ORGANIC LETTERS

2005
Vol. 7, No. 26
5857−5859

Practical Synthesis of Triaryl- and Triheteroarylmethanes by Reaction of Aldehydes and Activated Arenes Promoted by Gold(III) Chloride

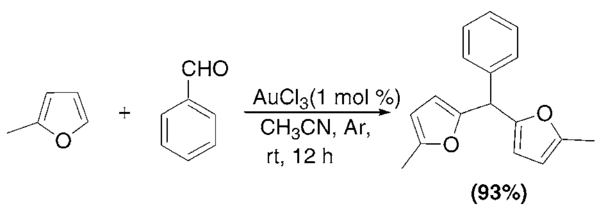
Vijay Nair,* K. G. Abhilash, and N. Vidya

Organic Chemistry Division, Regional Research Laboratory (CSIR), Trivandrum-695019, India

vijaynair_2001@yahoo.com

Received October 6, 2005

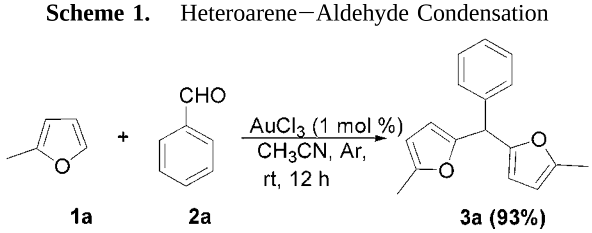
ABSTRACT



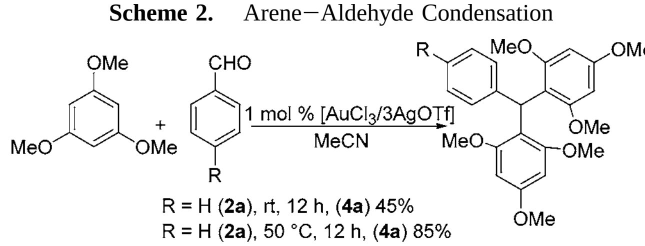
Electron-rich arenes condense efficiently with various aldehydes under the influence of $AuCl_3$, thus opening up a practical route to triarylmethanes, which have important applications. The mild conditions employed are especially noteworthy.

Since the discovery of the triphenylmethyl radical by Gomberg in 1900,[1] triaryl- and triheteroarylmethanes have attracted much attention from organic chemists and many such compounds have found widespread applications in synthetic, medicinal, and industrial chemistry.[2] Inter alia, the triarylmethyl derivatives are useful as protective groups,[3]

Scheme 1. Heteroarene−Aldehyde Condensation



Scheme 2. Arene−Aldehyde Condensation

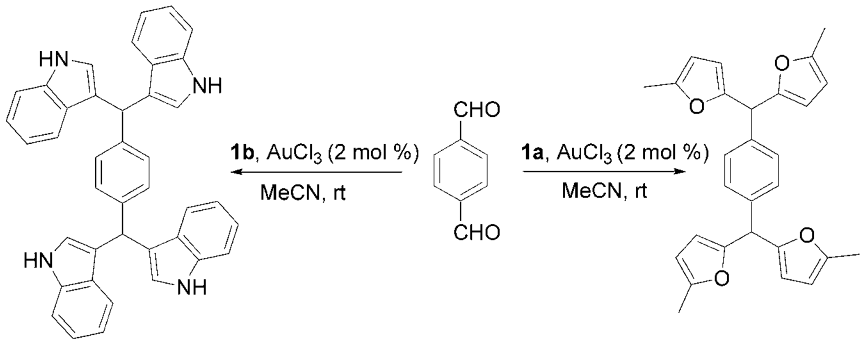


(1) Gomberg, M. *J. Am. Chem. Soc.* **1900**, *22*, 757.

(2) (a) Shchepinov, M. S.; Korshun, V. A. *Chem. Soc. Rev.* **2003**, *32*, 170. (b) Duxbury, D. F. *Chem. Rev.* **1993**, *93*, 381. (c) Schnitzer, R. J.; Hawking, F. *Experimental Chemotherapy*; Academic Press: New York, 1963; Vol. I.

