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QUINALDYL ETHERS AS LATENT CARBONYL FUNCTIONS

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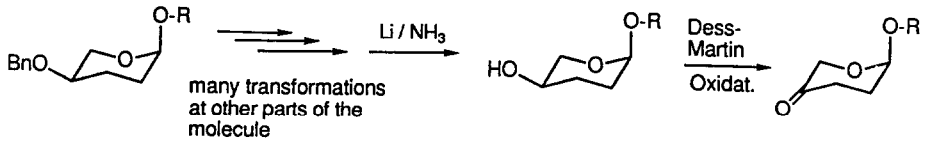
Abstract: *Ketones can be generated from secondary alcohols by converting the latter into quinaldine ethers followed by irradiaten (>320 nm). The quinaldine ethers can therefore be utilized as latent carbonyl groups. The quinaldine group is chemically inert during transformations at other parts of the molecule involving hydroboration, Grignard reagents, $LiAlH_4$, as well as bromine or ozone.*

During multistep synthesis of complicated structures those functional groups which are ultimately required in the target molecule have either to be protected en route or carried through the synthesis in latent form, which is unmasked in the last step of the synthesis. This applies in particular to ketone functions. If a long term protection of a carbonyl group is desired, the latter is frequently transformed into a 1,3-dioxolane, or a 1,3-dioxane derivative. However, if the number of transformations is to be kept at a minimum, it is preferable to use a latent carbonyl function, such as a C=C double bond. Similarly, alcohol functions are used frequently as pro-carbonyl groups. The alcohols, however, have themselves to be masked by protecting groups. Thus, in order to generate the desired keto function this protecting group has to be specifically removed in the presence of other protected alcohols at the end of the synthesis and oxidized to give the ketone. An arbitrary example is given from Danishefsky's triglycoside synthesis[1].



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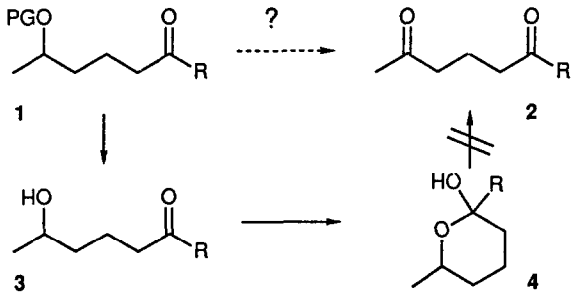
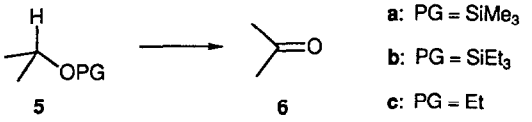
It would be more economical if a long term protecting group for an alcohol function would be available, which would allow the direct conversion into the desired ketone. Such a strategy becomes mandatory, if one has to generate a 1,4- or 1,5-dicarbonyl unit, e.g. **2** in the target molecule.

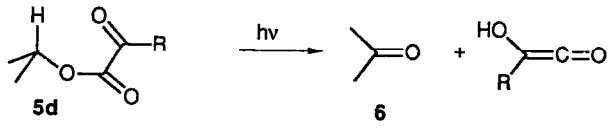


In such a case deprotection of the hydroxy group in **1** would generate the hydroxy ketone **3**, which could immediately cyclize to the pyranose **4**. In most cases the latter can no longer be oxidized to the target structure **2**. Out of such a situation we became interested in a protecting group, which would allow the direct transformation of **1** into **2**.

There are several examples known for a one pot conversion of a protected alcohol **5** into a ketone **6**[2,3].

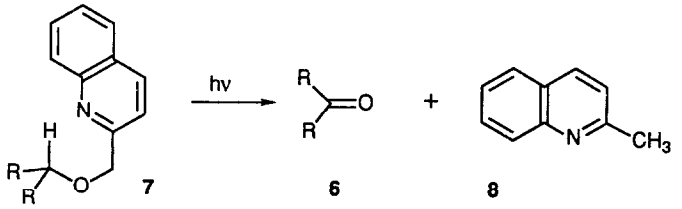


For instance, trimethylsilyl-(**5a**) or triethylsilyl-ethers **5b** have been oxidized with various oxidizing agents to the ketones **6**. At least in the more popular methods, Jones oxidation or Swern oxidation, it is not clear, whether the secondary alcohols are formed as intermediates. Of course, under forcing conditions, even ethyl ethers **5c** may be oxidized[3], but this is certainly unattractive for the final step in a synthesis of a labile multifunctional target molecule. It would be much more preferable to use a mild method for the conversion of **5** into **6**, which is specific for a particular protecting group, as has been found in a free radical fragmentation[2f] of 2-bromo benzyl ethers. Such specificity could also be found among the photochemically labile protecting groups[4]. Indeed photochemical generation of ketones have been reported for the substrates **5d**[5] having an α-ketoester-function.



