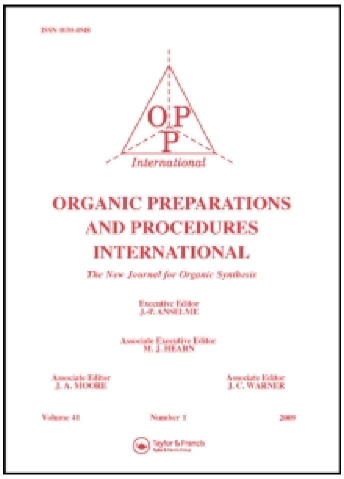

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THE PREPARATION OF DIHYDROXYDIPHENYLMETHANES CONTAINING NITRO GROUPS. II. UNSYMMETRICALLY SUBSTITUTED COMPOUNDS

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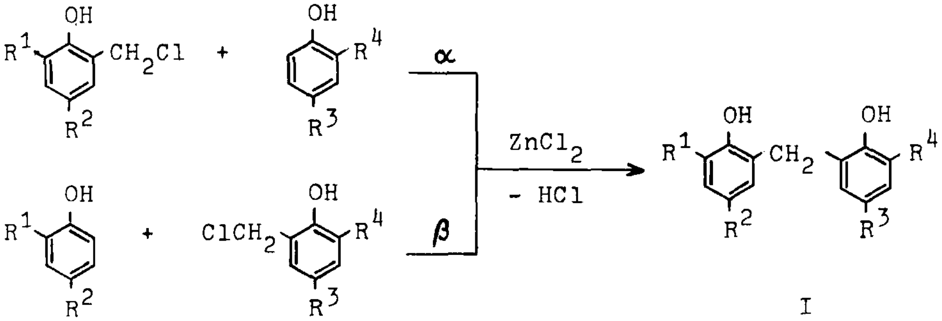
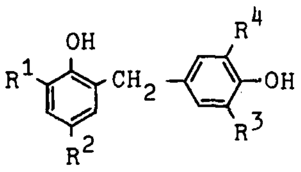
Recently we reported that dihydroxydiphenylmethanes substituted with nitro groups can readily be prepared by condensation of nitrophenols with formaldehyde.[1] However, in this way only symmetrically substituted products ($R^1 = R^4$, $R^2 = R^3$) can be obtained. Furthermore, a reactive ortho- or para-position should not remain in the condensation product.



I

	a	b	c	d	e	f	g
R^1 =	NO_2	NO_2	CH_3	H	NO_2	NO_2	NO_2
R^2 =	CH_3	CH_3	NO_2	NO_2	NO_2	NO_2	NO_2
R^3 =	NO_2	NO_2	NO_2	NO_2	CH_3	NO_2	NO_2
R^4 =	H	CH_3	H	H	NO_2	CH_3	H

Unsymmetrically substituted dihydroxydiphenylmethane compounds can be synthesized by condensation of chloromethylated nitrophenols with other nitrophenols. We have already reported two examples for this reaction (Ia, Ib),[2] which appears to be generally applicable. We have prepared both 2,2'-dihydroxydiphenylmethane derivatives (Ia-g) and 2,4'-dihydroxydiphenylmethane derivatives (IIa-d) in this way. Since the necessary chloromethylated nitrophenols are readily available,[3-5] this seems to be a very simple and convenient method.



II

		a	b	c	d
R^1	=	NO_2	H	CH_3	NO_2
R^2	=	CH_3	NO_2	NO_2	NO_2
R^3	=	NO_2	NO_2	NO_2	NO_2
R^4	=	CH_3	CH_3	CH_3	CH_3

As shown in the scheme (previous page), there are generally two pathways to prepare a certain compound (α,β). We have carried both of them out in the cases of Ia, Ib, IIa and IIb. Identical products were always obtained as shown by IR spectroscopy, thin layer chromatography, melting point and mixture melting point. These reactions can be considered as a structural proof but no particular advantage of one route (α) over the other (β) could be observed in these cases. However, for the preparation of the compounds with a dinitrophenol unit (Ie-g, IId), we only tried the condensation of 2-hydroxy-3,5-dinitrobenzyl chloride[4] with the corresponding nitrophenol (α). Considering the low reactivity of 2,4-dinitrophenol, the inverse reaction does not seem to be favorable in such a case.

