

Facile One-Pot Synthesis of Photochromic Pyrans

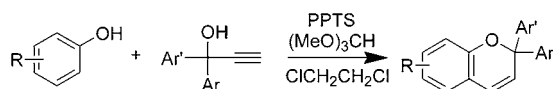
Weili Zhao and Erick M. Carreira*

Laboratorium für Organische Chemie, ETH-Hönggerberg HCI H335,
CH-8093 Zürich, Switzerland

carreira@org.chem.ethz.ch

Received August 25, 2003

ABSTRACT



Photochromic pyrans, including [3*H*]naphtho[2,1-*b*]pyrans, [2*H*]naphtho[1,2-*b*]pyrans, indeno-fused naphtho[1,2-*b*]pyrans, and heteroannulated pyrans, were synthesized in excellent yields through a facile one-pot procedure by reaction of propargyl alcohol and naphthol or phenol derivatives in the presence of 5 mol % PPTS and 2 equiv of (MeO)₃CH. Symmetrical and nonsymmetrical bispyrans can also be prepared using the protocol.

Diaryl-benzopyrans and naphthopyrans display highly desirable photochromic properties¹ and have thus been the subject of intense investigations aimed at developing novel materials with useful applications in the marketplace. For convenient access to designed photochromic compounds based on this structural motif, it is paramount that reliable, general synthetic methods be readily available. However, the various synthetic routes for the synthesis of diaryl-benzopyrans and naphthopyrans are limited with respect to yield and scope. Herein we report a synthetic method that leads to improved access to a wide range of pyrans involving acid-catalyzed reaction of propargyl alcohols and phenols or naphthols in the presence of (MeO)₃CH as a dehydrating agent.

There are three general approaches to diaryl benzopyrans or naphthopyrans. The first of these, the Kabbe synthesis, commences with chromanones and necessitates a multistep sequence of reactions.² The second method prescribes the reaction of aryl Grignard with benzocoumarins, followed by dehydration.³ The third and most expeditious involves the Claisen rearrangement of propargyl-aryl ethers prepared *in situ* from phenol or naphthol and a diaryl propargyl alcohol under acidic conditions.^{4–8} In general, these approaches lack

generality and provide the target photochromic compounds in poor yield contaminated with byproducts. In this respect, under the conditions of the condensation reaction of diaryl-propargyl alcohols with phenols or naphthols, the well-known Meyer–Schuster rearrangement reaction of the starting propargyl alcohol is competitive.^{7b,9} Additionally, under these conditions, the yield of pyran has been shown to be strongly dependent on the structure of the phenol or naphthol; thus, for example, in a report on the synthesis of 32 of heterocyclic

(4) (a) Iwai, I.; Ide, J. *Chem. Pharm. Bull.* **1963**, *11*, 1042. (b) Momodam, J.; Hara, T. U.S. Patent 5808100, 1998.

(5) (a) Tanaka, K.; Aoki, H.; Hosomi, H.; Ohba, S. *Org. Lett.* **2000**, *2*, 2133. (b) Moustrou, C.; Rebiere, N.; Samat, A.; Guglielmetti, R.; Yassar, A. E.; Dubest, R.; Aubard, J. *Helv. Chim. Acta* **1998**, *81*, 1293. (c) Heller, H. G.; Levell, J. R. U.S. Patent 5955520, 1999.

