.36.

N,N,O-Tris(*tert*-butoxycarbonyl)-10-amino-9-hydroxy-5-methoxy-1,4-anthraquinone (21): from *N,O,O*-triacyl derivative 12 (200 mg, 0.35 mmol) in toluene (10 mL); reaction time 24 h; purified by column chromatography (*n*-hexane/ethyl acetate, 1:1) (190 mg, 95%); mp 285–296 °C, dec; IR (KBr) 2998, 1770, 1730, 1690, 1670, 1610, 1575, 1395, 1270, 1140, 855, 805; ^{1}H NMR ($CDCl_3$) δ 7.82 (dd, 1H, J = 8.0, 0.7 Hz), 7.58 (t, 1H, J = 8.0 Hz), 7.02 (d, 1H, J = 8.0 Hz), 6.84, 6.78 (AB syst, 2H, J = 10.3 Hz), 3.90 (s, 3H), 1.56 (s, 9H), 1.23 (s, 18H); ^{13}C NMR ($CDCl_3$) δ 183.5, 157.9, 150.4, 149.9, 146.7, 140.2, 138.5, 135.0, 132.5, 130.4, 125.4, 123.3, 119.2, 115.8, 109.9, 84.2, 81.8, 56.0, 29.5, 27.6, 27.5; MS *m/z* 496 (M^+), 469, 369, 313, 269, 57 (100). Anal. Calcd for $C_{30}H_{35}NO_{10}$: C, 63.26; H, 6.19; N, 2.46. Found: C, 62.98; H, 6.18; N, 2.18.

N,N,O-Tris(2,2,2-trichloroethoxycarbonyl)-10-amino-9-hydroxy-1,4-anthraquinone (22): from *N,O,O*-triacyl derivative 13 (300 mg, 0.39 mmol) in toluene (15 mL); reaction time 2 h; purified by column chromatography (*n*-hexane/ethyl acetate, 3:1) (288 mg, 96%); mp 213–214 °C; IR (Nujol) 1795, 1750, 1670, 1630, 1615, 1570, 1310, 1290, 1260, 1210, 825, 785, 720; ^{1}H NMR ($CDCl_3$) δ 8.37 (m, 1H), 8.22 (m, 1H), 7.86 (m, 2H), 6.96 (s, 2H), 5.03 (s, 2H), 4.78 (s, 4H); MS *m/z* 765 (M^+) (1), 616, 396 (100), 265, 131, 95. Anal. Calcd for $C_{23}H_{12}NO_9Cl_9$: C, 36.09; H, 1.58; N, 1.83. Found: C, 35.77; H, 1.85; N, 1.88.

N,N,O-Tris(2,2,2-trichloroethoxycarbonyl)-10-amino-9-hydroxy-5-methoxy-1,4-anthraquinone (23): from *N,O,O*-triacyl derivative 14 (190 mg, 0.39 mmol) in toluene (15 mL); reaction time 2 h; purified by column chromatography (*n*-hexane/ethyl acetate, 3:1) (286 mg, 98%); mp 205–206 °C; IR (Nujol) 1830, 1790, 1740, 1670, 1610, 1575, 1280, 1220, 1120, 720; ^{1}H NMR ($CDCl_3$) δ 7.85 (dd, 1H, J = 0.9, 8.0 Hz), 7.66 (t, 1H, J = 8.0 Hz), 7.09 (dd, 1H, J = 8.0, 0.9 Hz), 6.88, 6.57 (AB syst, 2H, J = 10.4 Hz), 4.92 (s, 2H), 4.66 (s, 2H), 4.62 (s, 2H), 3.9 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 183.7, 183.2, 157.9, 157.0, 150.9, 149.2, 147.2, 140.4, 138.9, 132.2, 131.6, 125.0, 123.6, 116.5, 115.7, 111.0, 94.1, 93.9, 77.8, 75.4, 56.7; MS *m/z* 795 (M^+) (6), 619, 499, 428, 269, 131, 95 (100). Anal. Calcd for $C_{24}H_{14}NO_{10}CCl_9$: C, 36.23; H, 1.77; N, 1.76. Found: C, 36.51; H, 2.01; N, 1.44.

N,N,O-Tris(ethoxycarbonyl)-10-amino-9-hydroxy-1,4-anthraquinone (24): from *N,O,O*-triacyl derivative 15 (300 mg, 0.65 mmol) in toluene (20 mL); reaction time 5 h; purified by column chromatography (*n*-hexane/ethyl acetate, 3:1) (280 mg, 93%); mp 173–175 °C; identical in all respect with the product described above.