The condensation reaction requires temperatures of 100-120°

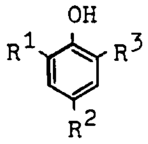
if mononitrohydroxybenzyl chlorides are condensed and 130-160° if 2-hydroxy-3,5-dinitrobenzyl chloride is used. Ordinarily it is necessary to use $ZnCl_2$ as catalyst, but with higher temperatures the condensation may be possible without a catalyst. This was shown in the preparation of Ia.[2] If the resulting dihydroxydiphenylmethane derivate still contains a free, reactive *ortho*- or *para*-position (Ia, Ic, Id, Ig, IIb), the nitrophenol must be used in a ten- to twenty-fold excess to avoid the formation of higher molecular weight condensation products. In the other cases, the stoichiometric amount of nitrophenol may be used, but still a three- to five-fold amount is preferable to obtain a homogeneous reaction mixture which increases the yield. The excess of nitrophenol can easily be removed by steam distillation (2-nitro-*p*-cresol, 6-nitro-*o*-cresol) or by dissolving in hot water (*p*-nitrophenol, 4-nitro-*o*-cresol).

Symmetrically substituted dihydroxydiphenylmethane derivatives can be prepared also by condensation of chloromethylated nitrophenols with the corresponding nitrophenols. Compared with the direct condensation with formaldehyde,[1] this is only favorable in the synthesis of Id[6] which can be prepared best in this way. On the other hand, tri- and tetranuclear compounds can be obtained by the same reaction.[2,7]

EXPERIMENTAL

Melting points were determined with a Mettler FP1. The values reported are the average of three values, differing by not more than ± 0,3°. Uncorrected values were determined by visual observation. Diacetates were prepared a) by refluxing the dihydroxydiphenylmethanes with an excess of acetic anhydride or b) by reaction with acetic anhydride in pyridine at room temperature. All products synthesized were chromatographically (TLC) pure.

General Procedure for the Condensation Reaction. The chloromethylated nitrophenol (III) and an excess of the nitrophenol (IV) were heated under nitrogen atmosphere while stirring. $ZnCl_2$ (about 0.2 g. per mmole of III) was added to the homogeneous molten mixture. The reaction was stopped when the HCl-evolution had subsided. The exact reaction data are given together with the further description of each compound. The excess of nitrophenol was removed by steam distillation (in the case of IVc and IVd) or by dissolving in boiling water (about 100 cm^3 per gram of IVa or IVb).



III or IV

		a	b	c	d	e
	R^1	H	CH_3	NO_2	NO_2	NO_2
III	R^2	NO_2	NO_2	CH_3	CH_2Cl	NO_2
	R^3	CH_2Cl	CH_2Cl	CH_2Cl	CH_3	CH_2Cl
	R^1	H	CH_3	NO_2	NO_2	
IV	R^2	NO_2	NO_2	CH_3	H	
	R^3	H	H	H	CH_3	

To remove the zinc compounds,the residue was dissolved in aqueous NaOH and reprecipitated by dropwise addition of the filtered alkaline solution to dilute aqueous HCl. The crude product was further purified as described for each compound.

2-(2-Hydroxy-5-nitro-benzyl)-6-nitro-p-cresol (Ia) by condensation of 0.02 mole IIIa with 0.2 mole IVc (4-6 hr. at 100-110°, 68%) or 0.02 mole IIIc with 0.3 mole IVa (8 hr. at 120-140° without $ZnCl_2$, 84%). Recrystallization from acetone or from glacial acetic acid/water yields a yellow, microcrystalline powder, mp. 204.1°, lit.[2] mp. 201-203°.

2-(2-Hydroxy-3-methyl-5-nitro-benzyl)-6-nitro-p-cresol (Ib) by condensation of 0.01 mole IIIb with 0.03 mole IVc (3 hr. at 100-120°, 55%) or 3.3 mmole IIIc with 3.6 mmole IVb (3 hr. at 115-120°, 71%). Recrystallization from ethanol yields small, yellow needles, mp. 195-196°, lit.[2] mp. 193-194°.

