Tetrahedron Letters 54 (2013) 7053–7055

Contents lists available at ScienceDirect

Tetrahedron Letters

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

An unusual involvement of $NaIO_4$ in the acetylation of bisphenol during attempted oxidative acetylation

Deepak Singh, Pradeep T. Deota *

Department of Applied Chemistry, Faculty of Technology & Engineering, The Maharaja Sayajirao University of Baroda, Vadodara 390 001, India

ARTICLE INFO

Article history:
Received 16 September 2013
Revised 11 October 2013
Accepted 15 October 2013
Available online 23 October 2013

Keywords:
Bisphenols
Bis-cyclohexadienone
Oxidative acetylation
Acetylation
Bis-triquinane

ABSTRACT

An unexpected behaviour of compilation of reagent sodium metaperiodate in acetic anhydride for acetylation of bisphenols was observed during attempted oxidative acetylation of bisphenols for the synthesis of a bis-acetoxy cyclohexadienone. The products were characterized by their spectral and analytical data and a probable mechanism for acetylation involving role of $NaIO_4$ is proposed.

The cyclohexadienone ketals, quinols and its congeners have enormous synthetic potential for the creation of molecular complexity in a stereocontrolled manner.[1] The use of cyclohexadienones as building blocks has accelerated the development of new methods towards total syntheses of various polyquinanes and other families of natural products.[1,2] These natural products possess diverse chemical behaviour and interesting biological profiles.[1,2]

Among the natural products triquinanes, a subset of rapidly growing group of polyquinanes, have aroused worldwide interest among organic chemists due to their fascinating molecular architecture and potent biological activity.[2] As a result numerous synthetic approaches have been developed for the construction of triquinane natural products since their discovery.[3]

Recently in 2010 Opatz and co-workers have encountered the six new triquinane sesquiterpenoids.[4] Out of the six, two members have a different type of molecular architecture composed of two triquinane skeletons, recognized as bis-triquinanes. The presence of two tricyclic frameworks with different functional groups and stereochemical complexity has further enhanced the interest in this family of compounds.

Inspired by the above report, we recently reported a novel method for quick assembly of the basic bis-triquinane skeleton **4** from bis-cyclohexadienone **1** by Diels–Alder cycloaddition and photochemical oxa-di-π-methane rearrangement[5] (Scheme 1).

Literature records a number of methods for the synthesis of cyclohexadienones by oxidation of phenols using a variety of reagents.[6a–d] However there is no report on the synthesis of bis-cyclohexadienone of type **1** excepting our own.[7] Previously we reported the synthesis of bis-cyclohexadienones by oxidative acetylation of tetramethyl bisphenol-F using LTA in benzene.[7] During the course of our work, it was found that the reaction of bisphenol-F to bis-cyclohexadienone can also be accomplished in toluene instead of benzene which is known for its carcinogenity.[8] However this method also has certain limitations for the oxidation of higher members of bisphenols.

In the area of synthesis of acetoxy cyclohexadienone we have previously reported the use of reagent $NaIO_4$ in Ac_2O for the synthesis of various types of acetoxy cyclohexadienonesby oxidative acetylation of structurally different phenols.[9]

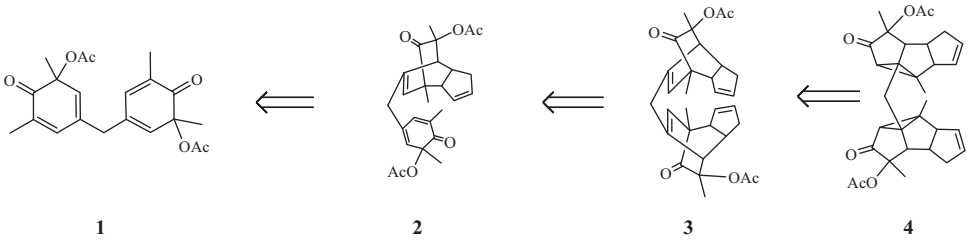
In search of another method, we explored the use of reagent $NaIO_4$ in Ac_2O for the synthesis of bis-acetoxy cyclohexadienones by oxidative acetylation of bisphenols. Thus bisphenol **5** was treated with $NaIO_4$ in Ac_2O at 75 °C for 3 h, which furnished the novel diacetates **10** rather than the expected bis-acetoxy cyclohexadienone **15**[12] (Scheme 2).

