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1,1-Dianisyl-2,2,2-trichloroethyl Ethers - A New Protection for the Hydroxyl Group

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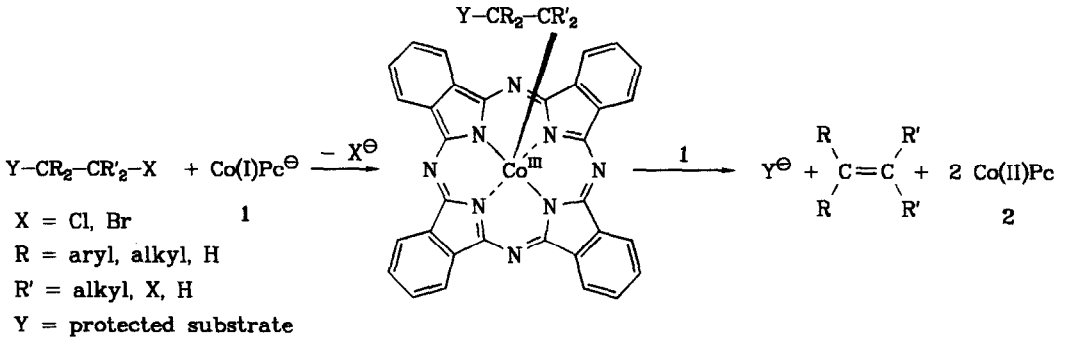
Abstract: ß-Haloalkyl protecting groups are well established. However, there was a lack of an appropriate protection, especially for carboxyl and vicinal hydroxyl groups. This problem was now solved by design of the 1,1-dianisyl-2,2,2-trichloroethyl group (DATE). The alkylation of model alcohols with the DATE moiety is described. The resulting ß-haloalkyl ethers proved to be remarkable stable against acids and bases. Deblocking of the model alcohols is achieved in high yields.

INTRODUCTION

In 1971 a new technique for the removal of ß-haloalkyl protecting groups was introduced (Scheme.1). Their cleavage is achieved by means of reductive fragmentation based on supernucleophile lithium cobalt(I)phthalocyanine (LiCo(I)Pc **1**)[1,2]. The advantage of this protecting group technique is „orthogonality"[3] to customary techniques and the very mild and neutral condition of fragmentation.



Scheme 1. Reductive fragmentation of ß-haloalkyl protected substrates

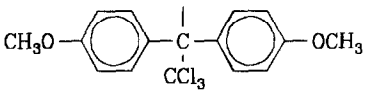
Several ß-haloalkyl groups were developed for the protection of a variety of functional groups. Thus the 2,2,2-trichloro-tert.-butyloxycarbonyl group (TCBOC)[2,4,5,6], the 2,2,2-trichloro-tert.-butyl group (TCB)[7,8]

and the 2,2,2-trichloroethyl group (TCE)[9,10] are well established. The TCBOC group is accepted as a reliable protecting group for the amino moiety of amino acids and for the exocyclic amino groups of nucleosides. Also hydroxyl groups are protectable by TCBOC, but migration between vicinal OH groups is observed. TCE is used for the protection of carboxyl and phosphate groups. A disadvantage of TCE esters is the lack of „orthogonality". TCE esters are sensitive towards bases due to possible deprotonation of the α-CH of the protecting moiety. The preparation of TCB esters of organic acids is achieved in low yields only. However, as a phosphate protecting group in the synthesis of oligonucleotides TCB proved to be successful. Attempts to synthesize TCB ethers failed. The only reaction observed during alkylation was elimination of the TCB moiety.

Within this set of „orthogonal" protective groups, there is still a lack of a ß-halogenated derivative, which esters are easy to prepare, sufficiently stable and rapidly cleavable by **1**. Furthermore, in ribonucleotide syntheses and sugar chemistry there is still the need of selective protection of hydroxyl groups. The ß-haloalkyl moiety should not migrate between vicinal hydroxyl groups and should be sufficiently stable towards acids and bases. The blocked carbohydrate moiety should be obtained in high yield and cleavage of the protecting group should be possible in quantitative yield.

RESULTS

All the above mentioned requirements for the selective protection of hydroxyl groups resulted in the conception of the ß-haloalkyl group DATE (1,1-**dia**nisyl-2,2,2-**t**rich**l**oro**e**thyl)[11].