N,N,O-Tris(ethoxycarbonyl)-10-amino-9-hydroxy-5-methoxy-1,4-anthraquinone (25): from *N,O,O*-triacyl derivative 16 (300 mg, 0.62 mmol) in toluene (20 mL); reaction time 10 h; purified by column chromatography (*n*-hexane/ethyl acetate, 3:1) (270 mg, 90%); mp 174–175 °C; IR (KBr) 2830, 1790, 1740, 1670, 1610, 1575, 1280, 1220, 1120, 720; ^{1}H NMR ($CDCl_3$) δ 7.91 (d, 1H, J = 8.5 Hz), 7.68 (dd, 1H, J = 8.5, 8.0 Hz), 7.12 (d, 1H, J = 8.0 Hz), 6.92, 6.88 (AB syst, 2H, J = 10.4 Hz), 4.47 (q, 2H, J = 7.2 Hz), 4.18 (q, 4H, J = 7.2 Hz), 3.96 (s, 3H), 1.52 (t, 3H), 1.13 (t, 6H): MS *m/z* 485 (M^+) (25), 413, 396, 352, 324, 296 (100), 268, 252. Anal. Calcd for $C_{24}H_{23}NO_{10}$: C, 59.38; H, 4.77; N, 2.88. Found: C, 59.38; H, 4.94; N, 2.85.

Diels–Alder Reaction of *N,N,O*- and *N,O,O*-Triacyl Derivatives with (*E*)-1,3-Bis[(trimethylsilyl)oxy]buta-1,3-diene. General Procedures. Method A. A solution of (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene and the *N,N,O*-triacyl derivative in a inert solvent (Table III) was refluxed under Ar until the starting material was consumed (disappearance of the *N,N,O*-triacyl derivative was monitored by TLC). The solvent was removed, and the residue was purified by crystallization from diethyl ether/*n*-hexane.

Method B. A solution of (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene and the *N,O,O*-triacyl derivative in toluene was refluxed under Ar until the starting material was consumed (disappearance of the *N,O,O*-triacyl derivative was monitored by TLC). The solvent was removed, and the residue was purified by crystallization from diethyl ether/*n*-hexane.

N,N,O-Tris(*tert*-butoxycarbonyl)-5-amino-12-hydroxy-7,9-bis[(trimethylsilyl)oxy]-6a,7,10,10a-tetrahydronaphthacene-6,11-dione (26). Method A. From *N,N,O*-triacyl derivative 20 (300 mg, 0.55 mmol) and (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene (1 mL, 4.60 mmol) in toluene (10 mL); reaction time 12 h (415 mg, 98%); mp 165–168 °C; IR (KBr) 1760, 1730, 1620, 1460, 1370, 1250, 1150; ^{1}H NMR ($CDCl_3$) δ 8.24 (m, 1H), 8.10 (m, 1H), 7.70 (m, 2H), 5.03 (dd, 1H, J = 6.0, 1.3 Hz), 4.67 (dd, 1H, J = 3.4, 6.0 Hz), 3.38 (t, 1H, J = 6.5 Hz), 3.09 (dd, 1H, J = 3.4, 6.5 Hz), 3.05 (d, 1H, J = 18.3 Hz), 2.14 (ddd, 1H, J = 1.3, 6.5 Hz), 1.65 (s, 9H), 1.39, 1.33 (s, 9H), 0.55 (s, 9H), –0.21 (s, 9H); ^{1}H NMR (C_6D_6) δ 8.26–8.20 (m, 2H), 5.07 (d, 1H, J = 5.9 Hz), 4.74 (dd, 1H, J = 3.1, 6.0 Hz), 3.10 (d, 1H, J = 18.3 Hz), 2.93–2.83 (m, 2H), 1.80 (m, 1H), 1.55 (s, 9H), 1.47, 1.39 (s, 9H), 0.26 (s, 9H), –0.03 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 196.9, 193.4, 153.1, 150.7, 150.4, 134.4, 134.0, 130.7, 129.8, 129.5, 127.6, 124.9, 124.5, 123.4, 105.6, 84.1, 83.1, 82.1, 68.4, 52.7, 44.6, 34.9, 31.8, 28.2, 27.6, 27.0, 22.8, 14.3, 0.5, –0.2; MS *m/z* 624 (M^+ – 2TMS), 598, 397, 239, 57 (100).

Method B: from *N,O,O*-triacyl derivative 11 (300 mg, 0.55 mmol) and (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene (1.40 mL, 6.07 mmol) in toluene (10 mL); reaction time 12 h (415 mg, 98%); mp 165–168 °C.

N,N,O-Tris(*tert*-butoxycarbonyl)-5-amino-12-hydroxy-4-methoxy-7,9-bis[(trimethylsilyl)oxy]-6a,7,10,10a-tetrahydronaphthacene-6,11-dione (27). Method A: from *N,N,O*-triacyl derivative 21 (300 mg, 0.53 mmol) and (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene (1.0 mL, 4.6 mmol) in toluene (10 mL); reaction time 12 h (411 mg, 96%); mp 158–160 °C; IR