We then attempted the reaction of other bisphenols **6**–**9** under the same reaction conditions using $NaIO_4$ in Ac_2O. In all the cases only acylated products were obtained however no product from oxidative acetylation was isolated[12] (Scheme 2, Table 1).

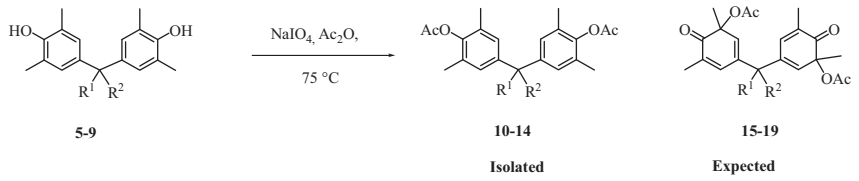
Literature records numerous reports in which $NaIO_4$ has been employed for the oxidation of phenols to cyclohexadienones and subsequent exploration towards the synthesis of a variety of

* Corresponding author. Tel.: +91 0265 2434188x415, 212; fax: +91 0265 2423898.
E-mail address: deotapt@yahoo.com (P.T. Deota).

0040-4039/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tetlet.2013.10.072



Scheme 1. Preparation of bis-triquinane **4** from bis-cyclohexadienone **1**.



5) R^1=CH_3, R^2=H; **6**) R^1=CH_3CH_2, R^2=H; **7**) R^1=$CH_3CH_2CH_2$, R^2=H; **8**) R^1=R^2=CH_3; **9**) R^1, R^2= -$(CH_2)_4$-

Scheme 2. Acetylation of bisphenol during attempted synthesis of bis-cyclohexadienone using $NaIO_4$ in Ac_2O.

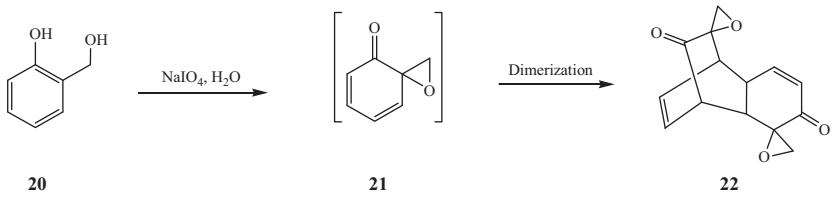
Table 1
Acetylation of bisphenols **5**–**9** using $NaIO_4$ in Ac_2O

Entry	Bisphenol	Diacetates	Time (h)	Yield (%)
1	5	10	3	88
2	6	11	3.5	87
3	7	12	3.5	87
4	8	13	4	84
5	9	14	4.5	88

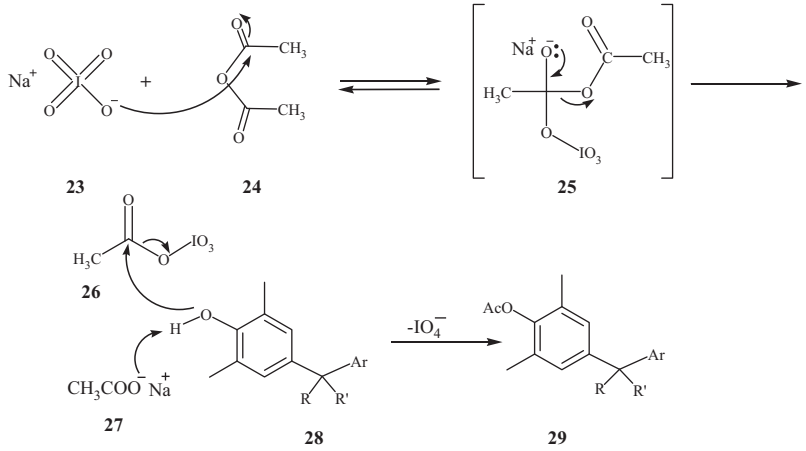
natural products[10,11] but there is no report for acetylation of phenol in the presence of $NaIO_4$.