2-(2-Hydroxy-5-nitro-benzyl)-4-nitro-o-cresol (Ic) by condensation of 0.01 mole IIIb with 0.15 mole IVa (2 hr. at 120°). Recrystallization from glacial acetic acid/water yields 67% of white crystals, mp. 253-255°.

Anal. Calcd. for $C_{14}H_{12}N_2O_6$ C, 55.27; H, 3.98; N, 9.21
Found C, 55.02; H, 4.01; N, 8.95

Diacetate of Ic yields small, white needles from ethanol, mp. 123.6°, after resolidification mp. 150.4°.

Anal. Calcd. for $C_{18}H_{16}N_2O_8$ C, 55.67; H, 4.15; N, 7.21
Found C, 55.97; H, 4.29; N, 6.94

2,2'-Methylenebis(4-nitrophenol) (Id) by condensation of 0.02 mole IIIa with 0.4 mole IVa (2 hr. at 120°). Recrystallization from glacial acetic acid/water yields 53% of pale yellow needles, mp. 269-271°, lit.[6] mp. 268°.

2-(2-Hydroxy-3,5-dinitro-benzyl)-6-nitro-p-cresol (Ie) by condensation of 0.01 mole IIIe with 0.03 mole IVc (4 hr. at 130-140° and 5 hr. at 150-160°). Recrystallization from glacial acetic acid and finally from glacial acetic acid/water yields 27% of dark yellow needles, mp. 188-194°.

Anal. Calcd. for $C_{14}H_{11}N_3O_8$
C, 48.15; H, 3.17; N, 12.03; O, 36.65
Found C, 47.96; H, 3.31; N, 12.32; O, 36.55

Diacetate of Ie yields yellow crystals from acetone/ethanol, mp. 170.6°.

Anal. Calcd. for $C_{18}H_{15}N_3O_{10}$

C, 49.89; H, 3.49; N, 9.70; O, 36.92; CH_3CO, 19.87

Found C, 50.19; H, 3.59; N, 9.40; O, 36.70; CH_3CO, 20.08

2-(2-Hydroxy-3,5-dinitro-benzyl)-4-nitro-o-cresol (If) by condensation of 0.01 mole IIIe with 0.05 mole IVb (4 hr. at 130-140° and 5 hr. at 140-150°). To remove impurities the crude product is extracted several times by small amounts of boiling chloroform. Recrystallization from glacial acetic acid yields 34% of pale yellow crystals, mp. 247,6°.

Anal. Calcd. for $C_{14}H_{11}N_3O_8$ C, 48.15; H, 3.17; N, 12.03

Found C, 48.27; H, 3.21; N, 11.82

Diacetate of If yields nearly white needles from ethanol, mp. 163.8°.

Anal. Calcd. for $C_{18}H_{15}N_3O_{10}$ C, 49.89; H, 3.49; N, 9.70

Found C, 50.17; H, 3.60; N, 9.61

2-(2-Hydroxy-3,5-dinitro-benzyl)-4-nitrophenol (Ig) by condensation of 0.05 mole IIIe with 0.5 mole IVa (7 hr. at 120-130°). Recrystallization from glacial acetic acid/water, using charcoal during the first times, finally yields 44% of grey-yellow crystals, mp. 202-204°.

Anal. Calcd. for $C_{13}H_9N_3O_8$

C, 46.58; H, 2.71; N, 12.54; O, 38.17

Found C, 46.27; H, 2.74; N, 12.72; O, 37.96

Diacetate of Ig yields pale yellow crystals from ethanol/petroleum ether (70-100°), mp. 104°.

Anal. Calcd. for $C_{17}H_{13}N_3O_{10}$

C, 48.70; H, 3.13; N, 10.10; CH_3CO, 20.53

Found C, 48.51; H, 3.06; N, 10.10; CH_3CO, 20.42

4-(2-Hydroxy-5-methyl-3-nitro-benzyl)-6-nitro-*o*-cresol (IIa) by condensation of 0.01 mole IIIc with 0.03 mole IVd (5 hr. at 100-120°, 66%) or 0.01 mole IIId with 0.03 mole IVc (3 hr. at 90-100° and 2 hr. at 100-110°, 85%). Recrystallization from glacial acetic acid/water yields yellow needles or larger, orange crystals, mp. 169.0°.