(KBr) 1810, 1770, 1715, 1460, 1370, 1280, 1145, 850; ^{1}H NMR ($CDCl_3$) δ 7.82 (dd, 1H, J = 8.5, 1.0 Hz), 7.59 (dd, 1H, J = 8.5, 8.4 Hz), 7.04 (d, 1H, J = 8.4 Hz), 4.91–4.86 (m, 2H), 3.93 (s, 3H), 3.56 (m, 1H), 3.19 (dd, 1H, J = 3.7, 4.4 Hz), 2.30–2.12 (m, 2H), 1.56 (s, 9H), 1.33, 1.21 (s, 18H), 0.12 (s, 9H), 0.07 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 202.3, 199.1, 193.6, 157.6, 151.0, 150.5, 150.2, 146.3, 134.1, 132.5, 129.9, 126.8, 125.8, 121.8, 115.8, 109.5, 105.6, 86.4, 84.2, 82.0, 81.7, 75.9, 64.8, 56.1, 54.9, 45.8, 29.3, 27.9, 27.8, 27.7, 0.2, 0.1; MS m/z 497, 446, 397, 377, 305, 253, 238, 147, 75, 57, 41(100). Anal. Calcd $C_{40}H_{57}NO_{12}Si_2$: C, 60.05; H, 7.18; N, 1.75. Found: C, 59.73; H, 7.04; N, 1.36.

Method B: from *N,O,O*-triacyl derivative **12** (300 mg, 0.53 mmol) and (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene (1.4 mL, 6.0 mmol) in toluene (10 mL); reaction time 13 h (396 mg, 94%); mp 158–160 °C.

***N,N,O*-Tris(2,2,2-trichloroethoxycarbonyl)-5-amino-12-hydroxy-7,9-bis[(trimethylsilyl)oxy]-6a,7,10,10a-tetrahydronaphthacene-6,11-dione (28). Method A**: from *N,N,O*-triacyl derivative **22** (800 mg, 1.05 mmol) and (*E*)-1,3-bis-[(trimethylsilyl)oxy]buta-1,3-diene (0.6 mL, 2.75 mmol) in benzene (30 mL); reaction time 24 h (1.04 g, 96%); ^{1}H NMR ($CDCl_3$) δ 8.23 (m, 1H), 8.15 (m, 1H), 8.18–8.13 (m, 2H), 6.19 (d, 1H, J = 6.8 Hz), 4.98 (s, 2H), 4.85, 4.74 (s, 4H), 4.62 (dd, 1H, J = 6.8, 3.5 Hz), 3.41 (t, 1H, J = 6.3 Hz), 3.10 (dd, 1H, J = 3.5, 6.3 Hz), 3.02 (d, 1H, J = 18.2 Hz), 2.14 (dd, 1H, J = 18.2, 6.3 Hz), 0.25 (s, 9H), –0.26 (s, 9H).

Method B. From *N,O,O*-triacyl derivative **13** (300 mg, 0.39 mmol) and (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene (0.22 mL, 1.03 mmol) in toluene (15 mL); reaction time 24 h (475 mg, 96%).

***N,N,O*-Tris(2,2,2-trichloroethoxycarbonyl)-5-amino-12-hydroxy-4-methoxy-7,9-bis[(trimethylsilyl)oxy]-6a,7,10,10a-tetrahydronaphthacene-6,11-dione (29). Method A**: from *N,N,O*-triacyl derivative **23** (100 mg, 0.12 mmol) and (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene (0.13 mL, 0.56 mmol) in benzene (15 mL); reaction time 24 h (112 mg, 94%); ^{1}H NMR ($CDCl_3$) δ 7.71 (dd, 1H, J = 7.9, 1.0 Hz), 7.55 (t, 1H, J = 7.9 Hz), 6.95 (d, 1H, J = 7.9 Hz), 4.86 (m, 1H), 4.54 (dd, 1H, J = 5.8, 3.7 Hz), 3.82 (s, 3H), 3.29 (t, 1H, J = 6.3 Hz), 2.97 (dd, 1H, J = 6.3, 3.7 Hz), 2.90 (d, 1H, J = 18.1 Hz), 2.03 (dd, 1H, J = 18.1, 6.3 Hz), 0.16 (s, 9H), –0.32 (s, 9H).

Method B: from *N,O,O*-triacyl derivative **14** (1 g, 1.26 mmol) and (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene (1.3 mL, 5.64 mmol) in toluene (30 mL); reaction time 24 h (1.125 mg, 94%).

***N,N,O*-Tris(ethoxycarbonyl)-5-amino-12-hydroxy-7,9-bis-[(trimethylsilyl)oxy]-6a,7,10,10a-tetrahydronaphthacene-6,11-dione (30). Method A**: from *N,N,O*-triacyl derivative **24** (110 mg, 0.24 mmol) and (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene (0.3 mL, 1.37 mmol) in CH_2Cl_2; reaction time 40 h (132 mg, 80%); mp 224–228 °C; IR (Nujol) 1760, 1670, 1630, 1590, 1440, 1375, 1280, 1220, 770; ^{1}H NMR ($CDCl_3$) δ 8.22 (m, 1H), 8.05 (m, 1H), 7.69 (m, 2H), 4.70 (d, 1H, J = 5.8 Hz), 4.62 (dd, 1H, J = 3.5, 5.8 Hz), 4.41 (m, 2H), 4.22 (m, 2H), 4.00 (m, 2H), 3.40 (t, 1H, J = 6.4 Hz), 3.10 (dd, 1H, J = 3.5, 6.4 Hz), 3.03 (d, 1H, J = 18.1 Hz), 2.10 (dd, 1H), 1.48 (t, 3H, J = 7.1 Hz), 1.16 (t, 3H, J = 7.1 Hz), 1.08 (t, 3H, J = 7.1 Hz), 0.25 (s, 9H), –0.28 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 196.9, 193.2, 153.0, 152.6, 152.5, 152.0, 145.0, 133.7, 133.4, 130.2, 130.1, 130.0, 127.5, 124.5, 124.0, 123.5, 105.1, 68.1, 65.4, 63.2, 63.0, 53.1, 44.3, 26.5, 14.2, 14.1, 14.0, 0.3, –0.4. Anal. Calcd for $C_{38}H_{43}NO_{11}Si_2$: C, 57.78; H, 6.32; N, 2.04. Found: C, 57.78; H, 6.38; N, 1.72.

