DINITRO-ISOBUTYLPHENOL AND DINITRO-ISOAMYLPHENOL[1]

By G. G. S. Dutton, T. I. Briggs,[2] and E. Merler

ABSTRACT

An unequivocal synthesis of ortho- and para-isobutyl and isoamyl phenols by the method of Klages is described. The resulting phenols were nitrated and characterized as their amine salts. The nitrophenols were prepared as part of a program for testing potential herbicides.

INTRODUCTION

It has been generally accepted that branching an alkyl side chain in a phenol lowers its phenol coefficient (6, 17). This has also proved to be true in the case of dinitroalkyl phenols as far as their herbicidal activity is concerned, with the exception of the ortho-(*sec*-butyl) isomer (5). In view of this apparent anomaly we desired to extend our previous work on the synthesis of dinitro-*n*-alkyl phenols (8) to isomers containing *sec*-alkyl groups.

Since rearrangements are known to occur when alcohols are condensed with an aromatic nucleus (10) we have preferred to use a modification of the method of Klages (11) whereby the desired alkyl group may be built up by reacting a methoxycarbonyl compound with a Grignard reagent. The resulting alcohol may then be dehydrated, the substituted ethylene hydrogenated, and on replacing the methoxyl group by hydroxyl the required phenol is obtained.

Since the isobutyl and isoamyl compounds were also needed for testing as herbicides the preparation of these phenols by the method of Klages and their subsequent nitration is described in this paper. A later communication will extend the use of this method to the preparation of *sec*-amyl and *sec*-hexyl phenols.

EXPERIMENTAL*

2-Isobutylphenol

(a) *2-Methyl-1-(o-methoxyphenyl)-1-propanol*

A Grignard reagent was prepared in the usual manner in an atmosphere of nitrogen using magnesium (37 gm., 1.5 moles), ether (250 cc.), and isopropyl bromide (196 gm., 1.5 moles) dissolved in ether (350 cc.). The reagent thus formed was treated with 2-methoxybenzaldehyde (102 gm., 0.75 mole) in ether (100 cc.) at 0°C. with vigorous stirring and then refluxed for five hours. The cooled solution was then slowly poured onto cracked ice and ammonium chloride. The ether layer was separated, washed, and dried. A small portion was evaporated and gave a negative test with 2,4-dinitrophenylhydrazine. Removal of the solvent from the main portion and distillation of the residual

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Contribution from the Department of Chemistry, University of British Columbia, Vancouver 8, B.C.
[2] *Present address, C.I.L., Nylon Division, Maitland, Ontario, Canada.*
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oil under vacuum gave 2-methyl-1-(*o*-methoxyphenyl)-1-propanol (98 gm., 73%) as a clear liquid boiling at 96°C. (1 mm.) and having n_D^{19}, 1.5235. Literature (12) b.p. 133°C. (14 mm.) and n_D^{16}, 1.524. Anal. calc. for $C_{11}H_{16}O_2$: OCH_3, 17.21%. Found: OCH_3, 17.30%. *Phenylurethane* m.p. 148°C. (from carbon tetrachloride). Anal. calc. for $C_{17}H_{21}NO_3$: N, 4.68; OCH_3, 10.36%. Found: N, 4.76; OCH_3, 10.30%.

(b) *2-Methyl-1-(o-methoxyphenyl)-1-propene*

2-Methyl-1-(*o*-methoxyphenyl)-1-propanol (5 gm.) was refluxed three hours with 20% sulphuric acid. There was thus obtained 2-methyl-1-(*o*-methoxy phenyl)-1-propene (4 gm., 90%) having b.p. 77°C. (1 mm.) and n_D^{23}, 1.5435. Literature (12) b.p. 109°C. (14 mm.) and n_D^{17}, 1.545. Anal. calc. for $C_{11}H_{14}O$: OCH_3, 19.13%. Found: OCH_3, 17.88, 17.80%. *Nitrosylchloride*, obtained in poor yield, m.p. 129°C. Anal. calc. for $C_{11}H_{14}ClNO_2$: N, 6.61%. Found: N, 7.00%.

