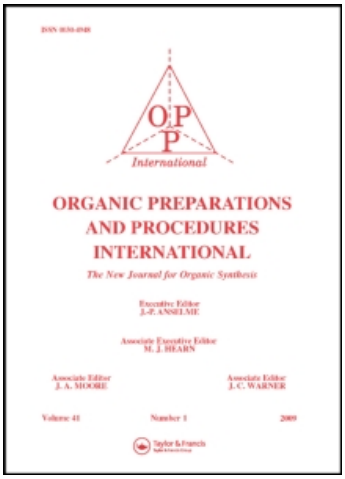

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V. Böhmer[a]; D. Rathay[a]; H. Kämmerer[a]
[a] Organisch-chemisches Institut der Johannes Gutenberg-Universität, Mainz, Germany

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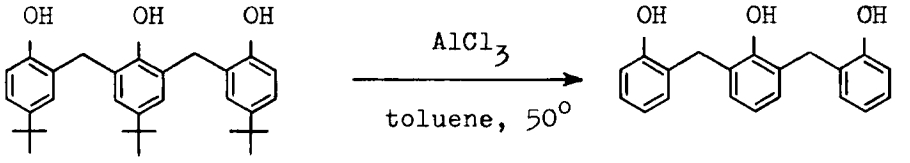
THE t-BUTYL GROUP AS A POSSIBLE PROTECTIVE GROUP IN THE SYNTHESIS OF OLIGO[HYDROXY-1,3-PHENYLENE]METHYLENES

V. Böhmer+, D. Rathay and H. Kämmerer

Organisch-chemisches Institut
der Johannes Gutenberg-Universität
Mainz, GERMANY

The stepwise synthesis of well defined oligo(hydroxy-1,3-phenylene)methylene compounds by condensation of hydroxy- or chloromethylated phenols with other phenols often requires the protection of reactive ortho- or para-positions. As pointed out previously,[1] halogen atoms may serve as excellent protective groups, which are normally completely stable during synthesis and readily cleaved under mild conditions. Nevertheless it would be advantageous to have a second protective group which could be independent of the first one.



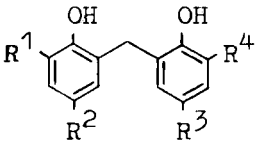
It has been reported by several authors,[2] that the t-butyl group may be eliminated from phenolic compounds by treatment with Lewis acids (e.g. $AlCl_3$), especially in the presence of aromatic compounds (such as benzene) which may serve as acceptor.[3] After we had started our investigations, it was re-

ported that for some dihydroxydiphenylmethanes certain conditions allow the elimination of t-butyl groups.[4,5]

Our experiments were most successful with $AlCl_3$ as catalyst in toluene. However, benzene or xylene gave similar results, while no reaction was observed in toluene in the presence of anisole. Though anisole should be a more reactive acceptor for the t-butyl group, apparently its complexation with the catalyst seems to predominate. Milder catalysts such as $TiCl_4$ and $AlCl_3$ in the presence of nitromethane in toluene were also tried. In the former case, no reaction occurred while in the latter many by-products could be observed by thin layer chromatography.

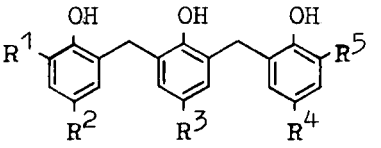
Preliminary experiments with t-butylcresols led to the use of 1.25 mole $AlCl_3$ per mole of t-butylcresol. Optimum yields of debutylated cresol (determined by gas chromatography) were obtained under these conditions in toluene at 90° after 60 min. After 30 min., 12 % of phenol could be detected beside 81 % of o-bromophenol from o-bromo-p-(t-butyl)-phenol, while after 120 min. refluxing, no trace of the desired p-nitrophenol could be observed from 2-t-butyl-4-nitrophenol.

With the di- and trinuclear compounds I and II, we were mainly interested in the elimination of t-butyl groups from para-positions because oligomers containing free ortho-positions often can be obtained without protective groups using a para substituted phenol in excess during the condensation reaction. Besides it was found,[5,6] that t-butyl groups are transferred more easily from the ortho-position, suggesting that the following conditions are also applicable to eliminate ortho-t-butyl groups. Using the molar ratio of 1.25 : 1



I

	R^1	R^2	R^3	R^4
a	H	t-Bu	t-Bu	H
b	CH_3	t-Bu	t-Bu	CH_3
c	Cl	t-Bu	t-Bu	Cl
d	Br	CH_3	t-Bu	H
e	H	H	H	H
f	CH_3	H	H	CH_3
g	Cl	H	H	Cl
h	Br	CH_3	H	H
i	H	CH_3	H	H