Method B. From *N,O,O*-triacyl derivative **15** (110 mg, 0.24 mmol) and (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene (0.3 mL, 1.37 mmol) in toluene (10 mL); reaction time 40 h (132 mg, 80%); mp 224–228 °C.

***N,N,O*-Tris(ethoxycarbonyl)-5-amino-12-hydroxy-4-methoxy-7,9-bis[(trimethylsilyl)oxy]-6a,7,10,10a-tetrahydronaphthacene-6,11-dione (31). Method A**: from *N,N,O*-triacyl derivative **25** (276 mg, 0.57 mmol) and (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene (1.4 mL, 6.0 mmol) in toluene; reaction time 1 h (300 mg, 73%); mp 143.5–145 °C; IR (Nujol) 1770, 1765, 1680, 1600, 1590, 1465, 1220, 1060, 795; ^{1}H NMR ($CDCl_3$) δ 7.81 (dd, 1H, J = 8.5, 0.95 Hz), 7.61 (dd, 1H, J = 8.5, 8.0 Hz), 7.03 (d, 1H, J = 8.0 Hz), 4.98 (d, 1H, J = 5.9 Hz), 4.62 (dd, 1H, J = 3.5, 5.9 Hz), 4.45–4.17 (m, 6H), 3.93 (s, 3H), 3.41 (t, 1H, J = 6.4 Hz), 3.08 (dd, 1H, J = 3.5, 6.4 Hz), 3.02 (d, 1H, J = 18.0 Hz), 2.12 (dd, 1 H), 1.49 (t, 3H, J = 7.1 Hz), 1.17 (t, 3H, J = 7.1 Hz), 1.07 (t, 3H, J = 7.1 Hz), 0.27 (s, 9H), –0.24 (s, 9H).

Method B: from *N,O,O*-triacyl derivative **16** (276 mg, 0.57 mmol) and (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene (1.4 mL, 6.0 mmol) in toluene (10 mL); reaction time 1 h (300 mg, 73%); mp 143.5–145 °C.

***N,N,O*-Tris(ethoxycarbonyl)-5-amino-12-hydroxy-7-[(trimethylsilyl)oxy]-6a,7,10,10a-tetrahydronaphthacene-6,11-dione and *N,N,O*-Tris(ethoxycarbonyl)-5-amino-12-hydroxy-10-[(trimethylsilyl)oxy]-6a,7,10,10a-tetrahydronaphthacene-6,11-dione**: from *N,N,O*-triacyl derivative **24** (100 mg, 0.22 mmol) and (*E*)-1-[(trimethylsilyl)oxy]buta-1,3-diene (150 mg, 1.05 mmol) in CH_2Cl_2 (6 mL); reaction time 18 h (99 mg, 75%). The crude was found to be a 1.5:1 mixture of regioisomers (estimated by ^{1}H NMR): ^{1}H NMR ($CDCl_3$) δ 8.24 (m, 1H), 8.05 (m, 1H), 7.72 (m, 2H), 5.86 (m, 2H), 4.52–3.99 (m, 7H), 3.41 (m, 1H), 3.25–2.96 (m, 2H), 2.08 (m, 1H), 1.54–1.10 (m, 9H), –0.24, –0.25 (s, 9H).

***N,N,O*-Tris(ethoxycarbonyl)-5-amino-12-hydroxy-7-[(trimethylsilyl)oxy]-6a,7,8,9,10,10a-hexahydronaphthacene-6,9,11-trione (32)**. A solution of adduct **30** (60 mg, 0.088 mmol) in THF (2 mL) and 1.6 μL of 12 N HCl was kept at 0 °C for 6 h under Ar. The mixture was poured into water, and the solution was extracted with CH_2Cl_2. The organic layer was washed with water and dried ($MgSO_4$). The solvent was removed, and the residue was recrystallized from diethyl ether/*n*-hexane (46 mg, 85%); mp 138–140 °C; IR (KBr) 1795, 1790, 1715, 1690, 1290, 1120; ^{1}H NMR ($CDCl_3$) δ 8.22 (m, 1H), 8.06 (m, 1H), 7.73 (m, 2H), 4.75 (m, 1H), 4.40 (m, 2H), 4.22 (m, 2H), 3.98 (m, 2H), 3.65 (td, 1H, J = 1.3, 6.8 Hz), 3.39–3.34 (m, 2H), 2.54 (m, 2H), 2.32 (dd, 1H, J = 7.2, 15.8 Hz), 1.46 (t, 3H, J = 7.2 Hz), 1.17 (t, 3H, J = 7.1 Hz), 1.07 (t, 3H, J = 7.1 Hz), –0.26 (s, 9H).