(c) *2-Isobutylanisole*

2-Methyl-1-(*o*-methoxyphenyl)-1-propene (21 gm.) was dissolved in 95% ethanol (25 cc.) and Raney nickel catalyst added (about 5 gm.). Hydrogenation was carried out in an Aminco microhydrogenator at 500 p.s.i. and 50°C. yielding 2-isobutylanisole (16 gm., 76%) boiling at 55°C. (0.1 mm.) and having n_D^{25}, 1.5005. Anal. calc. for $C_{11}H_{16}O$: OCH_3 18.89%. Found: OCH_3, 18.40, 18.45%. The *sulphonamide* m.p. 103°C. was prepared by treating the alkylanisole with chlorosulphonic acid and ammonia according to the method of Huntress and Carten (9). Anal. calc. for $C_{17}H_{17}NO_3S$: N, 5.76, OCH_3, 12.75%. Found: N, 5.71; OCH_3, 12.62%.

(d) *2-Isobutylphenol*

2-Isobutylanisole (9 gm.) was treated with pyridine hydrobromide (11.5 gm.) and glacial acetic acid (1.3 cc.) and the whole heated under reflux at 200°C. for five hours (15). The cooled mixture was then poured into water and the organic layer extracted with ether. The ether layer was successively washed with dilute hydrochloric acid, sodium bicarbonate solution, and water. After drying and removal of solvent, fractionation gave a quantitative yield of 2-isobutylphenol b.p. 51°C. (0.01 mm.) and n_D^{24}, 1.5171. Literature (3) b.p. 86°C. (6 mm.). Anal. calc. for $C_{10}H_{14}O$: C, 80.0; H, 9.33%. Found: C, 79.8, 79.7; H, 9.24, 9.24%. *3,5-Dinitrobenzoate* m.p. 84°C. Anal. calc. for $C_{17}H_{16}N_2O_6$: N, 8.13%. Found: N, 8.09%.

4-Isobutylphenol

(a) *2-Methyl-1-(p-methoxyphenyl)-1-propanol*

By means of a Grignard reaction from isopropyl bromide and anisaldehyde there was obtained 2-methyl-1-(*p*-methoxyphenyl)-1-propanol (67%) boiling at 103°C. (1 mm.) and having n_D^{24}, 1.5215. Literature (16) b.p. 157°C. (21 mm.) and n_D^{20}, 1.5210. Anal. calc. for $C_{11}H_{16}O_2$: OCH_3, 17.21%. Found OCH_3, 17.40%. Phenylurethane m.p. 77°C. Literature (16) 82°C. Anal. calc. for $C_{17}H_{21}NO_3$: N, 4.68%. Found: N, 4.58%.

(b) *2-Methyl-1-(p-methoxyphenyl)-1-propene*

The above carbinol was dehydrated with 20% sulphuric acid to give 2-methyl-1-(*p*-methoxyphenyl)-1-propene (71%) boiling at 81°C. (1 mm.) and having n_D^{24}, 1.5470. Literature (4) b.p. 118°C. (15 mm.). Anal. calc. for $C_{11}H_{14}O$: OCH_3, 19.13%. Found: OCH_3, 18.90%. The *nitrosyl chloride*, obtained in very poor yield, melted at 133°C. Anal. calc. for $C_{11}H_{14}ClNO_2$: N, 6.61%. Found: N, 6.53%.

(c) *4-Isobutylanisole*

The ethylene obtained above was hydrogenated as before, yielding 4-isobutylanisole (72%) boiling at 68°C. (1 mm.) and having n_D^{25}, 1.4975. Literature (4) b.p. 123°C. (15 mm.) and n_D^{24}, 1.4980 (19). Anal. calc. for $C_{11}H_{16}O$: OCH_3, 18.89%. Found: OCH_3, 18.95, 18.88%. The *sulphonamide* m.p. 205°C., was obtained in poor yield. Anal. calc. for $C_{11}H_{17}NO_3S$: N, 5.76%. Found: N, 5.65%.

