Chinese Chemical Letters xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Chinese Chemical Letters

journal homepage: www.elsevier.com/locate/cclet

Original article

Triphenylphosphine-*m*-sulfonate/carbon tetrabromide as an easily recoverable catalyst system for the efficient synthesis of xanthene and xanthenone derivatives under solvent-free conditions

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ARTICLE INFO

Article history:
Received 11 November 2013
Received in revised form 17 December 2013
Accepted 2 January 2014
Available online xxx

Keywords:
Xanthene
Xanthenone
Naphthol
Aldehyde

ABSTRACT

A solid complex, readily prepared from commercially available sodium triphenylphosphine-*m*-sulfonate (TPPMS) and carbon tetrabromide, can be used as an easily recoverable and reusable catalyst system for one-pot condensation of 2-naphthol with aldehydes to construct 14-aryl(alkyl)-14*H*-dibenzo[*a*,*j*]-xanthene derivatives and one-pot condensation of 2-naphthol with aldehydes and cyclic 1,3-dicarbonyl compounds to construct 12-aryl(alkyl)-8,9,10,12-tetrahydrobenzo[*a*]xanthen-11-one derivatives.

1. Introduction

Xanthenes exhibit a range of important biological activities such as anti-inflammatory, anti-viral, and anti-bacterial properties [1]. Moreover, due to their spectroscopic properties, xanthenes are used as dyes and fluorescent materials for the visualization of biomolecules [2]. Xanthenones, especially tetrahydroxanthenones, are also an important class of compounds for their distinct structural features and great potential for further transformations [3]. Therefore, the synthesis of xanthene and xanthenone derivatives is of great importance [4]. The development of green and practical methods to construct these skeletons is still highly desired.

Recently, commercially available sodium triphenylphosphine-*m*-sulfonate (TPPMS) was developed as an ion-tagged reagent to mediate a facile Wittig reaction [5]. Afterwards, we demonstrated the use of the TPPMS/CBr_4 complex as a highly efficient catalyst system for the preparation of acetals from aldehydes, the tetrahydropyranylation of alcohols, and Friedel–Crafts alkylation of indoles with carbonyl compounds to produce bis(indolyl)alkane products (BIAs) (Scheme 1) [6]. These reactions utilize the TPPMS/CBr_4 system as a solid complex, which is stable and can be stored easily. The catalyst is soluble in relatively polar organic solvents but can be easily recovered from the reaction mixture by adding a non-polar solvent such as ether. Furthermore, the recovered catalyst can be reused. Multicomponent condensation reaction is a powerful tool for the construction of molecular complexity and structural diversity. Due to their use of one-pot and inherently simple experimental procedure, the development of more sustainable and greener multicomponent reactions is highly desired. As a part of our ongoing program to explore new catalytic activities for this solubility controllable TPPMS/CBr_4 complex, an efficient one-pot condensation of 2-naphthol with aldehydes to construct 14-aryl(alkyl)-14*H*-dibenzo[*a*,*j*]xanthenes derivatives and one-pot condensation of 2-naphthol with aldehydes and cyclic 1,3-dicarbonyl compounds to construct 12-aryl(alkyl)-8,9,10,12-tetrahydrobenzo[*a*]xanthen-11-one derivatives is introduced in this paper (Scheme 1).

2. Experimental

2.1. Typical procedure for the synthesis of 12-aryl(alkyl)-8,9,10,12-tetrahydrobenzo[a]xanthen-11-ones

A mixture of 1,3-dicarbonyl compounds (**3**, 1.2 mmol) and TPPMS/CBr_4 complex (0.05 mmol) was heated to 100 °C; 2-naphthol (**1**, 1 mmol) and the appropriate aldehyde (**2**, 1 mmol) were then added under stirring. After the reaction was completed (as indicated by TLC), DCM (2 mL) and ether (2 mL) were added successively, and the solid TPPMS/CBr_4 complex was recovered by

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http://dx.doi.org/10.1016/j.cclet.2014.01.023

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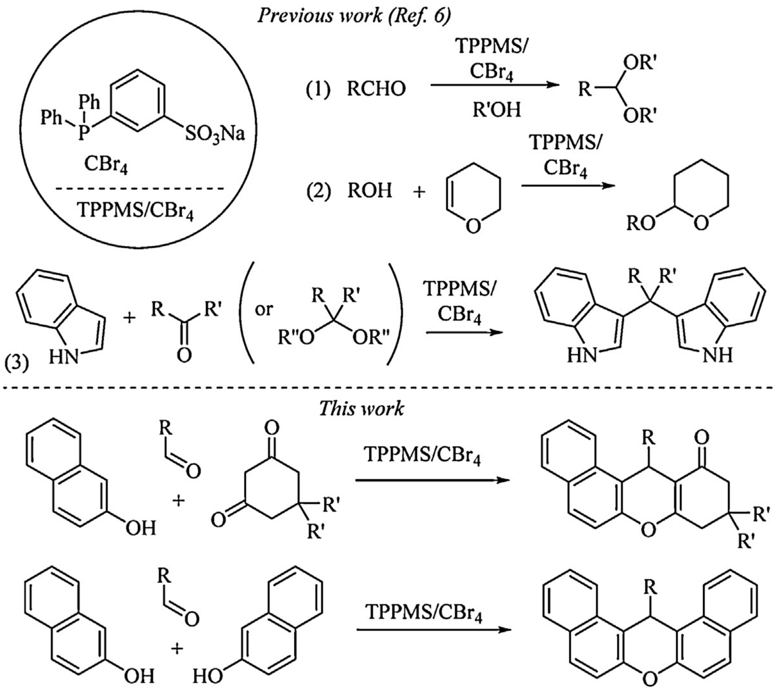