***N,N,O*-Tris(ethoxycarbonyl)-5-amino-7,12-dihydroxy-6a,7,8,9,10,10a-hexahydronaphthacene-6,9,11-trione (33). Method A.** A solution of adduct **30** (26 mg, 0.04 mmol) in THF (2 mL), 0.008 mL of 3 N HCl, and 0.008 mL H_2O_2 (30%) was kept at 0 °C for 3 h under Ar. The mixture was poured into water, and the solution was extracted with CH_2Cl_2. The organic layer was successively washed with water, NaCl solution, and water and dried ($MgSO_4$). The solvent was removed, and the residue was recrystallized from diethyl ether/*n*-hexane (18 mg, 83%); mp 120–124 °C; IR (Nujol) 3450, 1780, 1775, 1710, 1695, 1210; ^{1}H NMR ($CDCl_3$) δ 8.31 (m, 1H), 8.09 (m, 1H), 7.79 (m, 2H), 4.53 (m, 1H), 4.42 (q, 2H), 4.29–4.13 (m, 4H), 3.64–3.46 (m, 2H), 3.23 (dd, 1H, J = 4.1, 15.3 Hz), 2.69 (d, 2H, J = 12.6 Hz), 2.66 (dd, 1H, J = 4.4, 12.6 Hz), 2.46 (dd, 1H, J = 5.9, 15.3 Hz), 1.55 (br s, 1H), 1.47 (t, 3H, J = 7.1 Hz), 1.19 (t, 6H, J = 7.1 Hz).

Method B. A solution of **32** (50 mg, 0.08 mmol) in THF (2 mL), 0.016 mL of 3 N HCl, and 0.016 mL H_2O_2 (30%) was kept at 0 °C under Ar for 5 h. The mixture was poured into water, and the solution was extracted with CH_2Cl_2. The organic layer was successively washed with water, NaCl solution, and water and dried ($MgSO_4$). The solvent was removed, and the residue was recrystallized from diethyl ether/*n*-hexane (30 mg, 72%); mp 120–124 °C.

***N,N,O*-Tris(*tert*-butoxycarbonyl)-5-amino-12-hydroxy-7-[(trimethylsilyl)oxy]-6a,7,8,9,10,10a-hexahydronaphthacene-6,9,11-trione (34) and *N,N,O*-Tris(*tert*-butoxycarbonyl)-5-amino-7,12-dihydroxy-6a,7,8,9,10,10a-hexahydronaphthacene-6,9,11-trione (35)**. A solution of adduct **26** (616 mg, 0.80 mmol) in THF (50 mL) and 0.08 mL of 3 N HCl was kept at 0 °C under Ar for 15 min. The mixture was poured into water, and the solution was extracted with CH_2Cl_2. The organic layer was washed with water and dried ($MgSO_4$). The solvent was removed, and the residue was recrystallized from diethyl ether/*n*-hexane: ^{1}H NMR ($CDCl_3$) δ 8.22 (m, 1H), 8.11 (m, 1H), 7.75 (m, 2H), 4.77 (m, 1H), 4.50 (m, 1H), 3.60 (t, 1H, J = 8.2 Hz), 3.64–3.42 (m, 2H), 3.40–3.30 (m, 2H), 3.15 (dd, 1H, J = 5.7, 19.6 Hz), 2.66 (d, 2H, J = 5.7 Hz), 2.54 (m, 2H), 2.43 (dd, 1H, J = 8.1, 19.6 Hz), 2.32 (dd, 1H, J = 8.1, 17.0 Hz), 1.60 (s, 9H), 1.57 (s, 9H), 1.34 (s, 9H), 1.33 (s, 9H), 1.30 (s, 9H), 1.29 (s, 9H), –0.02 (s, 9H).

***N,N,O*-Tris(2,2,2-trichloroethoxycarbonyl)-5-amino-12-hydroxy-7-[(trimethylsilyl)oxy]-6a,7,8,9,10,10a-hexahydronaphthacene-6,9,11-trione (36)**. A solution of adduct **28** (1.146 g, 1.15 mmol) in THF (20 mL) and 0.2 mL of 3 N HCl was kept at 0 °C under Ar for 5 min. The mixture was poured into