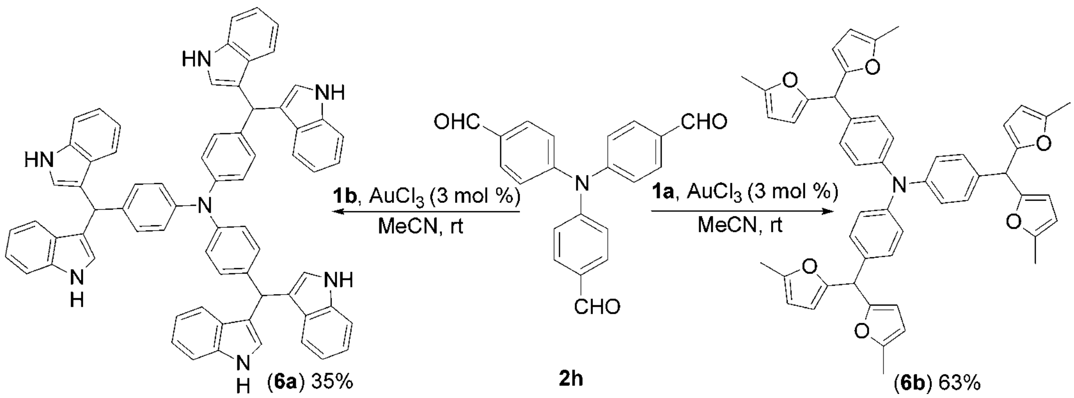
10.1021/ol052423h CCC: $30.25
Published on Web 11/30/2005

Scheme 3. Dialdehyde Condensations



(**5a**) 95% **2g** (**5b**) 51%

Scheme 4. Toward Dendritic Architectures



(**6a**) 35% **2h** (**6b**) 63%

photochromic agents,[4] and dyes.[5] Ring hydroxylated triarylmethanes have been reported to exhibit antitumor and antioxidant activities.[6] Also, bisheteroarylmethanes are of interest to the food industry as natural components of certain food and beverage items as well as flavor agents in coffee.[7] Although a number of methods are available for the synthesis of triarylmethanes, most of them are multistep processes and/or require harsh reaction conditions.[8]

In the quest to develop a mild and practical protocol for the synthesis of triaryl-/triheteroarylmethanes, it was speculated that gold(III), which has recently been shown to catalyze a variety of C−C bond forming reactions,[9,10] might be ideal for effecting the condensation of aldehydes and activated arenes. The preliminary results that illustrate the efficiency and versatility of $AuCl_3$-promoted condensation to afford triaryl- and triheteroarylmethanes are described in this letter.

In the first example, 2-methyl furan (**1a**) was treated with benzaldehyde (**2a**) in the presence of $AuCl_3$ (1 mol % based on the aldehyde) in acetonitrile (Scheme 1).

After stirring the reaction mixture at room temperature for 12 h, the bis(5-methylfur-2-yl)phenylmethane **3a** was

(3) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; Wiley: New York, 1999.

(4) (a) Aldag, R. Photochromism based on dissociation processes. In *Photochromism: Molecules and Systems*; Dürr, H., Bouas-Laurent, H., Eds.; Elsevier: London, 1990. (b) Irie, M. *J. Am. Chem. Soc*. **1983**, *105*, 2078.

(5) (a) Rys, P.; Zollinger, H. *Fundamentals of the Chemistry and Application of Dyes*; Wiley-Interscience: New York, 1972. (b) Muthyala, R.; Katritzky, A. R.; Lan, X. *Dyes Pigm.* **1994**, *25*, 303.

(6) Mibu, N.; Sumoto, K. *Chem. Pharm. Bull*. **2000**, *48*, 1810.

(7) Katritzky, A. R.; Xie, L.; Fan, W.-Q. *J. Org. Chem.* **1993**, *58*, 4376.

(8) (a) Schick, J. W.; Crowley, D. J. *J. Am. Chem. Soc.* **1951**, *73*, 1377. (b) Ungnade, H. E.; Crandall, E. W. *J. Am. Chem. Soc.* **1949**, *71*, 2209. (c) Pratt, E. F.; Green, L. Q. *J. Am. Chem. Soc.* **1953**, *75*, 275. (d) Katritzky, A. R.; Gupta, V.; Garot, C.; Stevens, C. V.; Gordeev, M. F. *Heterocycles* **1994**, *38*, 345. (e) Katritzky, A. R.; Toader, D. *J. Org. Chem.* **1997**, *62*, 4137. (f) Riad, A.; Mouloungui, Z.; Delmas, M.; Gaset, A. *Synth. Commun*. **1989**, *19*, 3169.