5d 6

This function serves admirably well for specific conversion of **5** into **6**, yet it can hardly be considered as a protecting group, since the α-ketoesters are as chemical vulnerable as the carbonyl groups they should ultimately provide. In search for a chemical more inert group, which still allows a photochemical conversion of **5** into **6** we found a report by Stermitz[6] on the photochemistry of quinaldine derivatives:



7 6 8

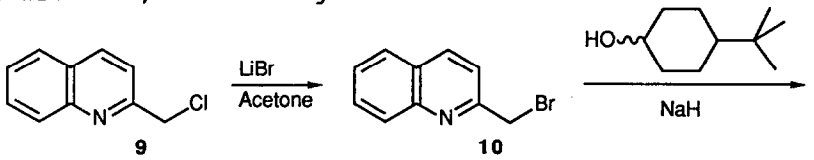
a: R = H

b: R = Alkyl

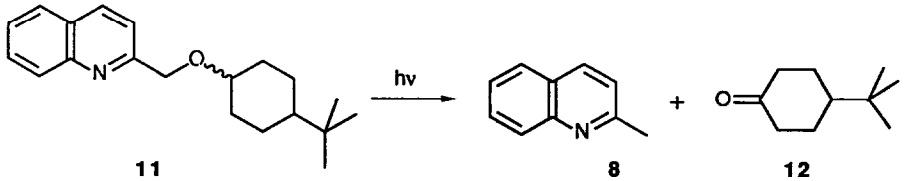
On photolyses of **7a** an 78% yield of quinaldine (**8**) was attained. The formation of formaldehyde was qualitatively established. This led us to investigate the potential of 2-quinolinemethyl ethers (quinaldine ethers) **7b** as latent carbonyl groups.

Photochemical Cleavage of 4-t-Butylcyclohexyl-2-quinolinemethyl ether 11

Quinaldine ethers can be formed[7] from 2-chloromethylquinoline (**9**)[8], which is available from Aldrich. In our hands, we preferred to convert **9** to the more reactive bromomethyl compound **10**[9]. Caution: **10**, like other benzylic bromides, is a strong skin irritant.



9 10

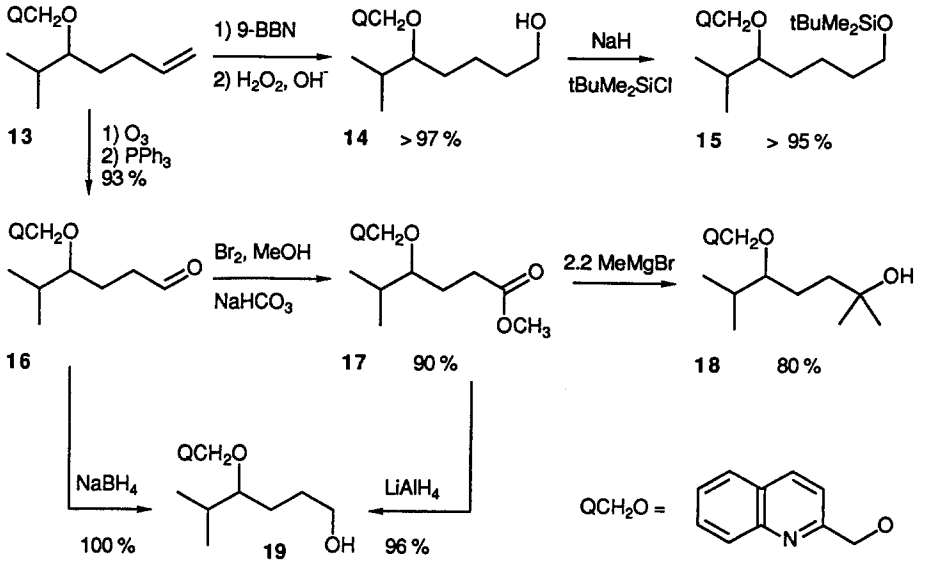


11 8 12

On reaction of 4-t-butylcyclohexanol (cis/trans-mixture) with **10** in the presence of sodium hydride the ether **11** was formed in 91% yield. Photolysis experiments were carried out with a 150 W medium pressure mercury lamp in a duran glass apparatus ($\lambda > 300$ nm). 5 h photolyses of a 0.008 m solution of **11** in benzene[6] led to the formation of t-butyl-cyclohexanone (**12**) in 61% yield. Higher concentrations should not be detrimental, as it has been reported for the photolysis of 2-alkyl-quinolines[10] that the quantum yield of this singlet reaction[6] increases with concentrations up to 1.2 m. Rather than changing the concentration, we found that a change in the solvent to acetonitrile allowed the photolyses of **11** to proceed more rapidly: a 2.5 h irradiaton furnished 85% of t-butylcyclohexanone (**12**). A change to t-butanol as solvent led to inferior results. In summary, the quinaldine ethers are not only readily obtained, they also lead to the ketones **12** in good yield.