water and was extracted with CH_2Cl_2. The organic layer was successively washed with water, NaCl solution, and water and dried ($MgSO_4$). The solvent was removed, and the residue was recrystallized from diethyl ether/*n*-hexane (920 mg, 95%); mp 124–127 °C; IR (Nujol) 1820, 1790, 1720, 1685, 1610, 1275, 1120; ^1H NMR ($CDCl_3$) δ 8.28–8.16 (m, 2H), 7.88–7.79 (m, 2H), 4.75 (m, 1H), 4.98 (s, 2H), 4.85, 4.74 (s, 4H), 3.67 (t, 1H, J = 6.1 Hz), 3.43 (m, 1H), 3.36 (m, 1H), 2.59 (m, 2H), 2.38 (dd, 1H, J = 16.0, 6.1 Hz), –0.23 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 204.5, 196.4, 192.0, 151.4, 150.2, 149.2, 145.5, 133.5, 132.2, 131.1, 131.0, 130.2, 126.9, 124.4, 123.4, 94.2, 94.1, 75.3, 73.8, 54.5, 48.6, 46.3, 37.4, 29.6, –0.6; MS m/z 749, 732, 449, 147, 75 (100), 50.

***N,N,O*-Tris(2,2,2-trichloroethoxycarbonyl)-5-amino-9,12-dihydroxynaphthacene-6,11-dione (38).** A solution of adduct **28** (1.140 g, 1.14 mmol) in THF (20 mL) and 0.6 mL of 3 N HCl was kept at 0 °C under Ar for 5 h. The mixture was poured into water, and the solution was extracted with CH_2Cl_2. The organic layer was washed with water and dried ($MgSO_4$). The solvent was removed, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate, 3:1) to yield 567 mg (65%) of **38**: mp 215–220 °C: IR (Nujol) 3440, 3380, 1815, 1790, 1675, 1605, 1585, 1275, 1120; ^1H NMR (DMSO-d_6) δ 11.19 (br s, 1H), 8.35–8.10 (m, 2H), 8.07 (d, 1H, J = 8.6 Hz), 8.02–7.95 (m, 2H), 7.45 (d, 1H, J = 2.5 Hz), 7.27 (dd, 1H, J = 8.6, 2.5 Hz), 5.22 (s, 2H), 4.87 (s, 4H). Anal. Calcd for $C_{27}H_{14}O_{10}NCl_9$: C, 38.99; H, 1.68; N, 1.68. Found: C, 39.12; H, 1.98; N, 1.99.

***N,N,O*-Tris(2,2,2-trichloroethoxycarbonyl)-5-amino-12-hydroxy-4-methoxy-7-[(trimethylsilyl)oxy]-6a,7,8,9,10,10a-hexahydronaphthacene-6,9,11-trione (37).** A solution of adduct **29** (1.3 g, 1.26 mmol) in THF (20 mL) and 0.6 mL of 3 N HCl was kept at 0 °C under Ar for 5 min. The mixture was poured into water, and the solution was extracted with CH_2Cl_2. The organic layer was successively washed with water, NaCl solution, and water and dried ($MgSO_4$). The solvent was removed, and the residue was recrystallized from diethyl ether/*n*-hexane (1.10 g, 92%); mp 125–130 °C; IR (Nujol) 1820, 1800, 1725, 1710, 1290, 1220, 1120, 750; ^1H NMR ($CDCl_3$) δ 7.91 (dd, 1H, J = 8.4, 0.9 Hz), 7.72 (dd, 1H, J = 8.4, 8.1 Hz), 7.07 (d, 1H, J = 8.1 Hz), 4.90 (m, 1H), 4.78 (s, 2H), 4.75, 4.69 (s, 4H), 3.9 (s, 3H), 3.58 (m, 1H), 3.30 (m, 1H), 3.20 (d, 1H, J = 19.0 Hz), 2.97 (dd, 1H, J = 18.6, 4.2 Hz), 2.53 (m, 1H), 2.30 (m, 1H), –0.27 (s, 9H); MS m/z 863, 757, 685, 566, 494, 392, 320, 44(100). Anal. Calcd for $C_{31}H_{28}NO_{12}Cl_9Si$: C, 39.04; H, 2.96; N, 1.47. Found: C, 39.30; H, 3.10; N, 1.52.

5-Amino-12-hydroxy-7-[(trimethylsilyl)oxy]-6a,7,8,9,10,-10a-hexahydronaphthacene-6,9,11-trione (39). A solution of **36** (234 mg, 0.59 mmol) in THF (5 mL), Zn dust (600 mg, 9.17 mmol), acetic acid (1 mL), and 1 M KH_2PO_4 (0.6 mL) was stirred at rt for 5 min. The mixture was extracted with CH_2Cl_2. The organic layer was washed with water and dried ($MgSO_4$). The solvent was removed, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate, 1:1) to give **36** (164 mg, 71%): mp 114–116 °C; IR (KBr) 3440, 3350, 1710, 1630, 1600, 1240, 1220, 1050, 830; ^1H NMR ($CDCl_3$) δ 13.33 (s, 1H), 8.50 (m, 1H), 7.98 (m, 1H), 7.79–7.27 (m, 4H), 4.69 (m, 1H, J = 2.8 Hz), 3.63 (m, 1H), 3.48 (m, 1H), 3.35 (dd, 1H, J = 6.4, 18.0 Hz), 2.68–2.51 (m, 2H), 2.40 (m, 1H), –0.35 (s, 9H); MS m/z 397 (M^+) (55), 381, 296, 239, 147 (100).