II

	R^1	R^2	R^3	R^4	R^5
a	H	t-Bu	t-Bu	t-Bu	H
b	CH_3	CH_3	t-Bu	CH_3	CH_3
c	Br	CH_3	t-Bu	CH_3	H
d	Br	CH_3	CH_3	t-Bu	H
e	H	H	H	H	H
f	CH_3	CH_3	H	CH_3	CH_3
g	Br	CH_3	H	CH_3	H
h	Br	CH_3	CH_3	H	H
i	H	CH_3	H	CH_3	H
j	H	CH_3	CH_3	H	H

between catalyst and hydroxy groups the dinuclear compounds Ia-d could be debutylated quantitatively within 1 - 3 hrs. even at 50°. Pure products Ie-g were obtained in 65 - 90 % yield and no difference in the reactivity of Ia and Ib[5,6] could be observed under these conditions. No limitation of the reaction time is necessary in the case of Ia and Ib, because Ie and If are stable under these conditions as has been shown by thin layer chromatography. On the other hand Id forms Ii instead of Ih as main product after 8 hrs.

The "higher reactivity" of the dinuclear compounds I (50°) in comparison with t-butylcresols (90°) is certainly caused by the fact that the effective concentration of the catalyst

is larger in the former case. If we assume, that each hydroxy group reacts with one molecule of $AlCl_3$, the ratio of the remaining $AlCl_3$ is 2 : 1. However, in 2,2'-dihydroxydiphenylmethanes also the two hydroxy groups may react with one molecule $AlCl_3$ forming chelate structures; thus, the excess of $AlCl_3$ is even higher. This means that for all compounds, the best conditions must be established by a series of experiments.

This was confirmed by the trinuclear compounds II. Under the same conditions as compounds I ($AlCl_3$ / OH = 1.25 / 1, 50°, 1 - 3 hrs.), IIa and IIb could be debutylated to yield 70 - 80 % of pure IIe and IIf which seem to be stable under these conditions. However, IIi and IIj were obtained as main products from IIc and IId even after 1 hr., indicating that the bromine atom in ortho-position is eliminated much faster from these compounds than from Id. On the other hand, IIg and IIh could be obtained within 5 - 7 min.

Attempted debutylation of linear tetranuclear compounds was not successful up to present because the purification was complicated by products resulting from side reactions in these cases. However, a cyclic tetranuclear compound bearing two t-butyl groups in para-position could be successfully debutylated which probably reflects the greater stability of cyclic compounds.[7] During this synthesis bromine was used in earlier stages to protect one ortho-position. The results in the present paper suggest, that the reverse order will be possible too, i. e. elimination of the t-butyl group in an earlier step and cleavage of the halogen atom in a later step of the synthesis. This clearly enlarges the possibilities.

EXPERIMENTAL

The starting compounds were synthesized according to the literature.[5,7-9,13] IIb was prepared as described below.

2,6-Bis-(2-hydroxy-3,5-dimethyl-benzyl)-4-t-butylphenol (IIb)

A mixture of 21.0 g. (0.1 mole) of 2,6-bis-hydroxymethyl-4-t-butylphenol[8] and 122 g. (1 mole) of 2,4-dimethylphenol was heated with stirring to 90°; then 30 ml. of conc. HCl were added. After 3 hrs., additional 10 ml. of conc. HCl were added and the temperature was raised to 100° and heating continued for a further 2 hrs. Excess dimethylphenol was removed by steam distillation, and the residue was recrystallized from acetone/water or ethanol/water, to yield 26.6 g. (63 %) of white crystals, mp. 181-183°.

Anal. Calcd for $C_{28}H_{34}O_3$: C, 80.35; H, 8.19
Found: C, 80.31; H, 8.20

^{1}H NMR (DMSO-d_6): δ = 1.19 (9 H, s, $C(CH_3)_3$), 2.17 (12 H, s, CH_3), 3.89 (4 H, s, CH_2) and 6.18-7.09 ppm (6 H, m, aromatic protons).

General Procedure for the Transbutylation Reaction. A solution of the t-butyl substituted di- or trinuclear compound in an appropriate amount of dry toluene (ca. 10 ml. per g.) was added with stirring to a mixture of $AlCl_3$ (1.25 mole per mole of OH-groups) and toluene (ca. 5 ml. per g. of $AlCl_3$) kept at 50°. The reaction was stopped by the addition of 10 % hydrochloric acid (20 ml. per g. of $AlCl_3$), the organic layer was separated, washed with water, dried over Na_2SO_4 and evaporated. The crude product was further purified as described for each compound. The reaction time was established in each case by a series of experiments which were followed by thin layer

chromatography and best results were obtained under these conditions with the times indicated for the individual reactions.

2,2'-Methylenebisphenol (Ie) from 2,2'-methylenebis(4-t-butylphenol) (Ia):[9] Reaction time 3 hrs., recrystallization from methanol/water, 86 %, mp. 118°, lit.[5,10] mp. 118°, 119°.

6,6'-Methylenebis(o-cresol) (If) from 6,6'-methylenebis(4-t-butyl-o-cresol) (Ib):[5] Reaction time 1 hr., recrystallization from glacial acetic acid/water, 80 %, mp. 126°, lit.[11] mp. 126-127°.

