

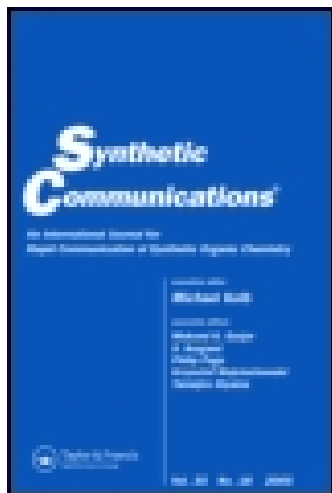
This article was downloaded by: [University of Kent]

On: 20 November 2014, At: 14:53

Publisher: Taylor & Francis

Informa Ltd Registered in England and Wales Registered Number: 1072954

Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/lcyc20>

An Unusual Synthesis of Phthalaldehyde

Ernest Wenkert ^a & Haripada Khatuya ^a

^a Department of Chemistry (0506) , University of California-San Diego , La Jolla, CA, 92093, USA

Published online: 17 Sep 2007.

To cite this article: Ernest Wenkert & Haripada Khatuya (1999) An Unusual Synthesis of Phthalaldehyde, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 29:14, 2413-2417, DOI: [10.1080/00397919908086247](https://doi.org/10.1080/00397919908086247)

To link to this article: <http://dx.doi.org/10.1080/00397919908086247>

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <http://www.tandfonline.com/page/terms-and-conditions>

AN UNUSUAL SYNTHESIS OF PHTHALALDEHYDE[#]

Ernest Wenkert* and Haripada Khatuya[†]

Department of Chemistry (0506), University of California-San Diego,
La Jolla, CA 92093, USA

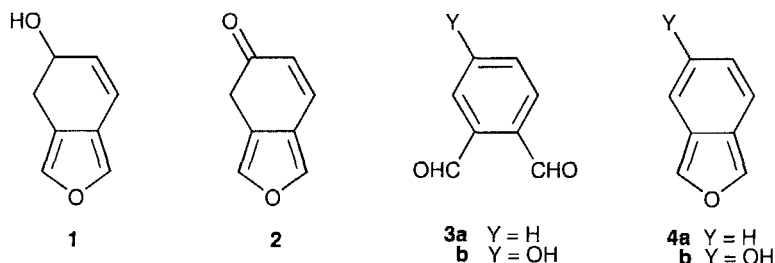
Abstract: A variety of oxidizing agents convert 5-hydroxy-4,5-dihydroisobenzofuran into phthalaldehyde. Other oxidizing agents produce both phthalaldehyde and its 4-hydroxy derivative.

5-Hydroxy-4,5-dihydroisobenzofuran **1** is a bicyclic furan alcohol, easily prepared from furfuryl alcohol by conversion into its propargyl ether followed by a Kanematsu reaction.¹ In connection with a natural product synthesis project ketone **2** was needed as starting material. Hence alcohol **1** was subjected to oxidation.

[#] Dedicated to the memory of *Dr. P. C. Rakshit*, Ramakrishna Mission Residential College, Narendrapur, West Bengal, India.

^{*} To whom correspondence should be addressed.

[†] Present Address: The R. W. Johnson P. R. I., 3535 General Atomics Court, Suite 100, San Diego, CA 92121, USA.

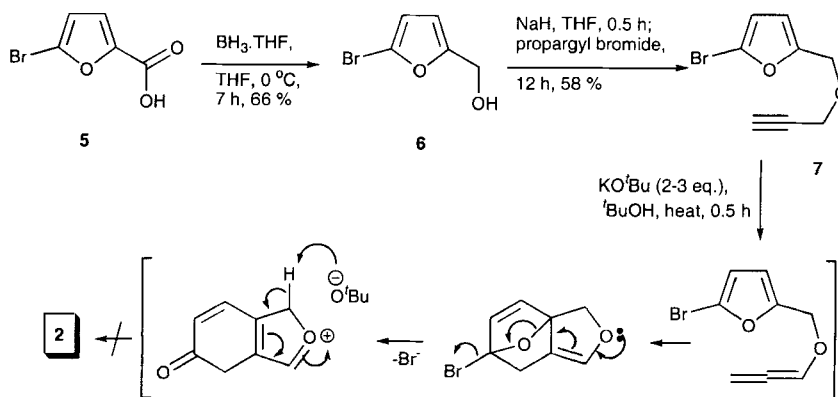


Despite the use of a variety of oxidizing agents (i: CAN/H₂O/2 h; ii: *t*-BuOCl/py/CCl₄/4 h; iii: DMSO/(COCl)₂-Et₃N/CH₂Cl₂; iv: *m*-ClC₆H₄CO₃H/CH₂Cl₂/1 h; v: *t*-BuOOH/VO(acac)₂/C₆H₆/3 h) none of the reactions (at ambient temperature) led to the desired ketone **2**, but, instead, produced phthalaldehyde **3a** in 37-50% yields. Oxidation in a refluxing aqueous SeO₂ suspension for 10 min furnished **3a** in 64% yield.