(6) (a) Coelho, P. J.; Carvalho, L. M.; Abrantes, S.; Oliveira-Campos, A. M. F.; Dubest, R.; Samat, A.; Guglielmetti, R. *Tetrahedron* **2002**, *58*, 9505. (b) Coelho, P. J.; Carvalho, L. M.; Rodrigues, S.; Oliveira-Campos, A. M. F.; Dubest, R.; Aubard, J.; Samat, A.; Guglielmetti, R. *Tetrahedron* **2002**, *58*, 925. (c) Oliveira, M. M.; Carvalho, L. M.; Moustrou, C.; Samat, A.; Guglielmetti, R.; Oliveira-Campos, A. M. F. *Helv. Chim. Acta* **2001**, *84*, 1163. (d) Coelho, P. J.; Carvalho, L. M.; Silva, J.; Oliveira-Campos, A. M. F.; Samat, A.; Guglielmetti, R. *Helv. Chim. Acta* **2001**, *84*, 117. (e) Martin, C. I.; Coelho, P. J.; Carvalho, L. M.; Oliveira-Campos, A. M. F.; Samat, A.; Guglielmetti, R. *Helv. Chim. Acta* **2003**, *86*, 570. (f) Frigoli, M.; Moustrou, C.; Samat, A.; Guglielmetti, R. WO 01/04233, 2001.

(7) (a) Rickwood, M.; Marsden, S. D.; Hepworth, J. D.; Gabbutt, C. D. U.S. Patent 5520853, 1996. (b) Harie, G.; Samat, A.; Guglielmetti, R. *Tetrahedron Lett.* **1997**, *38*, 3075. (c) Von Gemert, B. U.S. Patent 5645767, 1997. (d) Knowles, D. B.; Von Gemert, B. U.S. Patent 5464567, 1995.

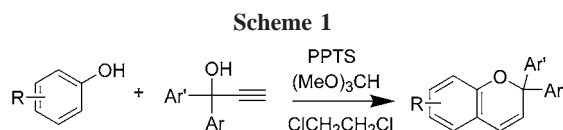
(8) (a) Pozzo, J. L.; Samat, A.; Guglielmetti, R.; Lokshin, V.; Minkin, V. *Can. J. Chem.* **1996**, *74*, 1649. (b) Kumar, A. U.S. Patent 5411679, 1995.

(9) Swaminathan, S.; Narayanan, K. V. *Chem. Rev.* **1971**, *71*, 429.

(1) Gemert B. V. Benzo and Naphthopyrans (Chromenes). In *Organic Photochromic and Thermochromic Compounds*; Crano, J. C., Guglielmetti, R., Eds.; Plenum Press: New York, 1999; Vol. 1, Chapter 3.

(2) (a) Gabbutt, C. D.; Hartley, D. J.; Hepworth, J. D.; Heron, B. M.; Kanjia, M.; Rahman, M. *Tetrahedron* **1994**, *50*, 2507. (b) Kabbe, H.; Widdig, A. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 247.

(3) Cottam, J.; Livingstone, R. *J. Chem. Soc.* **1965**, 6646.



[3*H*]-naphtho-[2,1-*b*]pyran compounds, the yields ranged from 4 to 40%.^{4b} In recent reports, the use of PPTS as a catalyst for preparation of sensitive benzopyrans and naphthopyrans is documented,^{5b,6} leading to yields ranging from 9 to 78%.