(d) *4-Isobutylphenol*

4-Isobutylanisole was demethylated as before yielding 4-isobutylphenol (75%) boiling at 60°C. (0.01 mm.). On standing the oil solidified and recrystallization gave the pure phenol m.p. 52°C. This phenol was first reported as a solid by Barber and Haslewood (2) who give m.p. 51–52°C. Anal. calc. for $C_{10}H_{14}O$: C, 80.0; H, 9.33%. Found: C, 80.0, 80.1; H, 9.36, 9.30%. *3,5-Dinitrobenzoate* m.p. 131°C. Anal. calc. for $C_{17}H_{16}N_2O_6$: N, 8.13%. Found: N, 8.08%.

2-Isoamylphenol

(a) *3-Methyl-1-(o-methoxyphenyl)-1-butanol*

By means of a Grignard reaction from isobutyl bromide and 2-methoxybenzaldehyde there was obtained the impure alcohol as a tan colored solid. Recrystallization from benzene – petroleum ether (30–60°C.) yielded pure *3-methyl-1-(o-methoxyphenyl)-1-butanol* as a white solid melting at 73°C. (Attempted distillation caused dehydration.) Anal. calc. for $C_{12}H_{18}O_2$: OCH_3, 15.97%. Found: OCH_3, 15.93, 15.95%. *Phenylurethane* m.p. 107°C. Anal. calc. for $C_{18}H_{23}NO_3$: N, 4.47; OCH_3, 9.90%. Found: N, 4.40; OCH_3, 9.90, 9.92%.

(b) *3-Methyl-1-(o-methoxyphenyl)-1-butene*

The above carbinol was dehydrated as before yielding *3-methyl-1-(o-methoxyphenyl)-1-butene* (50%) boiling at 82°C. (1 mm.) and having n_D^{18}, 1.5430. Anal. calc. for $C_{12}H_{16}O$: OCH_3, 17.60%. Found: OCH_3, 17.51, 17.55%. The *nitrosyl chloride*, obtained in good yield, melted at 137°C. Anal. calc. for $C_{12}H_{16}ClNO_2$: N, 5.79; OCH_3, 12.80%. Found: N, 5.98; OCH_3, 12.67, 12.61%.

(c) *2-Isoamylanisole*

The ethylene obtained above was hydrogenated giving a quantitative yield of 2-isoamylanisole b.p. 75°C. (0.5 mm.) and n_D^{18}, 1.4995. Anal. calc. for $C_{12}H_{18}O$: OCH_3, 17.40%. Found: OCH_3, 17.43, 17.37%. *Sulphonamide* m.p. 113°C. Anal. calc. for $C_{12}H_{19}NO_3S$: N, 5.44; OCH_3, 12.06%. Found: N, 5.37; OCH_3, 12.09%.

TABLE I

DINITRO-ISOBUTYL AND ISOAMYL PHENOLS AND THEIR AMINE SALTS*

Dinitrophenol	B.p., °C. (0.1 mm.)	Yield, %	Piperidine salt				Morpholine salt				Cyclohexylamine salts			
			Formula	M.p., °C.	Nitrogen, %		Formula	M.p., °C.	Nitrogen, %		Formula	M.p., °C.	Nitrogen, %	
					Calc.	Found			Calc.	Found			Calc.	Found
4,6-Dinitro-2-isobutyl**	130	66	$C_{15}H_{23}N_3O_5$	187	12.92	12.84	$C_{14}H_{21}N_3O_6$	168	12.84	12.84	$C_{16}H_{25}N_3O_5$	193	12.38	12.39
2,6-Dinitro-4-isobutyl	143	55	$C_{15}H_{23}N_3O_5$	189	12.92	12.95	$C_{14}H_{21}N_3O_6$	164	12.84	12.82	$C_{16}H_{25}N_3O_5$	192	12.38	12.32
4,6-Dinitro-2-isoamyl**	140	57	$C_{16}H_{25}N_3O_5$	167	12.39	12.48	$C_{15}H_{23}N_3O_6$	190	12.32	12.29	$C_{17}H_{27}N_3O_5$	188	11.90	11.89
2,6-Dinitro-4-isoamyl	154	55	$C_{16}H_{25}N_3O_5$	176	12.39	12.47	$C_{15}H_{23}N_3O_6$	169	12.32	12.32	$C_{17}H_{27}N_3O_5$	185	11.90	11.94

*All the salts are yellow, orange, or red.