The Chemical Stability of Quinaldine Ethers

A prerequisite for the use of quinaldine ethers as latent carbonyl groups is their inertness under the common synthetic transformations. In order to evaluate this aspect, the quinaldine ether **13** was prepared (95%) and subjected to representative sequences of transformations:

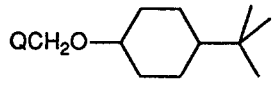
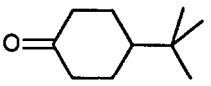
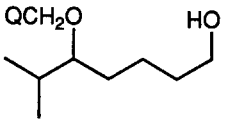
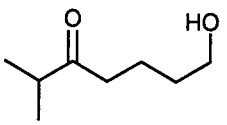
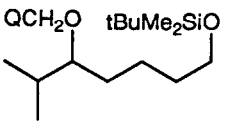
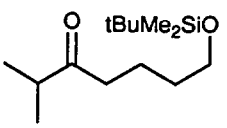
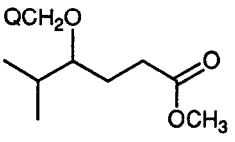
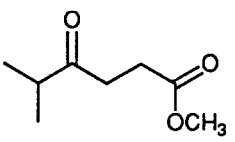
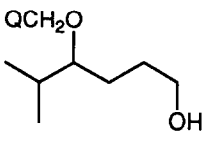
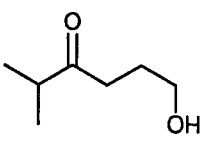


The high yields obtained attest the quinolinylmethyl group good chemical resistance against hydroboration, oxidations (ozone or bromine), reduction ($NaBH_4$, $LiAlH_4$), and Grignard additions. These findings back the proposal[7] to use quinaldine ethers as hydroxyl protecting groups.

Photolytic Generation of Ketones from 2-Quinolinemethyl Ethers

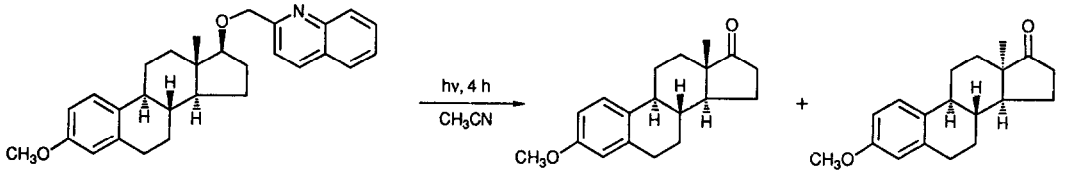
Reassured about the chemical stability of the quinaldine ethers we looked more closely at their direct photolytic conversion into ketones. Results of representative photolysis experiments are collected in the table.

Table: Irradiation of the 2-Quinolinylmethyl Ethers

Starting Ethers	Product Ketones	Yield (%)
11 	**12** 	85
14 	**20** 	65
15 	**21** 	62
17 	**22** 	61
19 	**23** 	61

We found that the open chain quinaldine ethers formed the desired ketones in only moderate yields of 60-65%. Longer irradiation time did not lead to higher yields. It became apparent that the rate of photo-cleavage leveled off rapidly, because the coproduct formed, the quinaldine **8**, serves as an internal filter. This, however, is not the decisive factor. Rather, the ketone products themselves turned out to be photolabile under the conditions applied. Thus, when a mixture of the ketoester **22** and quinaldine **8** was irradiated for the usual period, the ketone could only be re-

covered in 75% yield. The likely fate of the ketones is, that it undergoes Norrish type I cleavage (α-cleavage) to give side products. In this respect, the substrates **14**, **15**, **17**, **19** chosen provide ketones **20** - **23**, which are photochemically rather labile, because these ketones are α-branched. It is therefore understandable, that the photolyses of the cyclohexanol derivative **11** leading to an α,α'-unsubstituted ketone **12** did so in higher yield. The complication by a Norrish type I cleavage should be even more troublesome if an α-tertiary ketone[11] is to be generated. For this reason we examined the photolysis of the ether **24**:



24 **25** 72 % + **26** 12 %

The primary photoproduct, the ketone **25**, was obtained in good yield. Yet the lumi-ketone **26**[12] was isolated alongside. Thus, it is this secondary photolysis of the desired ketones we have to worry about. This secondary photo-cleavage could be eliminated by using a longer wave length irradiation. Unfortunately, the absorption of the quinoline moiety (λ_{max} 315 nm)[13] in comparison to that of the ketone, e.g. **22** (λ_{max} 326 and 341 nm) allows no further leeway towards longer wavelength.

The present study was aimed at the development of a protective group for secondary alcohols, that allows the direct photochemical generation of ketones. The 2-quinolinemethyl group serves this purpose. The quinolinemethyl ethers **7** are readily obtained and possess high chemical stability. Photoconversion of **7b** to the ketones proceeds with moderate to good yields. The efficiency of this conversion is limited by a secondary photodegradation of the desired ketones.

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EXPERIMENTAL

All temperatures quoted are not corrected. - ^{1}H NMR and ^{13}C-NMR: Bruker AM 300. - Column chromatography: Kieselgel 60 (230 - 400 mesh, Merck, Darmstadt). - Irradiation: Heraeus medium pressure mercury lamp Q150.

1. 2-Bromomethylquinoline (**10**): To a solution of 7.00 g (39 mmol) of 2-chloromethylquinoline (**9**) in 200 ml of THF was added 34.3 g (0.3 mol) of lithium bromide and the mixture was refluxed for 7 h. After addition of 75 ml of water the phases were separated and the aqueous phase was extracted twice with 100 ml of ether. The combined organic extracts were dried with $MgSO_4$ and concentrated to give a quantitative yield of **10** [9].