(9) For reviews, see: (a) Dyker, G. *Angew. Chem.* **2000**, *112*, 4407; *Angew. Chem., Int. Ed*. **2000**, *39*, 4237. (b) Hashmi, A. S. K. *Gold Bull.* **2003**, *36*, 3. (c) Hashmi, A. S. K. *Gold Bull*. **2004**, *37*, 51. (d) Arcadi, A.; Guiseppe, S. D. *Curr. Org. Chem*. **2004**, *8*, 795. (e) Hoffmann-Röder, A.; Krause, N. *Org. Biomol. Chem*. **2005**, *3*, 387.

(10) For selected examples, see: (a) Fukuda, Y.; Utimoto, K. *J. Org. Chem*. **1991**, *56*, 3729. (b) Asao, N.; Takahashi, K.; Lee, S.; Kasahara, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2002**, *124*, 12650. (c) Li, C.-J.; Yao, X. *J. Am. Chem. Soc*. **2004**, *126*, 6884. (d) Yang, C. G.; He, C. *J. Am. Chem. Soc*. **2005**, *127*, 6966. (e) Hashmi, A. S. K.; Schwarz, L.; Choe, J.-H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285. (f) Wei, C.; Li, C.-J. *J. Am. Chem. Soc*. **2003**, *125*, 9584. (g) Shi, Z.; He, C. *J. Am. Chem. Soc*. **2004**, *126*, 5964. (h) Luo, Y.; Li, C.-J. *Chem. Commun.* **2004**, 1930. (i) Reetz, M. T.; Sommer, K. *Eur. J. Org. Chem*. **2003**, 3485. (j) Reetz, M. T.; Sommer, K. Gold-catalyzed Hydroarylation of Alkynes. In *Handbook of C−H Transformations, Vol.1 (Applications in Organic* Synthesis); Dyker, G., Ed.; Wiley-VCH: Weinheim, Germany, 2005, pp 157−166, 268−269.

Table 1. Heteroarene Condensation Products with Yields

entry	R	R'	product with yield (%)[a]
1	1a	2b	3b, 90
2	1a	2c	3c, 76
3	1a	2d	3d, 77
4	1a	2e	3e, 65
5	1b	2b	3f, 92
6	1b	2c	3g, 99
7	1b	2d	3h, 78
8	1b	2e	3i, 76
9[b]	1c	2a	3j, 70
10[b]	1c	2c	3k, 32
11	1d	2a	3l, 93
12	1d	2b	3m, 85
13	1e	2d	3n, 64

[a] Isolated yield. [b] 1 mol % $AuCl_3$/3AgOTf was used.

isolated in 93% yield. Other heterocycles such as indole, 1-methyl indole, and 3-methyl indole also reacted well under the same conditions (Table 1). 2-Methyl thiophene on reaction with benzaldehyde under the above conditions yielded 35% of the adduct. The yield rose to 70% when the catalyst system was changed to 1 mol % of $AuCl_3$/3AgOTf.[11] Various heterocyclic and aryl aldehydes as well as aliphatic aldehydes underwent the reaction smoothly.

An electron-rich arene, 1,3,5-trimethoxybenzene, required the catalytic system $AuCl_3$/3AgOTf and a slightly elevated temperature (50 °C) to condense effectively with benzaldehyde. However, with a more activated electrophile (4-nitro benzaldehyde), the reaction took place at room temperature to afford the tris adduct in good yield (Scheme 2).

With the perception that the reaction, if successful with polyaldehydic compounds, would allow an unprecedented entry into the dendritic arena, a few exploratory reactions were carried out. Thus, terephthalaldehyde was reacted with indole and 2-methyl furan, and in both cases, good yields of the condensation products were obtained (Scheme 3).

The condensation of tris[(4-formyl)phenyl]amine with heteroarenes yielded even more fascinating molecules (Scheme 4). Evidently, these products, in principle, can serve as core structures for dendritic architectures.

In summary, it has been demonstrated that electron-rich aromatic systems undergo an efficient condensation reaction with various aldehydes under the influence of gold(III). It is reasonable to expect that the present work will find much use in the synthesis of triaryl- and triheteroarylmethanes, which are very valuable compounds in many respects.

Acknowledgment. Financial assistance from Council of Scientific and Industrial Research (CSIR), Government of India, is acknowledged.

Supporting Information Available: Experimental procedures and characterization data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

OL052423H

(11) A 1:3 mixture of $AuCl_3$ and AgOTf acts as a better catalyst system, though it is not clear what the active species is. See ref 10i for a discussion.