5-Amino-12-hydroxy-4-methoxy-7-[(trimethylsilyl)oxy]-6a,7,8,9,10,10a-hexahydronaphthacene-6,9,11-trione (40). A solution of **37** (300 mg, 0.31 mmol) in THF (10 mL), Zn dust (910 mg, 13.92 mmol), acetic acid (1.3 mL), and 1 M KH_2PO_4 (0.91 mL) was stirred at rt for 5 min. The mixture was extracted with CH_2Cl_2. The organic layer was washed with water and dried ($MgSO_4$). The solvent was removed, and the residue was purified by column chromatography (*n*-hexane/ethyl acetate, 1:1) to give **40** (96 mg, 73%): mp 105 °C; IR (Nujol) 3440, 1730, 1600, 1260, 1240, 845; ^1H NMR ($CDCl_3$) δ 13.20 (s, 1H), 10.69 (br s, 1H), 8.28 (br s, 1H), 8.02 (d, 1H, J = 8.1 Hz), 7.59 (dd, 1H, J = 8.1, 7.1 Hz), 7.06 (d, 1H, J = 7.1 Hz), 4.62 (m, 1H), 4.04 (s, 3H), 3.57 (t, 1H, J = 7.1 Hz), 3.48 (d, 1H, J = 15.7 Hz), 3.27 (d, 1H, J = 7.0 Hz), 2.63–2.44 (m, 2H), 2.37 (dd, 1H, J = 15.7, 7.0 Hz), –0.34 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 206.2, 201.2, 195.4, 160.0, 149.8, 148.9, 130.9, 118.0, 111.9, 110.6, 110.3, 72.9, 56.6, 55.4, 49.9, 44.6, 37.6, 29.7, –0.7; MS m/z 427 (M^+) (100), 412, 308, 268, 143, 101, 73, 44.

9-Ethynyl-6,7,9,11-tetrahydroxy-5-imino-7,8,9,10-tetrahydronaphthacen-12-one (41). A solution of ethylmagnesium bromide, freshly prepared from Mg (233 mg, 9.58 mmol) and ethyl bromide (0.8 mL, 10.72 mmol), in THF (15 mL) was added over a period of 90 min to a saturated solution of acetylene in THF. During the addition acetylene was passed into the mixture. A solution of **39** (100 mg, 0.25 mmol) in THF (20 mL) was added, and the mixture was stirred for 30 min at 0 °C. Then the reaction mixture was stirred with a saturated aqueous solution of tartaric acid and ethyl acetate for 10 min. The organic layer was separated, washed with NaCl solution, dried, and evaporated. The residue was air-oxidized by dissolution in THF (10 mL), addition of 5% aqueous KOH (25 mL), and stirring at 0 °C. After 30 min, a saturated aqueous solution of tartaric acid (15 mL) and ethyl acetate (15 mL) were added. The organic layer was separated, washed with NaCl solution, and dried. The solvent was evaporated, and the residue was purified by column chromatography (ethyl acetate) to give **41** as a 5:2 mixture of epimers (estimated by ^1H NMR) (70 mg, 80%): mp 164–167 °C; IR (Nujol) 3370, 3300, 1615, 1575, 1380, 1080; ^1H NMR (DMSO-d_6) δ 16.23 (s, 1H), 15.70 (s, 1H); 12.75 (br s, 1H), 11.88 (br s, 1H), 10.01 (br s, 1H), 9.63 (br s, 1H), 8.53 (m, 1H), 8.35 (m, 1H), 7.93–7.77 (m, 2H), 6.10 (s, 1H), 5.55 (s, 1H), 5.48 (br s, 1H), 4.97 (t, 1H, J = 6.5 Hz), 4.71 (t, 1H, J = 3.4 Hz), 4.29 (s, 1H), 3.29 (s, 1H), 3.21 (s, 1H), 2.98, 2.71 (AB syst, 2H, J = 17.9 Hz), 2.40–1.86 (m, 2H); MS m/z 349 (M^+) (3), 313 (100), 290, 253, 228, 77, 44. Anal. Calcd for $C_{20}H_{15}NO_5$: C, 86.76; H, 4.33; N, 4.01. Found: C, 86.50; H, 4.02; N, 3.97.