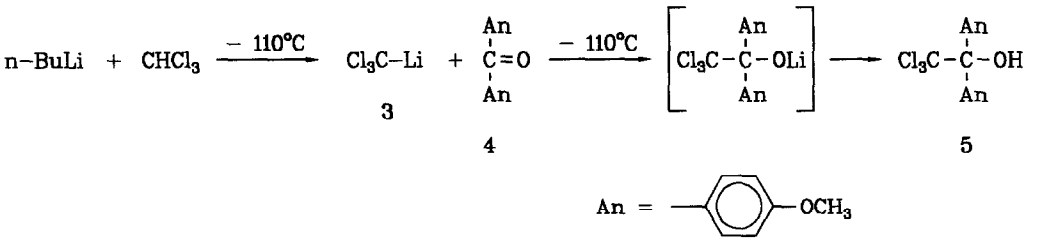


The DATE group

The lack of α-hydrogens should give DATE the stability towards bases. The stability in the presence of acids could be expected because of the electron withdrawing trichloromethyl group. The +M-effect of the anisyl moiety should diminish this -I-effect of the trichloromethyl group, so that alkylative esterification and etherification by suitable DATE derivatives should be possible. Moreover, this ß-haloalkylated derivative could easily cleaved by supernucleophile **1**, as an additional alternative to the well established zinc method.

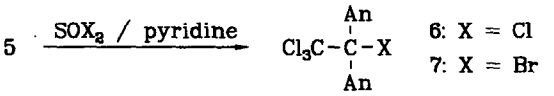
Starting from 1,1-dianisyl-2,2,2-trichloroethanol (DATE-OH **5**) the corresponding halogenides **6**, **7** and DATE p-toluenesulfonate (DATE-OTos **8**) or DATE trifluoromethanesulfonate (DATE-OTf) were studied as alkylating reagents for alcohols.

Due to the analogy of the DATE group towards DDT derivatives there has been great interest in the synthesis of DATE compounds. Until recently, no synthesis of DATE-OH **5** has been found except for the electrochemical oxidation of 1,1-dianisyl-2,2,2-trichloroethane. Depending on experimental conditions yields of just 5-30% have resulted[12]. We have carried out more than 30 experiments to screen any preparative strategy thinkable for preparing the DATE skeleton. Ultimately, only from the reaction of trichloromethyllithium (**3**)[13,14] with 4,4′-dimethoxybenzophenone (**4**) the desired product **5** could be isolated in 60% yields.



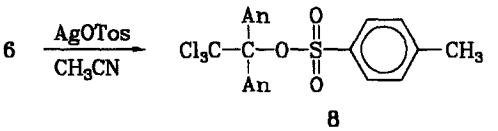
Scheme 2. Synthesis of DATE-OH **5**

The halogenides DATE-Cl **6** and DATE-Br **7** were prepared by treatment of **5** with thionyl chloride and thionyl bromide, respectively.



Scheme 3. Synthesis of DATE halogenides

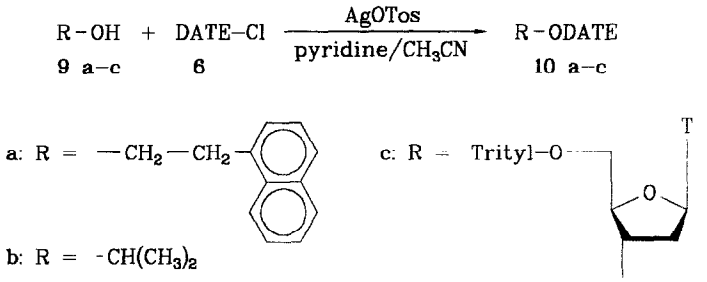
Using 2-propanol as a model alcohol, we found no alkylating potential in DATE-Cl **6** and only weak alkylating power in the case of DATE-Br **7**. In order to improve the alkylating power, we tried to synthesize several other derivatives of DATE. Attempts to prepare the p-toluenesulfonate (DATE-OTos **8**) and the trifluoromethanesulfonate (DATE-OTf) derivatives by the reaction of **5** and the corresponding sulfonic acid chlorides or anhydrides failed. However, **8** could be synthesized by treatment of DATE-Cl **6** with silver p-toluenesulfonate (silver tosylate, AgOTos) (Scheme 4), while the analogous synthesis of DATE-OTf could not be performed successfully. DATE-OTos **8** itself is stable at below temperatures in a moisture free environment.