2,2'-Methylenebis(6-chlorophenol) (Ig) from 2,2'-methylenebis(6-chloro-4-t-butylphenol) (Ic):[9] Reaction time 2 hrs., recrystallization from methanol/water, 63 %, mp. 137°, lit.[12] mp. 136°.

^{1}H NMR (DMSO-d_6): δ = 4.02 (2 H, s, CH_2) and 6.73-7.32 ppm (6 H, m, aromatic protons).

2-Bromo-6-(2-hydroxybenzyl)-p-cresol (Ih) from 2-bromo-6-(2-hydroxy-5-t-butyl-benzyl)-p-cresol (Id):[13] Reaction time 30 min., recrystallization from petroleum ether (70-110°), 89 %, mp. 140°.

Anal. Calcd for $C_{14}H_{13}BrO_2$: C, 57.34; H, 4.43; Br, 27.26
Found: C, 57.26; H, 4.20; Br, 27.28

^{1}H NMR (DMSO-d_6): δ = 2.15 (3 H, s, CH_3), 3.91 (2 H, s, CH_2) and 6.88-7.27 ppm (6 H, m, aromatic protons);
MS: m/e = 294/292 (72 %, M^+ for $^{81}Br/^{79}Br$), 201/199 (91 %, $M^+ - C_6H_4OH$).

2,6-Di(2-hydroxybenzyl)phenol (IIe) from 2,6-di(2-hydroxy-5-t-butyl-benzyl)-4-t-butylphenol (IIa):[9] Reaction time 1 hr., recrystallization from petroleum ether (70-110°), 79 %,

mp. 158°, lit.[14] mp. 158-159°.

2,6-Di(2-hydroxy-3,5-dimethyl-benzyl)phenol (IIf) from IIb: Reaction time 3 hrs., recrystallization from methanol/acetone/water, 69 %, mp. 165°.

Anal. Calcd for $C_{24}H_{26}O_3$: C, 78.50; H, 7.18
Found: C, 78.20; H, 7.08

The same compound was synthesized in a similar way using the chlorine atom to protect the para-position.[15]

2-(3-Bromo-2-hydroxy-5-methyl-benzyl)-6-(2-hydroxy-5-methyl-benzyl)-phenol (IIg) from 2-(3-bromo-2-hydroxy-5-methyl-benzyl)-6-(2-hydroxy-5-methyl-benzyl)-4-t-butylphenol (IIc):[13] Reaction time 7 min., purification by column chromatography on silica gel, eluent acetone/petroleum ether (70-110°) 4 : 1, 48 %, mp. 191°.

Anal. Calcd for $C_{22}H_{21}BrO_3$: C, 63.93; H, 5.12
Found: C, 63.84; H, 4.99

^{1}H NMR (acetone-d_6): δ = 2.17 (6 H, s, CH_3), 3.91 (4 H, s, CH_2) and 6.71-7.18 ppm (8 H, m, aromatic protons);
MS: m/e = 414/412 (56 %, M^+ for $^{81}Br/^{79}Br$), 306/304 (41 %, $M^+ - CH_3C_6H_4OH$).

2-(3-Bromo-2-hydroxy-5-methyl-benzyl)-6-(2-hydroxy-benzyl)-p-cresol (IIh) from 2-(3-bromo-2-hydroxy-5-methyl-benzyl)-6-(2-hydroxy-5-t-butyl-benzyl)-p-cresol (IId):[7] Reaction time 5 min., 77 % of a slightly contaminated product which was purified like IIg, mp. 188°C.

Anal. Calcd for $C_{22}H_{21}BrO_3$: C, 63.93; H, 5.12
Found: C, 64.05; H, 5.20

^{1}H NMR (acetone-d_6): δ = 2.14 (6 H, s, CH_3), 3.90 (4 H, s, CH_2) and 6.74-7.21 ppm (8 H, m, aromatic protons);

MS: m/e = 414/412 (40 %, M^+ for $^{81}Br/^{79}Br$), 320/318 (16 %, $M^+ - C_6H_5OH$).

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3. Since t-butylphenols behave like other alkylphenols during stepwise condensation, where halogen atoms can be used as protective groups in the usual way,[9] the t-butyl group might serve as an independent protective group if its elimination could also be achieved from oligomeric compounds without destroying the molecular structure. This was not necessarily to be expected because a benzyl cation shows a stability similar to that of a t-butyl cation. Indeed it was reported that the benzyl substituent may be transferred to aromatics in the presence of Friedel-Crafts catalysts [O. Tsuge and M. Tashiro, Bull. Chem. Soc. Japan, 38, 185 (1965), 40, 115, 125 (1967)], a reaction which would lead to the destruction or isomerization of the oligo(hydroxy-1,3-phenylene)methylene molecules.
4. However, in similar cases either no elimination was observed or the desired product could be obtained only in traces among large amounts of unidentified by-products.[6]
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