9-Ethynyl-6,7,9,11-tetrahydroxy-5-imino-4-methoxy-7,8,9,-10-tetrahydronaphthacen-12-one (42). A solution of ethylmagnesium bromide, freshly prepared from Mg (117 mg, 4.81 mmol) and ethyl bromide (0.41 mL, 5.18 mmol), in THF (5 mL) was added over a period of 90 min to a saturated solution of acetylene in THF. During the addition, acetylene was passed into the mixture. A solution of **40** (50 mg, 0.12 mmol) in THF (10 mL) was added, and the mixture was stirred for 30 min at 0 °C. Then the reaction mixture was stirred with a saturated aqueous solution of tartaric acid and ethyl acetate for 10 min. The organic layer was separated, washed with NaCl solution, dried, and evaporated. The residue was air-oxidized by dissolution in THF (5 mL), addition of 5% aqueous KOH (15 mL), and stirring at 0 °C. After 30 min, a saturated aqueous solution of tartaric acid (8 mL) and ethyl acetate (8 mL) were added. The organic layer was separated, washed with NaCl solution, and dried. The solvent was evaporated, and the residue was purified by column chromatography (ethyl acetate) to give **42** (35 mg, 79%): mp 164 °C; IR (KBr) 3400, 3280, 1580, 1270, 1160, 1140; ^1H NMR (DMSO-d_6) δ 15.50 (s, 1H), 13.72 (br s, 1H), 9.88 (br s, 1H), 7.97 (d, 1H, J = 7.6 Hz), 7.80 (t, 1H, J = 7.6 Hz), 7.57 (d, 1H, J = 7.6 Hz), 5.80 (s, 1H), 5.31 (m, 1H), 5.06 (m, 1H), 4.10 (s, 3H), 3.28 (s, 1H), 3.10, 2.75 (AB syst, 2H, J = 17.1 Hz), 2.20–1.81 (m, 2H); MS m/z 379 (M^+), 363 (100), 343, 319, 295, 252, 154, 126, 97, 43.

(±)-4-Demethoxy-5-iminodaunomycinone (3). To a solution of **41** (20 mg, 0.06 mmol) in acetone (15 mL) were added HgO (200 mg, 0.92 mmol) and 1.26 M H_2SO_4 (13 mL). The reaction mixture was heated for 15 min, and then 1 N HCl (10 mL) and CH_2Cl_2 were added at rt. The organic layer was separated and dried, and the solvent was evaporated. The residue was purified by column chromatography (ethyl acetate) to give **3** (16 mg, 72%): mp 190–200 °C; IR (Nujol) 3350, 1710, 1610, 1590, 1130, 800; ^1H NMR (DMSO-d_6) δ 15.91 (s, 1H), 12.52 (br s, 1H), 9.41 (br s, 1H), 8.56 (d, 1H, J = 7.7 Hz), 8.39 (dd, 1H, J = 7.5, 1.4 Hz), 7.95 (td, 1H, J = 1.4 Hz), 7.87 (t, 1H), 5.95 (d, 1H), 5.36 (d, 1H, J = 4.3 Hz), 4.99 (m, 1H), 2.85, 2.74 (AB syst., 2H, J = 16.7 Hz), 2.27 (s, 3H), 2.18 (dd, 1H, J = 12.5, 5.2 Hz), 2.08 (dd, 1H, J = 12.5, 4.8 Hz); MS m/z 368 (M^+ + 1) (19), 367 (M^+) (7), 350, 332, 307, 279, 253, 187, 57, 43 (100).

(±)-5-Iminodaunomycinone (4). To a solution of **42** (10 mg, 0.03 mmol) in acetone (8 mL) were added HgO (100 mg, 0.46 mmol) and 1.26 M H_2SO_4 (12.5 mL). The reaction mixture was heated for 15 min and then 1 N HCl (5 mL) and CH_2Cl_2 were added at rt. The organic layer was separated and dried, and the solvent was evaporated. The residue was purified by column chromatography (ethyl acetate) to give **4** (7 mg, 70%): mp 222–228 °C; IR (Nujol) 3400, 1715, 1265, 1095, 800; ^1H NMR (DMSO-d_6) δ 15.79 (s, 1H), 13.63 (br s, 1H), 9.80 (br s, 1H), 8.07 (d, 1H,

J = 7.7 Hz), 7.86 (t, 1H, J = 7.7 Hz), 7.63 (d, 1H), 5.94 (s, 1H), 5.50 (d, 1H, J = 4.4 Hz), 5.00 (m, 1H), 4.12 (s, 3H), 2.95, 2.76 (AB syst, 2H, J = 18.6 Hz), 2.27 (s, 3H), 2.17–1.94 (m, 2H); MS m/z 397 (M^+) (5), 381, 379, 361, 346, 342, 338 (100), 319, 295, 272, 202, 171, 126, 88, 43.

To confirm the identity of the synthetic product, a suspension of (+)-daunomycinone (8 mg, 0.02 mmol) (obtained by acidic hydrolysis of a sample of natural (+)-daunomycin), methanol (4 mL), and 30% aqueous ammonia (4 mL) was stirred at rt for 3 h, and then ethyl acetate was added. The organic layer was separated and dried, and the solvent was evaporated. The residue was purified by column chromatography (ethyl acetate) to give a violet product (7 mg, 90%), the spectral data of which were identical to those described above.

(±)-Daunomycinone (5). To a solution of 4 (6 mg, 0.015 mmol) in dioxane (4 mL) was added 20% H_2SO_4 (4 mL). The mixture was stirred at rt for 6 days, and ethyl acetate was added. The organic layer was separated and dried, and the solvent was evaporated. The residue was purified by column chromatography (n-hexane/ethyl acetate, 1:10) to give 5 (4.5 mg, 75%). The ^1H NMR spectrum of the product was identical with that reported in the literature.[17b,c]

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