Scheme 4. Synthesis of DATE-OTos **8**

The fact that DATE-OTos **8** proved to be rather unstable and DATE-OTf not to be isolatable shows that this compounds are highly reactive, but moreover difficult to handle. Therefore **8** was prepared *in situ* and so it is possible to convert alcohols into DATE ethers **10a-c** by a one pot procedure using the desired alcohol, DATE-Cl **6** and silver tosylate. Thereby, the ease of successful alkylation of model alcohols **9a-c** could be demonstrated (Scheme 5).

The DATE ethers **10a-c** are remarkable stable towards acidic and basic conditions, respectively. For example, after 20 hours at ambient temperature the following environments showed no impact on these ethers: conc. hydrochloric acid / methanol / dioxane (1:2:2 v/v/v); dichloroacetic acid / dichloromethane (3:97 v/v); conc. ammonia / dioxane (1:1 v/v).

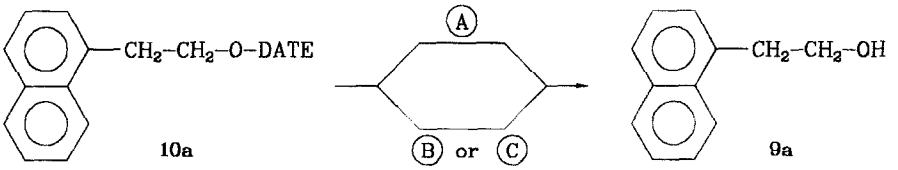


Scheme 5. Alkylation of model alcohols

To achieve the cleavage of model ether **10a** the lithium cobalt(I)phthalocyanine technique was applied (Scheme 6). While the basic fragmentation mechanism took place smoothly a six defold of LiCo(I)Pc **1** was required for quantitative reaction. This is in contrast to previous experiences with ß-trichloroalkyl protecting groups (two equivalents are required for quantitative fragmentation) and is due to further dehalogenations of the primary builded vinylhalogenide 1,1-dianisyl-2,2-dichloroethene.

Here we demonstrate the first example of using LiCo(I)Pc **1** as a deblocking reagent for aliphatic alcohols protected as O-ß-haloalkyl ethers. The cleavage of ß-bromoethylphenyl ether[1] could be already performed, but here the relatively strong acidity of phenol eases the fragmentation significantly.

Compound **10a** could also be cleaved classically by the application of zinc using either 80% acetic acid or zinc bromide as coreagents, however resulting yields are slightly lower than achieved by the LiCo(I)Pc method.



(A) 6 x Li[Co(I)Pc] / MeOH
(B) Zn(act.) / $ZnBr_2$
(C) Zn(act.) / 80% acetic acid

Scheme 6. Cleavage of the DATE protective group

Summarizing these results, it is obvious that the DATE group features unambigious blocking and deblocking characteristics while being stable to most any relevant reaction conditions. The DATE group cannot only be a powerful element in an arsenal of protection techniques, but it is also the ideal candidate for regioselective OH-protections, e.g. in chemical RNA syntheses. The application of the DATE group as a 2'-OH protection in chemical RNA syntheses is now under investigation.

EXPERIMENTAL

The ^1H NMR and ^{13}C NMR spectra were obtained by a Bruker AM 360 with TMS as the internal standard with the ^1H NMR at 360.13 MHz, and the ^{13}C NMR at 90.556 MHz. Mass spectra were obtained on a

Varian MAT CH-5 (70 eV) instrument. Melting points are uncorrected and were determined with a Büchi SMP-20 apparatus. Elemental analyses were performed by the Microchemical laboratory of the Institute of Organic Chemistry, Technical University, Munich. Flash chromatography[15] was done on a column of Silica gel 60, 15-40 μm (Merck). Thin layer chromatography was performed on Silica gel 60 F_{254} plates (Merck). If necessary, the solvents were purified and dried by the usual methods. Moisture and oxygen sensitive compounds are handled under an atmosphere of dry and oxygen free nitrogen.