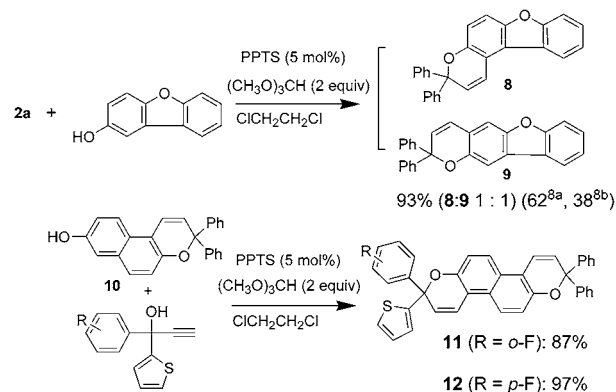
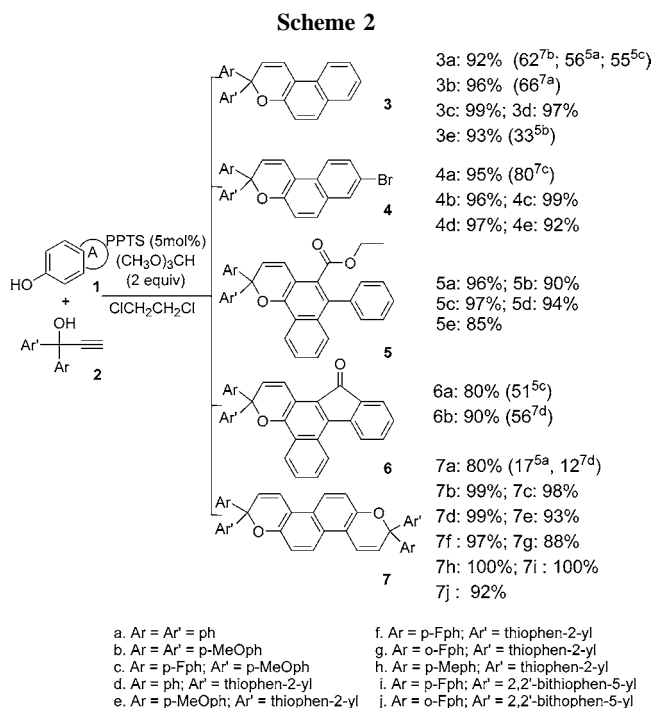
Our initial studies in this area focused on the use of PPTS as a catalyst (5%) in the reaction of 1,1-diphenyl-2-propyn-1-ol and 2-naphthol as model substrates. Under the standard conditions, the reaction was extremely slow, affording 2% adduct after 1 week. Interestingly, we observed a dramatic improvement in the course of the reaction when (MeO)₃CH was used as an additive. Under optimal conditions, treatment of diarylpropargyl alcohol (1.05–1.1 equiv) and aromatic phenols or naphthols (1 equiv) in ClCH₂CH₂Cl with 2 equiv of (MeO)₃CH and 5 mol % PPTS furnished the desired product in high yields.

As shown in Scheme 2, the experimental protocol is widely applicable, including both [3*H*]naphtho[2,1-*b*]pyrans and [2*H*]naphtho[1,2-*b*]pyrans and indeno-fused naphtho[1,2-*b*]pyrans, as well as heteroannulated pyrans. For comparison purposes, the yields reported in the literature are included in parentheses. The yields obtained under the conditions we describe herein offer considerable improvement over those previously reported.

The unique advantages of the method can be appreciated in the preparation of bisnaphthopyran derivatives **7**, which have otherwise been previously obtained in only low yields.^{5a,c} Under the conditions reported herein, an excellent yield of **7** was obtained, and analytically pure bisnaphthopyran could be obtained by simple filtration of the cold reaction mixture. Additionally, unsymmetrical bisnaphthopyrans can be prepared. Thus, in the reaction of the mononaphthopyran **10**¹⁰ with thienyl propargyl alcohols, **11** and **12** can be obtained in 87 and 97% yields, respectively.

In conclusion, we have developed a facile one-pot synthesis of photochromic pyran and bispyran compounds by reaction of propargyl alcohols and naphthol derivatives in

(10) Compound **10** was prepared in 50% yield by adding slowly a solution of 1,1-diphenyl-2-propyn-1-ol (1.0 mmol) in 1,2-dichloroethane (4 mL) into a boiling suspension of 2,6-dihydroxynaphthalene (1.1 mmol), PPTS (0.05 mmol), and trimethyl orthoformate (2.0 mmol) in 1,2-dichloroethane (5 mL), followed by 2 h reflux.



the presence of 5 mol % PPTS and 2 equiv of (MeO)₃CH. The method permits convenient access to a wide range of photochromic pyran systems and, importantly, should enable access of novel, interesting materials that have only been previously accessed in poor yields with some difficulties.

Acknowledgment. We thank the ETH for an internal research grant (TH-Gesuch).

Supporting Information Available: Characterization data for compounds **3–12**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

OL035599X