The above results indicate that no oxidation had taken place at the site of the hydroxy group of alcohol **1**. Instead, the latter had undergone dehydration induced by either Lewis acid catalysis of the oxidizing agent or by solvolysis of an intermediate ester of an inorganic acid. The resultant metastable isobenzofuran¹ **4a** would be expected to suffer oxidation at its furan α -position, affording phthalaldehyde **3a** as product. Had the desired oxidation occurred, ketone **2** might not have survived, since its enol is metastable 5-hydroxyisobenzofuran **4b**, vulnerable at its furan α -site and en route to 4-hydroxyphthalaldehyde **3b**. This scenario actually could be observed, when four more oxidizing systems were studied.

Manganese dioxide oxidation in refluxing dioxane (18 h) yielded a 1:2 **3a-3b** mixture, while PCC in CH_2Cl_2 ($-78\text{ }^\circ\text{C}$, 9 h; then $22\text{ }^\circ\text{C}$, 18 h) gave a 1:1 **3a-3b** mixture. Treatment of alcohol **1** with PDC in CH_2Cl_2 as under the PCC oxidation conditions afforded a 1:2 product mixture, though the reaction at $22\text{ }^\circ\text{C}$ (18 h) furnished the aldehydes in 4:1 ratio. Oxidation with DDQ in dioxane at $22\text{ }^\circ\text{C}$ led to a 1:1 product ratio, whereas in refluxing dioxane (18 h) aldehydes **3a** and **3b**² were produced in a 2:1 combination, respectively. Since the dialdehyde yields were in the 51-78% range, the oxidations of alcohol **1** represent a reasonable method of synthesis of phthalaldehyde **3a** and/or its 4-hydroxy derivative **3b**.

Scheme: Furan ring transfer (FRT) study



In the absence of success of the **1**→**2** conversion a Kanematsu reaction sequence was investigated, which was expected to yield ketone **2** without recourse to an oxidation (**Scheme**). 5-Bromofuroic acid **5** was reduced with borane and the

resultant 5-bromofurfuryl alcohol **6** was alkylated immediately with propargyl bromide. Exposure of 5-bromofurfuryl propargyl ether **7** to Kanematsu reaction conditions unfortunately yielded only intractable material.

Experimental:

General. M.p.: Reichert micro hotstage; uncorrected. IR spectra (cm^{-1}): IBM 9000 spectrophotometer. ^1H - and ^{13}C -NMR spectra (CDCl_3 solutions): *General Electric QE-300* spectrometer. MS spectra: Hewlett-Packard 5890 GC-MS spectrometer. TLC: *EM Laboratories* precoated silica gel 60F-25 on 0.2 mm plates; column: *EM Laboratories* 60-200 mesh silica gel (elution with EtOAc/hexane mixtures); MPLC: *Merck Laboratory* (A, B, C) silica gel columns, *Fluid metering, Inc.* pump.

Phthalaldehyde (3a): A mixture of alcohol **1** (115 mg, 0.845 mmol) and SeO_2 (47 mg, 0.423 mmol) in H_2O (5 ml) was refluxed for 10 min. The cooled mixture was filtered through a SiO_2 pad and the latter washed with ether. The aqueous solution was extracted with ether and the combined ether solutions were washed with brine and dried (Na_2SO_4). Evaporation of the extract under vacuum furnished phthalaldehyde **3a** (73 mg, 64%). Mp 55-57 °C (lit. Mp 54-55 °C).³ ^1H -NMR (CDCl_3): δ 7.77 (*dd*, 2H, $J = 3.3, 5.5$ Hz, H-C(4), H-C(5)); 7.95 (*dd*, 2H, $J = 3.3, 5.5$ Hz, H-C(3), H-C(6)); 10.49 (*s*, 2H, CHO). ^{13}C -NMR (CDCl_3): δ 130.7 (C(3), C(6)); 133.5 (C(4), C(5)); 136.0 (C(1), C(2)); 192.2 (CO).

References and Note:

1. K. Hayakawa, Y. Yamaguchi and K. Kanematsu, *Tetrahedron Lett.*, 1985, **26**, 2689.
2. **4-Hydroxyphthalaldehyde (3b)**: ^1H -NMR (CDCl_3): δ 2.00 (br. s, 1H), 7.20 (dd, 1H, $J = 2.4, 8.4$ Hz), 7.43 (d, 1H, $J = 2.4$ Hz), 7.87 (d, 1H, $J = 8.4$ Hz), 10.28 (s, 1H), 10.59 (s, 1H). ^{13}C NMR (CDCl_3): δ 117.0, 120.0, 128.6, 134.9, 138.6, 161.9, 191.4, 192.6.
3. C. V. Greco and F. C. Pellegrini, *Synth. Commun.*, 1971, **1**, 307.

(Received in the USA 19 January 1999)