1,1-Dianisyl-2,2,2-trichloroethanol (DATE-OH 5)

In a 500 mL three necked flask 7.3 mL (90mmol) $CHCl_3$, 100 mL THF, 25 mL diethyl ether and 25 mL petroleum benzine (bp.: 30-40° C) are mixed and cooled to -115° C by means of a pentane/liquid nitrogen bath. 36 mL of a 2.5 M solution of n-butyllithium in hexane (90 mmol) are added in a manner that the temperature does not rise above -105° C. The resulting suspension is stirred for 15 min. Within 17 min a precooled solution of 15.0 g (61.9 mmol) 4,4'-dimethoxybenzophenone (**4**) in 125 mL $CHCl_3$ is dropped into this suspension at a temperature ≤ - 105° C. After 15 min under vigorous stirring at a temperature between -110° and -90° C the reaction mixture is hydrolyzed with 15 mL acetic acid in 15 mL $CHCl_3$. The solution is washed with water and the organic layer is dried over $MgSO_4$. The brown oil remaining after evaporation is purified by flash chromatography (hexane / ethyl acetate; 85 : 15 v/v). The product is recrystallized from $CHCl_3$ / hexane. Yield: 13.2 g (59 %). Mp.: 88° C. R_f = 0.32 (hexane / ethyl acetate; 85 : 15 v/v). *^1H NMR ($CDCl_3$)* δ: 3.45 (s, 1H, OH; D_2O-exchange); 3.78 (s, 6H, OCH_3); 6.82 (d, 4H, m-H_{anisyl}, $J_{m\text{-}H,o\text{-}H}$ = 9.0 Hz); 7.61 (d, 4H, o-H_{anisyl}, $J_{o\text{-}H,\ m\text{-}H}$ = 9.0 Hz) ppm. *^{13}C NMR ($CDCl_3$)* δ: 55.2 (OCH_3); 87.1 (DATE-C); 106.8 (CCl_3); 112.6 (m-C_{anisyl}); 130.7 (o-C_{anisyl}); 133.0 (ipso-C_{anisyl}); 159.2 (p-C_{anisyl}) ppm. *MS (CI-Mode): m/z* 361/363/365 ($M^{\oplus}$ + 1; 1/1/0.5%); 343/345/347/349 ($M^{\oplus}$ + 1 - H_2O; 20/20/7/1%); 309/310/311/312/313 ($M^{\oplus}$ + 1 - HOCl; 10/2/7/2/1%); 243 ($M^{\oplus}$ + 1 - $CHCl_3$; 100%); 135 ($CH_3OPhCO^{\oplus}$; 3%). Anal. calcd. for $C_{16}H_{15}Cl_3O_3$: C, 53.14; H, 4.18. Found: C, 53.07; H, 4.13.

1,1-Dianisyl-1,2,2,2-tetrachloroethane (DATE-Cl 6)

A solution of 10 g (27.7 mmol) DATE-OH **5** in 30 mL benzene and 3.3 mL (41.1 mmol) pyridine is cooled down to 0° C. A mixture of 3 mL (41.1 mmol) thionyl chloride and 10 mL benzene is added slowly and stirred for 30 min. After evaporation the residue is dissolved in Et_2O and the precipitated pyridinium hydrochloride separated by filtration. After evaporation the product is recrystallized from ethyl acetate/hexane. Yield: 9.02 g (86 %). Mp.: 89°C. R_f = 0.56 (hexane/ethyl acetate; 85:15 v/v). *^1H NMR ($CDCl_3$)* δ: 3.80 (s, 6H, OCH_3); 6.80 (d, 4H, m-H_{anisyl}, $J_{m\text{-}H,o\text{-}H}$ = 9.1 Hz); 7.62 (d, 4H, o-H_{anisyl}, $J_{o\text{-}H,m\text{-}H}$ = 9.1 Hz) ppm. *^{13}C NMR ($CDCl_3$)* δ: 55.2 (OCH_3); 87.6 (DATE-C); 104.3 (CCl_3); 112.2 (m-C_{anisyl}); 132.3 (ipso-C_{anisyl}); 132.5 (o-C_{anisyl}); 159.4 (p-C_{anisyl}) ppm. *MS (EI-Mode): m/z* 343/345/347 ($M^{\oplus}$-Cl, 1/1/0.3 %); 308/310/312 ($M^{\oplus}$-Cl_2, 100/67/11 %); 273/275 ($M^{\oplus}$-Cl_3, 48/15 %); 238 ($M^{\oplus}$-Cl_4, 94 %); 119 ($CH_3OPhC^{\oplus}$, 27 %). Anal. calcd. for $C_{16}H_{14}Cl_4O_2$: C, 50.56; H, 3.71. Found: C, 50.60; H, 3.79.

