

Preparation of Ethyl 1-Hydroxy-2-naphthoates from
1H-2-Benzopyran-1-ones: A New Method

Frank M. Hauser* and Stefano A. Pogany

Department of Chemistry, Oregon Graduate Center, Beaverton, Oregon 97005

Received June 23, 1978

Lithio ethyl acetate is a superior reagent for the transformation of 1H-2-benzopyran-1-ones to naphthoates.

J. Heterocyclic Chem., 15, 1535 (1978)

Sir:

In recent papers we described the use of a modified Reformatsky reaction to regioselectively transform 3-methyl-1H-2-benzopyran-1-ones and 3-methylnaphtho-[2,3-c]pyran-1-ones to 1-hydroxy-3-methyl-2-naphthalene carboxylates and 1-hydroxy-3-methyl anthracene carboxylates, respectively (1,2). Although time consuming, the procedure afforded near quantitative yields of naphthoates **2a** and **2b** (Table I). However, the presence of methoxyl groups on the benzopyran precursors **1c** and **1d** cause a marked decrease in the yields of substituted naphthoates **2c** and **2d**. The reduced yields were traced to demethylation of the 8-methoxyl group of **1c** and **1d** by *in situ* generated zinc bromide.

Lithio ethyl acetate (4) is often used as a replacement for the Reformatsky reagent (5). We have investigated the use of this reagent to transform benzopyran-1-ones **1a-d** to naphthoates **2a-d** and have found that uniformly high yields (87-93%) of naphthoates are obtained, even when methoxylated precursors are used. Moreover, significantly less time is needed to conduct the reaction.

Preparation of Naphthoates **2a-d** (General Procedure).

Butyllithium (4.55 mmoles) and tetrahydrofuran (10 ml.) were added to a magnetically stirred solution of isopropylcyclohexylamine (4.55 mmoles) under nitrogen at 0°. The solution was stirred for 20 minutes at 0°, for 5 minutes at 25° and then cooled to -78°. Dry ethyl acetate (4.55 mmoles) was added and the solution stirred

for 30 minutes. The prepared anion was rapidly transferred through a teflon tube to a vigorously stirred solution of benzopyran **1a** or **1c** (2.27 mmoles) in demethylsulfoxide (5 ml.) and tetrahydrofuran (5 ml.) at 0°. After thirty minutes, the yellow reaction mixture was quenched with acetic acid (6 ml.) and stirred at room temperature for 48 hours. The tetrahydrofuran was evaporated at reduced pressure, the residue was taken up in ether (100 ml.) and the solution washed with water (2 x 25 ml.). The solvent was dried (magnesium sulfate), then evaporated to give impure naphthoates **2a-c**. Pure naphthoates were obtained by slug chromatography (silica gel, 30 g., dichloromethane).

Acknowledgement.

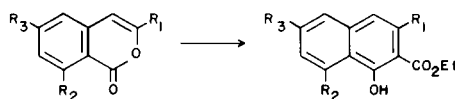
The authors wish to thank the National Cancer Institute of DHEW, grant number CA 18141 for support of this work.

REFERENCES AND NOTES

- (1) F. M. Hauser and R. P. Rhee, *J. Am. Chem. Soc.*, **99**, 4533 (1977).
- (2) F. M. Hauser and R. P. Rhee, *J. Org. Chem.*, **42**, 4155 (1977).
- (3) M. Pailer and O. Vostrowsky, *Monatsh. Chem.*, **102**, 951 (1971).
- (4) M. W. Rathke and A. Lindert, *J. Am. Chem. Soc.*, **93**, 2318 (1971).
- (5) M. W. Rathke, *Organic Reactions*, Vol. 22, John Wiley & Sons, Inc., New York, N. Y., 1975, p. 423.

Table I

Yields of Naphthoates from Isocoumarins



	R ₁	R ₂	R ₃	% Yield (BrZnCH ₂ CO ₂ Et)	% Yield (LiCH ₂ CO ₂ Et)	M.p. Naphthoates
a.	H	H	H	97	93	48-49° (lit. (3) 48-49.5°)
b.	CH ₃	H	H	97	92	58-59° (lit. (3) 56-59°)
c.	CH ₃	OCH ₃	H	69	91	69-70° (lit. (1,2) 68-70°)
d.	CH ₃	OCH ₃	OCH ₃	24	87	58-59° (lit. (2) 59°)