2. 4-t-Butyl-cyclohexyl 2-quinolinyl-methyl ether (**11**): A flask was charged with 2.02 g (9.1 mmol) of 2-bromomethylquinoline (**10**) and 0.2 g (8 mmol) of sodium hydride. The flask was purged with nitrogen and 40 ml of THF was added. The mixture was heated to reflux under stirring and a solution of 1.09 g (7 mmol) of 4-t-butylcyclohexanone (cis/trans-mixture) in 10 ml of THF was added dropwise. After 2 h reflux the cold mixture was hydrolyzed by dropwise addition of water. The phases were separated, and the aqueous phase was extracted twice with 20 ml of ether. The combined organic extracts were washed with 20 ml of brine, dried with $MgSO_4$ and concentrated. The residue was chromatographed with petroleum ether/ether = 4:1 to give 1.88 g (91%) of **11** as a white solid, m.p. 87-88°C. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.78, 0.81 (2s, 9H), 0.92 - 0.99 (m, 2H), 1.24 - 1.45 (m, 4H), 1.72 - 1.77 (m, 1H), 2.04 - 2.16 (m, 2H), 3.24 - 3.34 (m, 0.8H), 3.67 (broad s, 0.2H), 4.75 (s, 0.4H), 4.81 (s, 1.6H), 7.44 (dd, J = 7.4 and 7.5 Hz, 1H), 7.60 - 7.64 (m, 2H), 7.69 (d, J = 8.0 Hz, 2H), 7.87 (d, J = 8.5 Hz, 1H), 8.10 (d, J = 8.5 Hz, 1H). - ^{13}C NMR (75 MHz, $CDCl_3$): cis-isomer δ = 21.4, 27.4, 32.2, 32.5, 47.9, 71.2, 73.3, 119.3, 125.9, 127.4, 128.8, 129.3, 136.4, 147.4, 160.2.; trans-isomer, δ = 25.5, 27.5, 30.5, 32.7, 47.4, 71.5, 78.8, 119.4, 126.0, 127.5, 128.9, 129.3, 136.4, 147.4, 160.5.

$C_{20}H_{27}NO$ (297.4) Calcd. C 80.76 H 9.15 N 4.71
Found C 80.70 H 9.04 N 4.58

3. 6-Methyl-5-(2-quinolinylmethoxy)-1-heptene (**13**): 1.0 g (7.8 mmol) of 5-hydroxy-6-methyl-1-heptene were allowed to react as described under 2. Chromatography with petroleum ether/ether = 7:3 furnished 2.0 g (95%) of **13** as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.97 (d, J = 6.8 Hz, 3H), 0.99 (d, J = 6.8 Hz, 3H), 1.58 - 1.76 (m, 2H), 1.96 - 2.35 (m, 3H), 3.33 (dt, J = 7.3 and 4.7 Hz, 1H) 4.82 (d, J = 11.3 Hz, 1H), 4.88 (d, J = 11.3 Hz, 1H), 4.93 - 5.08 (m, 2H), 5.80 (ddt, J = 16.9, 10.3, and 6.7 Hz, 1H), 7.52 - 7.58 (m, 1H), 7.67 - 7.76 (m, 2H), 7.81 (d, J = 8.1 Hz, 1H), 8.04 (d, J = 8.3 Hz, 1H), 8.19 (d, J = 8.5 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.9, 18.4, 29.5, 30.1, 30.5, 73.3, 84.6, 114.5, 119.7, 126.1, 127.6, 129.0, 129.5, 136.5, 138.8, 145.5, 160.1.

$C_{18}H_{23}NO$ (269.4) Calcd. C 80.25 H 8.61 N 5.20
Found C 80.33 H 8.70 N 5.21

4. (+)3-Methoxy-17ß-(2-quinolinylmethoxy)-estra-1,3,5(10)-triene (**24**): 1.90 g (6.6 mmol) of (+)3-methoxy-estra-1,3,5(10)-trien-17ß-ol was converted to the quinaldine-ether **24** as described under 2. Chromatography with petroleum ether/ether = 1:1 afforded 2.21 g (78%) of **24** as a colorless solid, m.p. 132.5 - 133.5°C. - UV: ($CHCl_3$) λ_{max} (log ϵ) = 316 (3.62), 303 (3.54), 279 (3.76) nm. - $[\alpha]_D^{20}$ = +18,4 (c = 0.376) $CHCl_3$. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (s, 3H), 1.17 - 1.80 (m, 9H), 1.82 - 1.94 (m, 1H), 2.06 - 2.25 (m, 4H), 2.25 - 2.37 (m, 1H), 2.70 - 2.81 (m, 2H), 3.71 (dd, J = 7.1 and 7.0 Hz, 1H), 3.80 (s,

3H), 4.89 (s, 2H), 6.63 (d, J = 2.7 Hz, 1H), 6.72 (dd, J = 8.6 and 2.8 Hz, 1H), 7.14 (d, J = 8.2 Hz, 1H), 7.50 - 7.57 (m, 1H), 7.70 (d, J = 8.5 Hz, 1H), 7.73 (dd, J = 8.5 and 1.5 Hz, 1H), 7.84 (d, J = 8.1 Hz, 1H), 8.05 (d, J = 8.4 Hz, 1H), 8.20 (d, J = 8.5 Hz, 1H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.9, 23.3, 26.5, 27.3, 28.1, 29.9, 38.0, 38.8, 43.6, 44.1, 50.3, 55.3, 73.5, 89.4, 111.6, 114.0, 119.5, 126.2, 126.4, 127.6, 127.7, 129.0, 129.6, 132.8, 136.6, 138.1, 147.6, 157.6, 160.4.