***Ref.* (13).

(d) *2-Isoamylphenol*

2-Isoamylanisole was demethylated giving a quantitative yield of 2-isoamylphenol b.p. 64°C. (0.01 mm.) and n_D^{24}, 1.5120. Anal. calc. for $C_{11}H_{16}O$: C, 80.5; H, 9.82%. Found: C, 80.2, 80.4; H, 9.70, 9.71%. *3,5-Dinitrobenzoate* m.p. 92°C. Anal. calc. for $C_{18}H_{18}N_2O_6$: N, 7.82%. Found: N, 7.75%.

4-Isoamylphenol

(a) *3-Methyl-1-(p-methoxyphenyl)-1-butanol*

By means of a Grignard reaction from isobutyl bromide and anisaldehyde there was obtained 3-methyl-1-(*p*-methoxyphenyl)-1-butanol in crude form as an oil (60 gm., 68%). Attempted distillation caused obvious dehydration. It was not possible to obtain a phenylurethane.

(b) *3-Methyl-1-(p-methoxyphenyl)-1-butene*

The above carbinol was dehydrated giving *3-methyl-1-(p-methoxyphenyl)-1-butene*, in high yield, boiling at 91°C. (1 mm.) and having n_D^{27}, 1.5390. Anal. calc. for $C_{12}H_{16}O$: OCH_3, 17.60%. Found: OCH_3, 17.43, 17.43%. The *nitrosyl chloride* was obtained in good yield, m.p. 153°C. Anal. calc. for $C_{12}H_{16}ClNO_2$: N, 5.79; OCH_3, 12.80%. Found: N, 5.74; OCH_3, 12.16, 12.08%.

(c) *4-Isoamylanisole*

3-Methyl-1-(*p*-methoxyphenyl)-1-butene (75 gm.) was hydrogenated in the usual way and gave 4-isoamylanisole (58 gm., 78%) boiling at 78°C. (1 mm.) and having n_D^{27}, 1.4940. The literature (1) gives b.p. 121°C. (14 mm.) and n_D^{22}, 1.4995 (19). Anal. calc. for $C_{12}H_{18}O$: OCH_3, 17.40%. Found: OCH_3, 17.50, 17.50%. The *sulphonamide* was obtained in good yield and melted at 103°C. Anal. calc. for $C_{12}H_{19}NO_3S$: N, 5.45; OCH_3, 12.06%. Found: N, 5.51; OCH_3, 12.09, 12.05%.

(d) *4-Isoamylphenol*

4-Isoamylanisole (34 gm.) was demethylated as described above and yielded 4-isoamylphenol (29 gm., 94%) as an oil boiling at 68°C. (0.01 mm.) and having n_D^{25}, 1.5060. The literature (14) gives b.p. 245–250°C. (760 mm.) and n_D^{27}, 1.505. Anal. calc. for $C_{11}H_{16}O$: C, 80.5; H, 9.82%. Found: C, 80.3, 80.3; H, 9.80, 9.59%. The *3,5-dinitro-benzoate* melted at 124°C. Anal. calc. for $C_{18}H_{18}N_2O_6$: N, 7.82%. Found: N, 7.80%.

Nitration of the Phenols

The four phenols described above were then nitrated in the usual manner and the dinitrophenols thus formed were characterized as their piperidine, morpholine, and cyclohexylamine salts as described in an earlier communication (7). The relevant data are summarized in Table I.

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