Scheme 1. Application of easily recoverable TPPMS/CBr_4 catalyst system.

filtration. The liquid filtrate was evaporated to give the corresponding products. Further purification by recrystallization or flash chromatography was required in some cases.

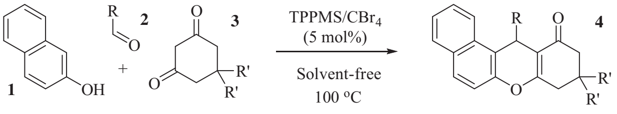
2.2. Typical procedure for the synthesis of 14-aryl(alkyl)-14H-dibenzo[a,j]xanthenes

A mixture of 2-naphthol (**1**, 2 mmol), the appropriate aldehyde (**2**, 1 mmol), and TPPMS/CBr_4 complex (0.1 mmol) was stirred at 110 °C. After the reaction was completed (as indicated by TLC), DCM (2 mL) and ether (2 mL) were added successively, and the solid TPPMS/CBr_4 complex was recovered by filtration. The liquid filtrate was evaporated and purified to give the corresponding products. Further purification by recrystallization or flash chromatography was required in some cases.

3. Results and discussion

Because a solvent-free protocol leads to a clean, efficient, and economical technology [7], a synthesis using solvent-free conditions was developed. The condensation reaction of 2-naphthol, benzaldehyde, and 5,5-dimethylcyclohexane-1,3-dione was first investigated under solvent-free conditions. After simple optimization of reaction conditions (TPPMS/CBr_4 5 mol%, 100 °C), designed tetrahydroxanthenone derivative **4a** was delivered with high yield (Table 1, entry 1). With the optimized conditions in hand, we then explored the generality and scope of this TPPMS/CBr_4 catalyzed transformation. The reactivity of various aldehydes was first examined as summarized in Table 1. In general, the TPPMS/CBr_4 complex was able to catalyze the reaction of both aryl and aliphatic aldehydes. Aryl aldehydes with electron-donating substituents and with electron-withdrawing substituents were all tolerant of the reaction conditions (Table 1, entries 2–10). The aldehydes with *ortho* or *meta* substituents delivered the corresponding xanthenones in high yields as well (Table 1, entries 4, 9, 10). The unprotected phenol group was tolerated in this reaction (Table 1, entry 5). The introduction of a halogen atom into this system made the methodology more useful for further transformation (Table 1, entries 6, 7). Aliphatic aldehydes also gave good yields of the corresponding xanthenones (Table 1, entries 11–13). The use of 1,3-cyclohexanedione in place of 5,5-dimethyl-1,3-cyclohexanedione also gave similar results, as shown in Table 1, entries 14–19. Encouraged by these good results, we next tested the condensation reaction of 2-naphthol with benzaldehyde to construct xanthene derivatives. After slight tuning of the reaction conditions (TPPMS/CBr_4 10 mol%, 110 °C), the desired product **5a** was achieved with complete conversion and an excellent isolated yield (Table 2, entry 1). The generality and scope of this transformation was also investigated, as shown in Table 2.

Table 1
Synthesis of 12-aryl(alkyl)-8,9,10,12-tetrahydrobenzo[*a*]xanthen-11-ones[a].



Entry	Aldehyde	R′	Time (min)	Product	Yield (%) [b]
1	C_6H_5CHO	Me	80	**4a**	84
2	4-MeC_6H_4CHO	Me	80	**4b**	86
3	4-$MeOC_6H_4CHO$	Me	40	**4c**	85
4	3-$MeOC_6H_4CHO$	Me	60	**4d**	82
5	4-OHC_6H_4CHO	Me	90	**4e**	79
6	4-ClC_6H_4CHO	Me	40	**4f**	85
7	4-BrC_6H_4CHO	Me	40	**4g**	85
8	4-$NO_2C_6H_4CHO$	Me	30	**4h**	90
9	3-$NO_2C_6H_4CHO$	Me	30	**4i**	86
10	2-$NO_2C_6H_4CHO$	Me	70	**4j**	83
11	$CH_3(CH_2)_3CHO$	Me	60	**4k**	84
12	$CH_3(CH_2)_5CHO$	Me	60	**4l**	81
13	$(CH_3)_2CHCHO$	Me	90	**4m**	78
14	C_6H_5CHO	H	60	**4n**	85
15	4-MeC_6H_4CHO	H	80	**4o**	84
16	4-$MeOC_6H_4CHO$	H	80	**4p**	85
17	4-ClC_6H_4CHO	H	40	**4q**	86
18	4-BrC_6H_4CHO	H	40	**4r**	87
19	4-$NO_2C_6H_4CHO$	H	30	**4s**	88

[a] Standard reaction conditions: **1** (1.0 mmol), **2** (1.0 mmol), **3** (1.2 mmol), TPPMS/CBr_4 (0.05 mmol), solvent-free, 100 °C.
[b] Isolated yields.