$C_{29}H_{33}NO_2$ (427.6) Calcd. C 81.46 H 7.78 N 3.28
Found C 81.72 H 7.88 N 3.22

5. 6-Methyl-5-(2-quinolinylmethoxy)-1-heptanol (14): 4.50 mmol of 9-borabicyclo[3.3.3]-nonane (obtained by evaporation of a hexane solution) was dissolved in 10 ml of anhydrous THF. A solution of 0.80 g (3 mmol) of 6-methyl-5-(2-quinolinylmethoxy)-1-heptene (13) in 3 ml of THF was added at room temperature. The reaction was quenched after 1 h by addition of 9 ml of ethanol, 4.5 ml of 6 N aqueous sodium hydroxide solution and 4.5 ml of 30% aqueous hydrogen peroxide. After heating for 1 h to 50°C, the aqueous phase was saturated with solid potassium carbonate. The organic phase was separated and the aqueous phase was extracted twice with 20 ml of ether. The combined organic phases were dried with $MgSO_4$ and concentrated. Chromatography with ether furnished 850 mg (100%) of the alcohol **14** as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (d, J = 6.8 Hz, 3H), 0.90 (d, J = 6.8 Hz, 3H), 1.32 - 1.60 (m, 6H), 1.91 (q, J = 6.7 Hz, 1H), 2.62 (broad s, 1H), 3.18 - 3.23 (m, 1H), 3.57 (t, J = 6.1 Hz, 2H), 4.75 (s, 2H), 7.40 - 7.48 (m, 1H), 7.57 - 7.66 (m, 2H), 7.73 (d, J = 8.1 Hz, 1H), 7.99 (d, J = 8.5 Hz, 1H), 8.09 (d, J = 8.5 Hz, 1H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.2, 18.4, 22.1, 30.1, 30.7, 33.0, 62.7, 73.3, 85.3, 119.9, 126.3, 127.6, 127.7, 128.9, 129.6, 136.7, 147.4, 160.1.

$C_{18}H_{25}NO_2$ (287.4) Calcd. C 75.23 H 8.77 N 4.87
Found C 75.11 H 9.02 N 4.72

6. 1-(t-Butyldimethylsilyloxy)-6-methyl-5-(2-quinolinylmethoxy)-heptane (15): To a suspension of 35 mg (1.5 mmol) of sodium hydride in 10 ml of THF was added at 0°C under argon a solution of 210 mg (0.73 mmol) of 6-methyl-5-(2-quinolinylmethoxy)-1-heptanol (14) in 2 ml of THF. After addition of 130 mg (0.87 mmol) of t-butyl-dimethyl-chlorosilane the mixture was allowed to reach room temperature. 5 ml of water was added, and the aqueous phase was extracted three times with 10 ml of ether. The combined organic phases were washed with 10 ml of brine, dried with $MgSO_4$ and concentrated. Chromatography using petroleum ether/ether = 4:1 furnished 235 mg (80%) of **15** as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = -0.01 (s, 6H), 0.85 (s, 9H), 0.92 (d, J = 6.8 Hz, 3H), 0.94 (d, J = 6.8 Hz, 3H), 1.46 - 1.54 (m, 6H), 1.90 - 2.00 (m, 1H), 3.18 - 3.28 (m, 1H), 3.56 (t, J = 6.2 Hz, 2H), 4.79 (s, 2H), 7.44 - 7.50 (m, 1H), 7.62 - 7.69 (m, 1H), 7.67 (d, J = 8.5 Hz, 1H), 7.76 (d, J = 8.1 Hz, 1H), 8.00 (d, J = 8.4 Hz, 1H), 8.13 (d, J = 8.5 Hz, 1H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = -5.4, 17.9, 18.1, 18.2, 21.9, 25.8, 29.9, 30.4, 33.0, 63.0, 73.2, 85.1, 119.6, 125.9, 127.4, 127.5, 128.8, 129.3, 136.3, 147.3, 160.1.

$C_{24}H_{39}NO_2Si$ (401.7) Calcd. C 71.77 H 9.79 N 3.49
Found C 71.98 H 9.83 N 3.43

7. 5-Methyl-4-(2-quinolinylmethoxy)-hexanal (16): To a solution of 1.5 g (5.6 mmol) of 6-methyl-5-(2-quinolinylmethoxy)-1-heptene (13) in 40 ml of dichloromethane was introduced at -78°C a stream of ozone until TLC indicated complete consumption of the olefin. Excess of ozone was purged with a stream of nitrogen. 1.46 g (5.6 mmol) of triphenylphosphine were added and the reaction mixture was allowed to reach room temperature. The solvents were removed i.vac. and the residue was chromatographed using petroleum ether/ether = 3:7

to give 1.41 g (93%) of the aldehyde **16** as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (d, J = 6.8 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H), 1.74 - 2.05 (m, 3H), 2.42 - 2.62 (m, 2H), 3.22 - 3.31 (m, 1H), 4.71 (d, J = 13.0 Hz, 1H), 4.80 (d, J = 13.0 Hz, 1H), 7.45 - 7.51 (m, 1H), 7.58 (d, J = 8.5 Hz, 1H), 7.62 - 7.70 (m, 1H), 7.76 (d, J = 8.1 Hz, 1H), 8.00 (d, J = 8.5 Hz, 1H), 8.13 (d, J = 8.5 Hz, 1H), 9.73 (p, J = 1.6 Hz, 1H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.4, 18.7, 22.7, 30.4, 40.5, 73.4, 84.3, 119.8, 126.3, 127.6, 127.7, 129.1, 129.6, 136.7, 147.5, 159.5, 202.2.

