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ORIGINAL ARTICLE

A Simple Alternative Method for the Synthesis of Aromatic Dialdehydes

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ABSTRACT
Aromatic dialdehydes were synthesized from 5-*t*-butylsalicylaldehyde and o-vanilline in good yields using paraformaldehyde, hydrobromic acid and catalytic amounts of sulfuric acid in one step which was previously unavailable with present methods.

Key Words: *aromatic dialdehydes, bromomethylation, 5-t-butylsalicylaldehyde, o-vanilline.*

1. INTRODUCTION

The recent growth of studies on multi-metallic compounds comes from the areas of homogeneous catalysis, magnetic exchange between paramagnetic centers and bioinorganic chemistry [1,3]. There are many multi-metal center proteins and enzymes in nature; prominent among these are many with homo and heterodinuclear metal centers [4,5]. Molecular systems having two or more redox active centers in close proximity, capable of cooperative interactions, are also of interest in relation to their potential as catalysts for reduction or oxidation reactions [6]. Considerable effort has thus been directed in recent years towards the synthesis of macrocyclic ligands capable of holding two or more metal ions [7].

The diphenolic dialdehyde 5,5`-di-*tert*-butyl-2,2`-dihydroxy-3,3`-methanediyldibenzaldehyde (**1**) is the building block of many macrocyclic Schiff base ligands [8,9]. However, the synthesis of **1** still remains problematic as the only reported method involves three steps from the known dialcohol 5,5`-di-*tert*-butyl-2,2`-dihydroxy-3,3`-methanediyldi benzenemethanol (Scheme 1) [8, 10]. The precursor dialcohol is obtained from p-*tert*-butylphenol in a few steps [11].

The preparation of the dialdehyde analogue 6,6`-dihydroxy-5,5`-dimethoxy-3,3`-ethylenedibenzaldehyde (2) involves only one step according to the reported methods [12, 13] however the reactions are very low yielding (23%).

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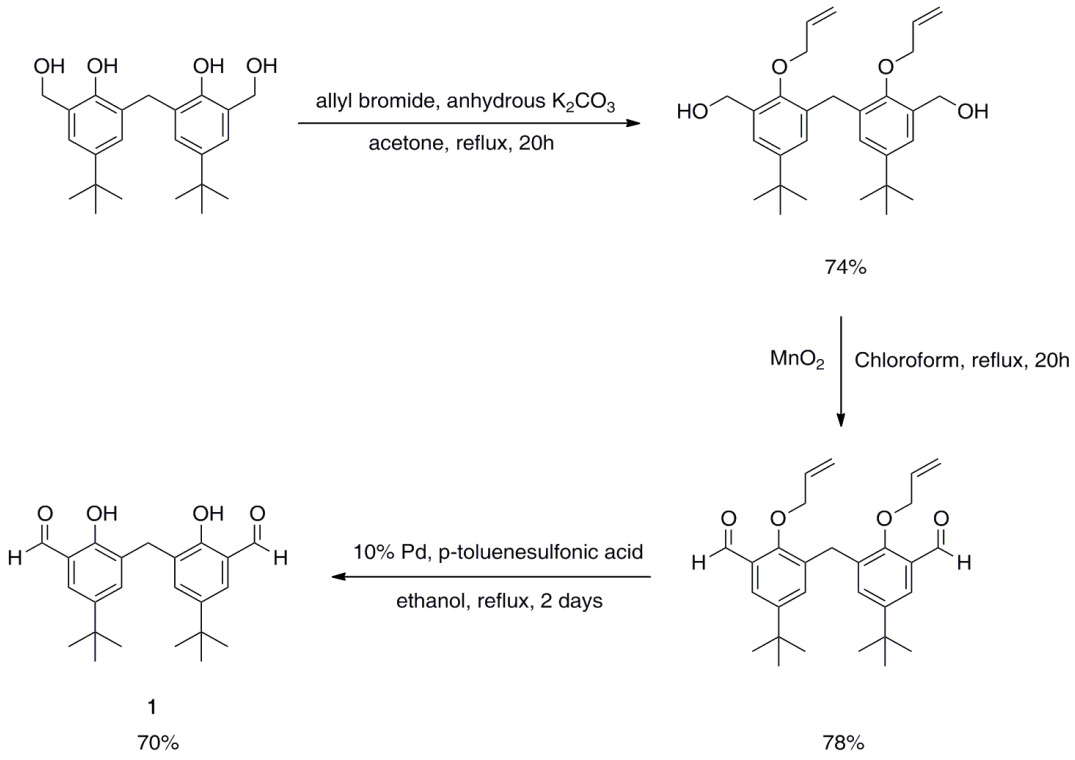


Scheme 1. The synthesis of dialdehyde 1 reported by McKee et. al.

With this new alternative method, we were able to synthesize aromatic dialdehydes 1 and 2 in good yields from 5-*t*-butysalicylaldehyde and o-vanilline in a single step.