1,1-Dianisyl-2,2,2-trichloroethyl bromide (DATE-Br 7)

DATE-Br **7** is synthesized in analogy to DATE-Cl **6** by the reaction of DATE-OH **5** and thionyl bromide. Yield: 5.60 g (48 %). Mp.: 94°C. R_f = 0.56 (hexane/ethyl acetate; 85:15 v/v). *^1H NMR ($CDCl_3$) δ:* 3.80 (s, 6H, OCH_3); 6.78 (d, 4H, m-H_{anisyl}, $J_{m\text{-}H,o\text{-}H}$=9.0 Hz); 7.68 (d, 4H, o-H_{anisyl}, $J_{o\text{-}H,m\text{-}H}$=9.0 Hz) ppm. *$^{13}C$ NMR ($CDCl_3$) δ:* 55.2 (OCH_3); 85.2 (DATE-C); 104.2 (CCl_3); 112.1 (m-C_{anisyl}); 133.0 (ipso-C_{anisyl});

133.5 (o-C_{anisyl}); 159.3 (p-C_{anisyl}) ppm. Anal. calcd. for $C_{16}H_{14}BrCl_3O_2$: C, 45.27; H, 3.32. Found: C, 45.15; H, 3.34.

1,1-Dianisyl-2,2,2-trichloroethyl p-toluenesulfonate (DATE-OTos 8)

To a solution of 2 g (5.3 mmol) DATE-Cl **6** in 40 mL acetonitrile 3 g (10.7 mmol) silver tosylate are added. After 30 min the precipitate is filtered off and the resulting clear solution is concentrated by evaporation. DATE-OTos **8** crystallizes at -20° C. Yield: 1.64 g (60 %). *^1H NMR ($CDCl_3$) δ:* 2.38 (s, 3H, CH_3); 3.82 (s, 6H, OCH_3); 6.77 (d, 4H, m-H_{anisyl}, $J_{m\text{-}H,o\text{-}H}$=9.1 Hz); 7.14 (d, 2H, m-H_{tolyl}, $J_{m\text{-}H,o\text{-}H}$=8.0 Hz); 7.46 (d, 2H, o-H_{tolyl}, $J_{o\text{-}H,m\text{-}H}$=7.9 Hz); 7.63 (d, 4H, o-H_{anisyl}, $J_{o\text{-}H,m\text{-}H}$=9.1 Hz) ppm. *$^{13}C$ NMR ($CDCl_3$)* δ: 21.6 (CH_3); 55.3 (OCH_3); 103.8 (CCl_3); 112.1 (m-C_{anisyl}); 127.4 (m-C_{tolyl}); 127.7 (ipso-C_{anisyl}); 129.1 (o-C_{tolyl}); 133.6 (o-C_{anisyl}); 135.7 (p-C_{tolyl}); 144.0 (ipso-C_{tolyl}); 160.4 (p-C_{anisyl}) ppm.

General procedure for the protection of alcohols as DATE ethers

To a solution of 3 g (7.9 mmol) DATE-Cl **6** and 6 mmol of the desired alcohol in 10 mL acetonitrile 1 mL (12.4 mmol) pyridine is added. This mixture is treated with 2.2 g (7.9 mmol) silver tosylate and stirred for 12-18 h at ambient temperature (in case of secondary alcohols it might be necessary to heat and/or to increase the ratio of **6** to secondary alcohol). The solvent is removed by evaporation, the residue dissolved in Et_2O and filtered. After evaporation of the solvent the product is purified by flash chromatography and recrystallized or distilled.