$C_{17}H_{21}NO_2$ (271.4) Calcd. C 75.25 H 7.80 N 5.16
Found C 75.23 H 7.70 N 5.16

8. Methyl 5-methyl-4-(2-quinolinylmethoxy)-hexanoate (**17**): A solution of 0.50 g (1.85 mmol) of 5-methyl-4-(2-quinolinylmethoxy)-hexanal (**16**) in 5 ml of methanol and 0.5 ml of water was buffered by addition of 3.3 g (0.04 mol) of sodium hydrogen-carbonate. 4.5 ml of a 2 M solution of bromine in methanol/water (9:1) was added dropwise. After stirring for 15 min, the excess of bromine was decolorized by addition of sodium thiosulfate. 100 ml of water were added, and the mixture was extracted three times with 20 ml each of ether. The combined organic phases were dried with $MgSO_4$ and concentrated. Chromatography with petroleum ether/ether = 1:1 furnished 0.50 g (90%) of the ester **17** as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (d, J = 6.9 Hz, 3H), 0.92 (d, J = 6.9 Hz, 3H), 1.70 - 2.02 (m, 3H), 2.30 - 2.50 (m, 2H), 3.23 - 3.29 (m, 1H), 3.56 (s, 3H), 4.71 (d, J = 13.1 Hz, 1H), 4.79 (d, J = 13.1 Hz, 1H), 7.43 - 7.49 (m, 1H), 7.60 (d, J = 8.5 Hz, 1H), 7.62 - 7.68 (m, 1H), 7.74 (d, J = 8.1 Hz, 1H), 7.98 (d, J = 8.3 Hz, 1H), 8.12 (d, J = 8.5 Hz, 1H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.4, 18.5, 25.3, 30.3, 30.4, 51.4, 73.2, 84.1, 119.6, 126.1. 127.6, 128.9, 129.4, 136.5, 147.5, 159.6, 174.2.

$C_{18}H_{23}NO_3$ (301.4) Calcd. C 71.73 H 7.69 N 4.65
Found C 71.48 H 7.69 N 4.67

9. 1,1,5-Trimethyl-4-(2-quinolinylmethoxy)-1-hexanol (**18**): To a solution of 150 mg (0.5 mmol) of methyl 5-methyl-4-(2-quinolinylmethoxy)-hexanoate (**17**) in 10 ml of ether was added at 0°C 0.4 ml of a 2.72 M solution of methyl magnesium bromide. After stirring for 30 min 10 ml of saturated aqueous NH_4Cl solution was added. The phases were separated and the aqueous phase was extracted twice with 10 ml of ether. The combined organic phases were dried with $MgSO_4$ and concentrated. Chromatography with ether furnished 120 mg (80%) of **18** as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.90 (d, J = 6.8 Hz, 3H), 0.94 (d, J = 6.8 Hz, 3H), 1.17 (s, 3H), 1.18 (s, 3H), 1.43 - 1.68 (m, 3H), 1.81 (broad s, 1H), 1.89 - 2.00 (m, 2H), 3.20 - 3.28 (m, 1H), 4.78 (s, 2H), 7.43 - 7.50 (m, 1H), 7.61 (d, J = 8.4 Hz, 1H), 7.62 - 7.69 (m, 1H), 7.76 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.5 Hz, 1H), 8.13 (d, J = 8.5 Hz, 1H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.2, 18.7, 24.7, 29.3, 29.7, 30.4, 30.7, 39.5, 70.8, 73.3, 85.7, 119.9, 126.3, 127.6, 127.7, 129.0, 129.6, 136.7, 147.5, 159.9.

$C_{19}H_{27}NO_2$ (301.4) Calcd. C 75.71 H 9.03 N 4.65
Found C 75.45 H 8.87 N 4.50

10. 5-Methyl-4-(2-quinolinylmethoxy)-1-hexanol (**19**): To a suspension of 21.8 mg (0.57 mmol) of lithium aluminiumhydride in 5 ml of THF was added a solution of 115 mg (0.38 mmol) of methyl 5-methyl-4-(2-quinolinylmethoxy)-hexanoate (**17**) in 2 ml of THF at 0°C. After stirring for 30 min at room temperature, 2 ml of water and subsequently 30 ml of 2 N aqueous sodium hydroxide solution were added. The mixture was stirred for 20 min and filtered through celite. The celite was washed throroughly with ether and the combined organic phases were dried with $MgSO_4$ and concentrated. Chromatography with ether fur-