Anal. Calcd. for $C_{15}H_{14}N_2O_6$ C, 56.60; H, 4.43; N, 8.80
Found C, 56.38; H, 4.41; N, 8.76

Diacetate of IIa yields small, yellow crystals from ethanol/petroleum ether (70-100°), mp. 149.5°.

Anal. Calcd. for $C_{19}H_{18}N_2O_8$
C, 56.72; H, 4.51; N, 6.96; O, 31.81
Found C, 57.03; H, 4.36; N, 6.91; O, 31.70

4-(2-Hydroxy-5-nitro-benzyl)-6-nitro-*o*-cresol (IIb) by condensation of 0.01 mole IIIa with 0.15 mole IVd (5 hr. at 110°, 83%) or 0.01 mole IIId with 0.15 mole IVa (6 hr. at 120°, 74%). Recrystallization from glacial acetic acid and from methanol/water or ethanol/water yields a yellow, microcrystalline product, mp. 203-206°.

Anal. Calcd. for $C_{14}H_{12}N_2O_6$ C, 55.27; H, 3.98; N, 9.21
Found C, 55.40; H, 3.87; N, 9.09

Diacetate of IIb yields small, white crystals from ethanol, mp. 111.1°.

Anal. Calcd. for $C_{18}H_{16}N_2O_8$ C, 55.67; H, 4.15; N, 7.21
Found C, 55.57; H, 4.33; N, 7.21

4-(2-Hydroxy-3-methyl-5-nitro-benzyl)-6-nitro-*o*-cresol (IIc) by condensation of 0.01 mole IIId with 0.03 mole IVb (7 hr. at 120°). Recrystallization from glacial acetic acid yields 87% of yellow needles, mp. 235,1°.

<u>Anal</u>. Calcd. for $C_{15}H_{14}N_2O_6$ C, 56.60; H, 4.43; N, 8.80
Found C, 56.57; H, 4.33; N, 8.59

Diacetate of IIc yields small, white crystals from ethanol, mp. 172.5°.

<u>Anal</u>. Calcd. for $C_{19}H_{18}N_2O_8$ C, 56.72; H, 4.51; N, 6.96
Found C, 56.94; H, 4.70; N, 6.99

<u>4-(2-Hydroxy-3,5-dinitro-benzyl)-6-nitro-o-cresol</u> (IId) by condensation of 0.01 mole IIIe with 0.05 mole IVd (10 hr. at 160°). Recrystallization from glacial acetic acid yields 37% of dark yellow crystals, mp. 213-215°. A purer product is obtained by column chromatography (silica gel, chloroform); bright yellow crystals from glacial acetic acid/water, mp. 221.3°.

<u>Anal</u>. Calcd. for $C_{14}H_{11}N_3O_8$ C, 48.15; H, 3.17; N, 12.03
Found C, 47.92; H, 3.32; N, 11.84

Diacetate of IId yields white crystals from ethanol, mp. 156.4°.

<u>Anal</u>. Calcd. for $C_{18}H_{15}N_3O_{10}$ C, 49.89; H, 3.49; N, 9.70
Found C, 50.13; H, 3.61; N, 9.52

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REFERENCES

1. W. Lotz and V. Böhmer, Org. Prep. and Proced. Int., <u>6</u>, 123 (1974)
2. H. Kämmerer and V. Böhmer, Makromol. Chem., <u>135</u>, 97 (1970).
3. C. A. Buehler, F. K. Kirchner and G. F. Deebel, Org. Syn. Coll. Vol., <u>3</u>, 468 (1967).
4. Ger. Pat., 1,247,326 (1967); CA <u>68</u> P 77960z (1968).
5. V. Böhmer and J. Deveaux, Org. Prep. and Proced. Int., <u>4</u>, 283 (1972).
6. F. D. Chattaway and R. M. Goepp, J. Chem. Soc., <u>1933</u>, 699.
7. V. Böhmer, J. Deveaux and H. Kämmerer, unpublished results.

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