1,1-Dianisyl-2,2,2-trichloroethyl-2-(1-naphthyl)ethyl ether (10a)

The eluant for flash chromatography is hexane/ethyl acetate 85:15, v/v. **10a** is recrystallized from $CHCl_3$/ hexane. Yield: 3.75 g (92 %). Mp.: 114°C. R_f= 0.73 (hexane/ethyl acetate; 75:25 v/v). *^1H NMR ($CDCl_3$) δ:* 3.45 (tr, 2H, CH_2, $J_{CH2,OCH2}$=7.2 Hz); 3.81 (s, 6H, OCH_3); 3.97 (tr, 2H, OCH_2, $J_{OCH2,CH2}$=7.3 Hz); 6.77 (d, 4H, m-H_{anisyl}, $J_{m\text{-}H,o\text{-}H}$=9.0 Hz); 6.80-7.46 (m, 4H, $H_{naphtyl}$); 7.49 (d, 4H, o-H_{anisyl}, $J_{o\text{-}H,m\text{-}H}$=9.0 Hz); 7.73-7.92 (m, 3H, $H_{naphtyl}$) ppm. *^{13}C NMR ($CDCl_3$)* δ: 34.2 (CH_2); 55.1 (OCH_3); 67.5 (OCH_2); 92.3 (DATE-C); 105.5 (CCl_3); 112.1 (m-C_{anisyl}); 123.8 (C-$8_{naphtyl}$); 125.4, 125.4 (C-$3_{naphtyl}$, C-$6_{naphtyl}$); 125.8 (C-$4_{naphtyl}$); 127.0 (C-$2_{naphtyl}$); 128.6 (C-$5_{naphtyl}$); 131.9 (ipso-C_{anisyl}); 132.0 (o-C_{anisyl}); 132.2 (C-$4a_{naphtyl}$); 133.7 (C-$8a_{naphtyl}$); 134.6 (ipso-$C_{naphtyl}$); 159.1 (p-C_{anisyl}) ppm. Anal. calcd. for $C_{28}H_{25}Cl_3O_3$: C, 65.19; H, 4.88. Found: C, 65.11; H, 5.02.

1,1-Dianisyl-2,2,2-trichloroethyl-(2-propyl) ether (10b)

In this case 2-propanol is used in a ten fold excess and the mixture stirred at ambient temperature. The eluant for flash chromatography is hexane/ethyl acetate 9:1, v/v. Yield: 1.9 g (60 %). Bp.: 210-235°C/ 0.01 torr. R_f= 0.56 (hexane /ethyl acetate; 9:1 v/v). *^1H NMR ($CDCl_3$)* δ: 1.21 (d, 6H, CH_3, $J_{CH3,CH}$=6.0 Hz); 3.84 (s, 6H, OCH_3); 4.10 (sept, 1H, CH, $J_{CH,CH3}$ = 6.0 Hz); 6.87 (d, 4H, m-H_{anisyl}, $J_{m\text{-}H,o\text{-}H}$ = 9.0 Hz); 7.69 (d, 4H, o-H_{anisyl}, $J_{o\text{-}H,m\text{-}H}$ = 9.0 Hz) ppm. *^{13}C NMR ($CDCl_3$)* δ: 24.3 (CH_3); 55.0 (OCH_3); 69.8 (CH); 92.7 (DATE-C); 106.3 (CCl_3); 111.8 (m-C_{anisyl}); 132.2 (ipso-C_{anisyl}); 132.8 (o-C_{anisyl}); 159.2 (p-C_{anisyl}) ppm. *MS (EI-Mode): m/z* 343/345/347 ($M^{\oplus}$-OiPr; 0.5/0.5/0.1%); 332/334 ($M^{\oplus}$-Cl_2; 0.8/0.2%); 285 ($M^{\oplus}$-CCl_3, 25%); 243 (($CH_3OPh)_2C{=}O^{\oplus}$-H; 89%); 135 ($CH_3OPhCO^{\oplus}$; 100%); 107 ($CH_3OPh^{\oplus}$; 10%). Anal. calcd. for $C_{19}H_{21}Cl_3O_3$: C, 56.52; H, 5.24. Found: C, 56.58; H 5.26.