nished 100 mg (96%) of the alcohol **19** as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, J = 6.8 Hz, 3H), 0.90 (d, J = 6.8 Hz, 3H), 1.50 - 1.72 (m, 4H), 1.94 (quint, J = 6.8 Hz, 1H), 2.45 (broad s, 1H), 2.82 - 3.00 (m, 1H), 3.20 - 3.27 (m, 1H), 3.61 (broad s, 1H), 4.73 (d, J = 13.1 Hz, 1H), 4.78 (d, J = 13.1 Hz, 1H), 7.41 - 7.46 (m, 1H), 7.57 (d, J = 8.5 Hz, 1H), 7.60 - 7.66 (m, 1H), 7.73 (d, J = 8.1 Hz, 1H), 8.00 (d, J = 8.5 Hz, 1H), 8.08 (d, J = 8.5 Hz, 1H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.7, 18.4, 26.2, 28.8, 30.3, 62.6, 72.9, 85.1, 119.7, 126.1, 127.4, 127.5, 128.7, 129.4, 136.5, 147.2, 159.5.

$C_{17}H_{23}NO_2$ (273.4) Calcd. C 74.69 H 8.48 N 5.12
Found C 74.23 H 8.22 N 5.17

11. 4-t-Butyl-cyclohexanone (**12**): A solution of 240 mg (0.80 mmol) of the quinaldine ether **11** in 100 ml of anhydrous acetonitrile was flushed with argon for 30 min. It was then irradiated with a medium pressure mercury lamp in an immersion reactor through a single layer of duran glass. The progress of the reaction was monitored by TLC. After 2.5 h the solution was concentrated and the residue was chromatographed with chloroform to yield 107.5 mg (85%) of **12** as a colorless solid. **12** was identified by comparison of m.p. and the NMR spectra with a commercial sample.

12. 2-Methyl-7-hydroxy-3-heptanone (**20**): A solution of 146 mg (0.5 mmol) of 6-methyl-5-(2-quinolinylmethoxy)-1-heptanol (**14**) in 65 ml of acetonitrile was irradiated for 3 h as described under 11. Chromatography with petroleum ether/ether = 3:7 gave 48 mg (65%) of the hydroxyketone **20** [14] as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.03 (d, J = 7.0 Hz, 6H), 1.43 - 1.65 (m, 4H), 2.04 (broad s, 1H), 2.44 (t, J = 7.0 Hz, 2H), 2.55 (hept. J = 7.0 Hz, 1H), 3.56 (t, J = 6.2 Hz, 2H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.2, 19.7, 32.2, 39.8, 40.8, 62.3, 215.0

13. 7-(t-Butyldimethylsilyloxy)-2-methyl-3-heptanone (**21**): A solution of 227 mg (0.56 mmol) of 1-(t-butyldimethylsilyloxy)-6-methyl-5-(2-quinolinylmethoxy)-heptane (**15**) in 70 ml of acetonitrile was irradiated for 2.5 h as described under 11. Chromatography with petroleum ether/ether (4:1) gave 90.6 mg (62%) of the ketone **21** as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 (t, J = 3.0 Hz, 6H), 0.85 (s, 9H), 1.04 (d, J = 6.9 Hz, 6H), 1.40 - 1.62 (m, 4H), 2.43 (t, J = 7.2 Hz, 2H), 2.56 (hept., J = 7.0 Hz, 1H), 3.57 (t, J = 6.2 Hz, 2H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = -5.2, 18.3, 18.4, 20.4, 26.0, 32.4, 40.2, 40.8, 63.0, 214.8.

$C_{14}H_{30}O_2Si$ (258.5) Calcd. C 65.06 H 11.70
Found C 65.09 H 11.67

14. Methyl 5-methyl-4-oxo-hexanoate (**22**): A solution of 192 mg (0.63 mmol) of methyl 5-methyl-4-(2-quinolinylmethoxy)-hexanoate (**17**) in 80 ml of acetonitrile was irradiated for 4 h as described under 11. Chromatography with petroleum ether/ether = 2:1 furnished 61.5 mg (61%) of the ketoester **22** [15] as a colorless oil. - UV (CH_3CN) λ_{max} (log ϵ) = 341 (1.04), 326 (1.17), 269 (1.98), 245 (2.29) nm. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.06 (d, J = 7.0 Hz, 6H), 2.52 (t, J = 6.6 Hz, 2H), 2.58 (hept., J = 7.0 Hz, 1H), 2.71 (t, J = 6.6 Hz, 2H), 3.60 (s, 3H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.1, 27.7, 34.7, 40.7, 51.6, 173.3, 212.5.

15. 2-Methyl-6-hydroxy-3-hexanone (**23**): A solution of 144 mg of 5-methyl-4-(2-quinolinylmethoxy)-1-hexanone (**19**) in 65 ml of acetonitrile was irradiated for 2 h as described under 11. Chromatography with petroleum ether/ether = 1:4 furnished 42 mg (61%) of the hydroxyketone **23** [16] as a colorless oil. - ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.04 (d, J = 7.0

Hz, 6H), 1.68 - 1.86 (m, 2H), 2.20 (borad s, 1H), 2.54 (t, J = 7.0 Hz, 2H), 2.57 (hept., J = 6.9 Hz, 1H), 3.58 (t, J = 6.1 Hz, 2H). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.3, 26.6, 37.1, 41.0, 62.3, 215.4.