2. EXPERIMENTAL

All chemicals were purchased from Merck and Sigma-Aldrich and used without any purification. Solvents were used as received from commercial suppliers. Silica gel F_{254} (Merck 5554) precoated plates were used for thin layer chromatography. For column chromatography silica gel 60 (Merck 7743) was used. IR spectra were recorded using a Mattson FTIR 1000. ^{1}HNMR and ^{13}CNMR spectra were carried out using a 400 MHz Varian NMR spectrometer at ambient temperature. Melting points were recorded with an electro thermal digital melting points apparatus.

2.1 Synthesis of 5,5`-di-tert-butyl-2,2`-dihydroxy-3,3`-methanediyldibenzaldehyde (1)

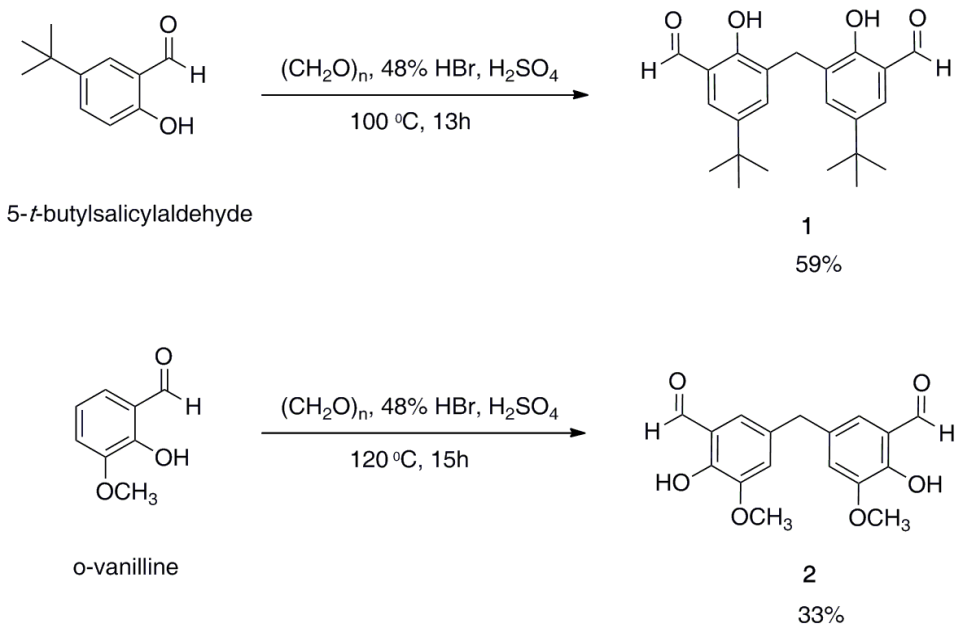
48% HBr (2.5 mL, 43.7 mmol) and a few drops of H_2SO_4 were added to the mixture of 5-*t*-butylsalicylaldehyde (2 mL, 11.7 mmol) and paraformaldehyde (262.5 mg, 8.7 mmol). The resulting solution was heated (100 °C) for 13 hours. The mixture was extracted with water and dichloromethane and the organic phase was evaporated under *vacuo*. The crude product was purified with column chromatography (3:1 hexanes: dichloromethane) to give the title compound as pale yellow crystals (59%). m.p. 179-180 °C. IR (NaCl): 3054, 2968, 2859, 1660, 1615, 1271, 1218, 737, 711 cm^{-1}. ^{1}HNMR (400 MHz, $CDCl_3$) δ (ppm): 11.18 (s, 2H, -OH), 9.86 (s, 2H, -CHO), 7.64 (s, 2H, Ar-H), 7.37 (s, 2H, Ar-H), 4.04 (s, 2H, -CH_2), 1.29 (s, 18H, CH_3). ^{13}CNMR (400 MHz, $CDCl_3$) δ (ppm): 197.09, 158.04, 142.53, 136.55, 128.20, 128.10, 119.97, 34.26, 31.43, 29.17. Anal. Calcd. for: $C_{23}H_{28}O_4$(%): C, 74.97; H, 7.66 Found: C, 74.47; H, 7.56.

2.2 Synthesis of 6,6`-dihydroxy-5,5`-dimethoxy-3,3`-methylenedibenzaldehyde (2)

48% HBr (2.7 mL, 49.3 mmol) and a few drops of H_2SO_4 were added to the mixture of o-vanilline (2 g, 13.1 mmol) and paraformaldehyde (295.9 mg, 9.9 mmol). The resulting solution was heated (120 °C) for 15 hours. The mixture was extracted with water and dichloromethane and the organic phase was evaporated under *vacuo*. The crude product was purified with column chromatography (3:1 hexanes: dichloromethane) to give the title compound as yellow crystals (33%). m.p. 151 °C. IR (NaCl): 2966, 2852, 1667, 1614, 1269, 1217, 739, 710 cm^{-1}. ^{1}HNMR (400 MHz, $CDCl_3$) δ (ppm): 10.97 (s, 2H, -OH), 9.88 (s, 2H, -CHO), 6.95 (d, J= 2 Hz, 2H, Ar-H), 6.91 (d, J= 2 Hz, 2H, Ar-H), 3.96 (s, 2H, -CH_2), 3.88 (s, 6H, -OCH_3). ^{13}CNMR (400 MHz, $CDCl_3$) δ (ppm): 196.34, 150.46, 148.54, 131.74, 123.86, 120.50, 118.70, 56.38, 40.41. Anal. Calcd. for: $C_{17}H_{16}O_6$(%): C, 64.55; H, 5.10 Found: C, 63.72; H, 5.04.