***3'-O-(1,1-Dianisyl-2,2,2-trichloroethyl)-5'-O-tritylthymidine* (10c)**

The ratio of alcohol **9c** : DATE-Cl **6** is 1:3. The reaction mixture is refluxed for 18 h. The eluant for flash chromatography is CH_2Cl_2/triethylamine 99:1, v/v. After chromatography triethylamine is removed by azeotrope evaporation with toluene. The resulting residue is recrystallized from CH_2Cl_2/hexane. Yield: 1.64 g (75 % relative to **9c**). Mp.: 125 - 135 °C. R_f = 0.78 (CH_2Cl_2/MeOH; 99:1 v/v). *^1H NMR ($CDCl_3$)* δ: 1.37 (s, 1H, 5-CH_3); 2.07 (m, 1H, H-2'A); 2.56 (dd, 1H, H-2'B, $J_{2'B,1'}$=5.2 Hz, J_{gem}=13.4 Hz); 3.01 (d, 1H, H-5'A, J_{gem}=10.5 Hz); 3.24 (d, 1H, H-5'B, J_{gem}=10.5 Hz); 3.77, 3.80 (s, s, 6H, OCH_3); 4.36 (s, 1H, H-4'); 4.71 (d, 1H, H-3', $J_{3',2'A}$=5.4 Hz); 6.59 (dd, 1H, H-1', $J_{1',2'A}$=9.3 Hz, $J_{1',2'B}$=5.2 Hz); 6.76 (d, 2H, m-H_{anisyl}, $J_{m\text{-}H,o\text{-}H}$=8.8 Hz); 6.81 (d, 2H, m-H_{anisyl}, $J_{m\text{-}H,o\text{-}H}$=8.8 Hz); 7.24 (br s, 15H, H_{trityl}); 7.51 (d, 4H, o-H_{anisyl}, $J_{o\text{-}H,m\text{-}H}$=8.8 Hz); 7.53 (s, 1H, H-6); 9.21 (br s, 1H, NH; D_2O-exchange) ppm. *^{13}C NMR ($CDCl_3$)* δ: 11.6 (5-CH_3); 40.5 (C-2'); 55.1, 55.2 (OCH_3); 64.0 (C-5'); 78.4 (C-3'); 84.8, 85.7 (C-1',C-4'); 87.3 (trityl-C); 93.3 (DATE-C); 105.0 (CCl_3); 111.1 (C-5); 112.3, 112.4 (m-C_{anisyl}); 127.3, 127.9, 128.4 (C_{phenyl}); 131.0, 131.4 (ipso-C_{anisyl}); 132.4, 132.7 (o-C_{anisyl}); 135.6 (C-6); 143.1 (ipso-C_{phenyl}); 159.3, 159.4 (p-C_{anisyl}); 150.4, 163.9 (C-2, C-4) ppm. Anal. calcd. for $C_{45}H_{41}Cl_3N_2O_7$: C, 65.26; H, 4.99; N, 3.38. Found: C, 64.78; H, 5.20; N, 3.21.

General method for the deblocking of DATE protected alcohols

- ***with zinc***

The DATE protected alcohol **10** (20 mmol) is dissolved a) in 20 mL MeOH/Et_2O (1:1, v/v) and stirred for 20 h with 1 g zinc (act.) and 1 g zinc bromide or b) in 30 mL 80% acetic acid/dioxane (1:2, v/v) and stirred for 20 h with 1 g zinc (act.). After filtration the reaction mixture is diluted with $CHCl_3$, washed with water until neutrality, dried over $MgSO_4$ and evaporated. Flash chromatography provides the pure alcohol **9** in yields about 70-80%.

- ***with Li[Co(I)Pc] (1)***[16, 17]

The DATE protected alcohol **10** (2 mmol) is dissolved in 100 - 150 mL methanol or acetonitrile (or a mixture of these solvents). After degasing of this solution 11.7 g (12.6 mmol) **1** are added and the green suspension stirred for 17 h at ambient temperature. To oxidize the excess of **1** the reaction flask is opened and vigorously stirred for 1 h (TLC analysis shows quantitative fragmentation of the starting material). The precipitated violet Co(II)Pc **2** is filtered off. After evaporation the residue is dissolved in Et_2O and washed with diluted acetic acid and saturated aqueous $NaHCO_3$. The organic fractions are dried over $MgSO_4$ and the solvent is removed with a rotary evaporator. After flash chromatography the alcohol **9** is obtained in 80-90% yield.

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