16. 3-Methoxy-estra-1,3,5(10)-trien-17-one (**25**, **26**): 201 mg (0.47 mmol) of (+)-3-methoxy-17β-(2-quinolinylmethoxy)-estra-1,3,5(10)-triene (**24**) in 120 ml of anhydrous acetonitrile were irradiated as described under 11. using a Heraeus TQ 180 lamp. After 4 h irradiation TLC indicated >90% conversion. The solvents were removed i.vac. and the crude product was chromatographed over 30 g of silica gel using petroleum ether/ethyl acetate = 6:1 to give 16 mg (12%) of the 13-α-compound **26** and 96 mg (72%) of the 13-β-compound **25**. Further elution with petroleum ether/ethyl acetate = 4:1 furnished 10 mg (5%) of the starting compound **24**.

25: M.p. 166°C, from methanol, cf. ref. [17]: 167.5 - 169°C. - $[\alpha]_D^{20}$: + 157° (c = 0,814, dioxane), ref. [18] $[\alpha]_D$: +159,8° (c = 1,227, dioxane). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8, 21.5, 25.1, 25.9, 29.6, 31.5, 35.8, 38.3, 43.9, 48.0, 50.4, 55.1, 111.5, 113.8, 126.3, 132.0, 137.7, 157.6, 228.8.

26: M.p. 128 - 129°C, from methanol, cf. ref. [19]: 129 - 130°C. - $[\alpha]_D^{20}$: -35° (c = 0,09, dioxane), ref. [19] $[\alpha]_D^{21}$: -43° (c = 0,5, dioxane). - ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.0, 25.1, 28.3, 28.4, 30.3, 33.1, 33.5, 41.4, 41.5, 49.2, 50.2, 55.2, 111.5, 113.7, 126.9, 132.0, 138.0, 157.5, 228.8.

References and Notes

1. Suzuki, K.; Sulikowski, A. G.; Friesen, R. W.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1990**, *112*, 8895.
2. a) Tolstikov, G. A.; Miftakhov, M. S.; Vostrikov, N. S.; Komissarova, N. G.; Adler, M. E.; Kuznetsov, O. M. *Zh. Org. Khim.* **1988**, *24*, 224; b) Mahrwald, R.; Theil, F.; Schick, H.; Palme, H.-J.; Nowack, H.; Weber, G.; Schwarz, S. *Synthesis* **1987**, 1012; c) Baker, R.; Rao, V. B.; Ravenscroft, P. D.; Swain, C. J. *Synthesis* **1983**, 572; d) Olah, G. A.; Ho, T.-L. *Synthesis* **1976**, 609; e) Jung, M. E. *J. Org. Chem.* **1976**, *41*, 1479; f) Curran, D.P.; Yu, H. *Synthesis* **1992**, 123.
3. Olah, G. A.; Gupta, B. G. B.; Fung, A. P. *Synthesis* **1980**, 897.
4. Pillai, V. N. R. *Synthesis* **1980**, 1.
5. a) Huyser, E. S.; Neckers, D. C. *J. Org. Chem.* **1964**, *29*, 276; b) Binkley, R. W.; Hehemann, D. G.; Binkley, W. W. *J. Org. Chem.* **1978**, *43*, 2573.
6. Stermitz, F. R.; Wei, C. C.; O'Donnell, C. M. *J. Am. Chem. Soc.* **1970**, *92*, 2745.
7. Usypchuk, L.; Leblanc, Y. *J. Org. Chem.* **1990**, *55*, 5344.
8. Mathes, W.; Schüly, H. *Angew. Chem.* **1963**, *75*, 235.
9. Brown, R. R.; Hammick, D. L.; Thewlis, B. H. *J. Chem. Soc (London)* **1951**, 1145.
10. Prathapan, S.; Loft, S.; Agosta, W. C. *J. Am. Chem. Soc.* **1990**, *112*, 3940.
11. Formosinho, S. J.; Arnaut, L. G. *Adv. Photochem.* **1991**, *16*, 67.
12. Crabbé, P.; Cruz, A.; Iriarte, J. *Can. J. Chem.* **1968**, *46*, 349.
13. Knight, S. B.; Wallick, R. H.; Balch, C. *J. Am. Chem. Soc.* **1955**, *77*, 2577.

14. Nikishin, G. I.; Kapustina, N. I.; Lubuzh, E. D.; Spektor, S. S.; Kaplan, E. P. *Izv. Akad. Nauk. SSSR, Ser. Khim.* **1980**, *11*, 2607; *Chem. Abstr.* **1981**, *94*, 191617e.
15. Kunkel, E.; Reichelt, I.; Reißig, H.-U. *Liebigs Ann. Chem.* **1984**, 802.
16. Fuji, K.; Node, M.; Usami, Y. *Chem. Lett.* **1986**, 961.
17. Cohen, A.; Cook, J. W.; Hewett, C. L. *J. Chem. Soc. (London)* **1935**, 445.
18. Goldberg, M. W.; Studer, S. *Helv. chim. Acta* **1942**, *25*, 1553.
19. Butenandt, A.; Wolff, A.; Karlson, P. *Ber. dtsch. Chem. Ges.* **1941**, *74*, 1308.