3. RESULTS AND DISCUSSION

We performed the reactions by heating paraformaldehyde, 48% hydrobromic acid and catalytic amounts of sulfuric acid with the appropriate salicylaldehyde derivatives (Scheme 2). These are the conditions for bromomethylation of aromatic compounds such as phenols [14].



Scheme 2. Synthesis of the aromatic dialdehydes 1 and 2

Considering the conditions of the reaction, it seems likely that the initial step involves reaction of the salicylaldehyde derivative with paraformaldehyde to form the hydroxyalkyl compound and then the HBr converts this to the bromomethylation product [15-17] which combines with a second aldehyde molecule in the final step to afford the desired aromatic dialdehydes.

Diphenolic dialdehydes such as **1** and **2** have previously been used to synthesize polynucleating macrocycles by Schiff base condensation with diamines [8,9] however their usage has been limited presumably due to the difficult procedures for their synthesis and low reaction yields. It is no doubt that the dialdehydes reported here will now find some new application fields as they can be obtained easily with this alternative method.

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REFERENCES

[1] Cairns, C. J. and Busch, D. H., "Intramolecular ferromagnetic interactions in polynuclear metal complexes", ***Coord. Chem. Rev***., 69, 1, (1986).

[2] Murray, K. S., "The magnetochemistry of homo- and hetero- tetranuclear first row d-block complexes", ***Adv. Inorg. Chem.***, 43, 261, (1995).

[3] Que, L., J. Chem. Soc., ***Dalton Trans.***, 3933, (1997).

[4] Que, L., "Metal Clusters in Proteins", ***ACS Symposium series***, 372, (1988).

[5] Bertini, I. "Handbook on Metallo proteins", ***Marcel Dekker***, (2001).

[6] Bosnich, B., "Cooperative bimetallic redox reactivity", ***Inorg. Chem***., 38, 2554, (1999).

[7] Zhu, H. B., Hu, D. H., Dong, H. Z., Li, G. X. and Gou, S. H., "Selective synthesis of [2+2] macrocyclic Schiff bases from chiral 1,4-diamines", ***Chin. J. Chem.*** 25, 343-345, (2007).

[8] Fontecha, J. B., Goetz, S. and McKee, V., "Di- tri- and tetracopper(II) complexes of a pseudocalixarene macrocycle", ***Angew. Chem. Int. Ed***., 41, 23, 4553-4556, (2002).

[9] Fontecha, J. B., Goetz, S. and McKee, V., "Dinuclear complexes of a pseudocalixarene macrocycle: structural consequences of intramolecular hydrogen bonding", ***Dalton Trans***., 923-929, (2005).

[10] Goetz, S., Fontecha, J. B. and McKee, V., "5,5'-Di-tert-butyl-2,2'-dihydroxy-3,3'-methanediyldibenzaldehyde and its allyl-protected dialcohol and dialdehyde precursors", ***Acta Cryst***., C60, 776-780, (2004).

[11] Dhawan, B. and Gutsche, C. D., "Calixarenes, oxocalixarenes", ***J. Org. Chem***., 48, 1536-1539, (1983).

[12] Jiao, G., Li, X., Cao, R. and Li, M., "Tetra-μ_2-acetato-κ^8 *O*:*O*′-bis[(isoquinoline-κ*N*)copper(II)]", ***Acta Cryst***., E61, 4298-4299, (2005).

[13] Odabaşoğlu, M., Albayrak, Ç. and Büyükgüngör, O., "Bis(3-formyl-4-hydroxy-5 methoxyphenyl)methane" ***Acta Cryst***., E62, 239-240, (2006).

[14] Smith, M. B. and March, J., ***March`s Advanced Organic Chemistry***, 5th Ed., 11, 721, (2001).

[15] Belen`kii, L. I., Vol`kenshtein, Yu. B. and Karmanova, I. B., ***Russ. Chem. Rev***., 46, 891, (1977).

[16] Ogata, Y. and Okano, M., "Kinetics of the chloromethylation of mesitylene in aqueous acetic acid", ***J. Am. Chem. Soc.,*** 78, 5423, (1956).

[17] Olah, G. A. and Yu, S. H., "Protonated chloromethyl alcohol and chloromethyl esters. Proof for the intermediacy of the elusive chloromethyl alcohol", ***J. Am. Chem. Soc***. 97, 2293, (1975).