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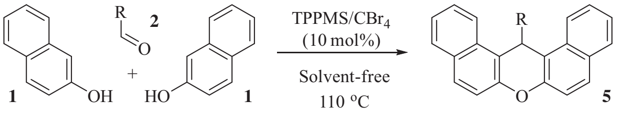
Table 2
Synthesis of 14-aryl(alkyl)-14*H*-dibenzo[*a*,*j*]xanthenes[a].



Entry	Aldehyde	Time (min)	Product	Yield (%) [b]
1	C_6H_5CHO	30	**5a**	90
2	$4\text{-}MeC_6H_4CHO$	20	**5b**	92
3	$4\text{-}MeOC_6H_4CHO$	30	**5c**	90
4	$3\text{-}MeOC_6H_4CHO$	50	**5d**	89
5	$4\text{-}OHC_6H_4CHO$	25	**5e**	91
6	$4\text{-}ClC_6H_4CHO$	20	**5f**	96
7	$4\text{-}BrC_6H_4CHO$	20	**5g**	97
8	$4\text{-}NO_2C_6H_4CHO$	15	**5h**	95
9	$3\text{-}NO_2C_6H_4CHO$	20	**5i**	95
10	$2\text{-}NO_2C_6H_4CHO$	40	**5j**	94
11	$CH_3(CH_2)_3CHO$	50	**5k**	88
12	$CH_3(CH_2)_5CHO$	50	**5l**	89
13	$(CH_3)_2CHCHO$	60	**5m**	86

[a] Standard reaction conditions: **1** (2.0 mmol), **2** (1.0 mmol), TPPMS/CBr_4 (0.05 mmol), solvent-free, 110 °C.
[b] Isolated yields.

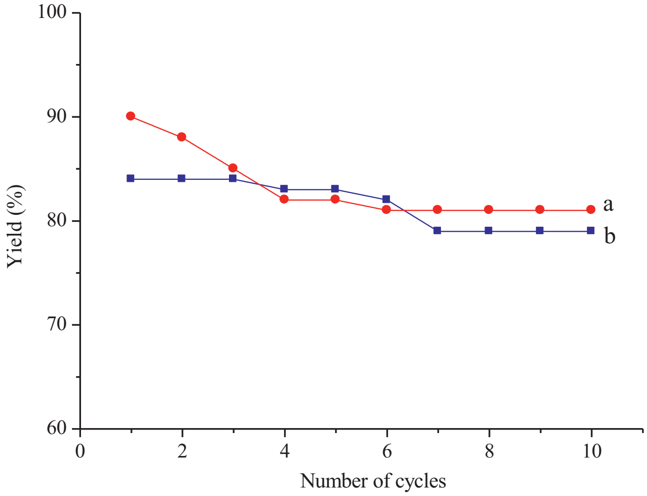


Fig. 1. Studying reusablility of TPPMS/CBr_4 in the synthesis of xanthenes and xanthenones.

In both of the reactions, the separation and recovery of the catalyst system was simply carried out by precipitation with DCM and ether after the reaction. The recovered catalyst could be reused without loss of catalytic activity. We demonstrated this with the reaction of 2-naphthol with benzaldehyde (Fig. 1, curve a) and the reaction of 2-naphthol with benzaldehyde and 5,5-dimethylcyclohexane-1,3-dione (Fig. 1, curve b) using recovered TPPMS/CBr_4 system for ten cycles without distinctly diminished yield.

To evaluate the practicality of our method [8], the reaction between 2-naphthol and benzaldehyde and the reaction between 2-naphthol, benzaldehyde and 5,5-dimethylcyclohexane-1,3-dione were performed on a larger scale (50 mmol) in a single batch, and no yield loss was observed (83%, 88% isolated yield respectively). That is to say, herein we present a practical and scalable synthetic entry to the xanthene and xanthenone derivatives.

4. Conclusion

In conclusion, we have demonstrated that the TPPMS/CBr_4 complex is a highly efficient catalyst for the preparation of 14-aryl(alkyl)-14*H*-dibenzo[*a*,*j*]xanthenes and 12-aryl(alkyl)-8,9,10,12-tetrahydrobenzo[*a*]xanthen-11-ones under solvent-free conditions. The catalyst is stable and can be stored easily. It is easily separable and can be recovered and reused without loss of catalytic activity for 10 cycles. Further applications of TPPMS/CBr_4 complex on the extension of this protocol are ongoing in our group.

Acknowledgments

We thank the National Natural Science Foundation of China (Nos. 21002080, 21262029) and the Specialized Research Fund for the Doctoral Program of Higher Education (No. 20106203120003) of the Education Ministry for financially supporting this work.

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