Adler and Holmberg have first reported the syntheses of various types of cyclohexadienones from a wide variety of phenols with $NaIO_4$.[10] The spiroepoxy cyclohexadienones obtained by Adler oxidation of *o*-hydroxy benzyl alcohol have tremendous synthetic importance in the syntheses of triquinanes, ovalicin and other natural products[11] (Scheme 3).

It was thought that the acetylation of phenol might be taking place due to nucleophilic attack of phenolic OH on a carbonyl of acetic anhydride without the involvement of $NaIO_4$. To test this hypothesis, bisphenol **5** was heated under reflux in Ac_2O, however the formation of acetylated product was not observed. This indicated some role of $NaIO_4$ in the acetyaltion of bisphenol.



Scheme 3. Oxidation of phenol using $NaIO_4$.



Scheme 4. Acetylation of bisphenols using $NaIO_4$ in Ac_2O.

Table 2
The acetylation of bisphenol **5** in Ac_2O using different reagents

Entry	Reagent	Temp (°C)	Time (h)	Yield (%)
1	$NaIO_4$	75	3	88
2	KIO_4	75	1.5	90
3	CH_3COONa	120	3.5	82
4	CH_3COOH	118	6	80[a]

[a] The reaction did not reach completion, yield is based on the recovery of starting materials.

We have proposed a probable mechanism for the formation of the acetylated products of bisphenols (Scheme 4). Periodate perhaps attacks first on the carbonyl carbon of the anhydride **24** to generate sodium acetate **27** and ethanoylperiodate **26** via intermediate **25**. The sodium acetate thus formed is a conjugate base which initiates the nucleophilic reaction of bis-phenol **28** with ethanoylperiodate **26** to give the acetylated product **29**. Acetylation of two hydroxyls in the bisphenol molecule may be synchronous or stepwise.

In the support of the above proposed mechanism we have also studied the acetylation of bisphenol **5** in Ac_2O with KIO_4, CH_3COONa and CH_3COOH (Table 2).

It was found that the use of KIO_4 shortens the reaction time as compared to $NaIO_4$. This may be due to the formation of a conjugate base CH_3COOK that releases the acetate ion more easily than CH_3COONa. (Table 2) The reaction of **5** in Ac_2O with CH_3COONa requires higher temperature and a longer reaction time than with $NaIO_4$. This indicates the involvement of species **26** in acetylation during the reaction of bisphenols with $NaIO_4$ or KIO_4 in Ac_2O. We have also attempted the acetylation of **5** in Ac_2O in the presence of CH_3COOH. The reaction with CH_3COOH not only required a high temperature and longer time but did not reach completion even under reflux (Table 2).

This Letter presents the involvement of $NaIO_4$ in the acetylation of bisphenols and a probable mechanism is also proposed.

Acknowledgments

The authors are thankful to Prof. Neelima Kulkarni, Prof. S. R. Shah and Prof. A. V. Bedekar of the Department of Chemistry, Faculty of Science, The M. S. University of Baroda for their help in getting the NMR and mass spectral analysis.

References and notes

1. (a) Magdziak, D.; Meek, S. J.; Pettus, T. R. R. *Chem. Rev.* **2004**, *104*, 1383; (b) Singh, V. K. *Acc. Chem. Res.* **1999**, *32*, 324; (c) Hsu, D. S.; Chou, Y. Y.; Tung, Y. S.; Liao, C. C. *Chem. Eur. J.* **2010**, *16*, 3121; (d) Mcclure, C. K.; Kiessling, A. J.; Link, J. S. *Org. Lett.* **2002**, *5*, 3811.
2. (a) Mehta, G.; Srikrishna, A. *Chem. Rev.* **1997**, *97*, 671; (b) Liao, C. C.; Peddinti, R. K. *Acc. Chem. Res.* **2002**, *35*, 856; (c) Coleman, R. S.; Grant, E. B. *J. Am. Chem. Soc.* **1995**, *117*, 10889.
3. Comer, F. W.; Trotter, J. *J. Chem. Soc. Phys. Org.* **1966**, *1*, 11.
4. Liermann, J. C.; Schuffler, A.; Wollinsky, B.; Birnbacher, J.; Kolshorn, H.; Anke, T.; Opatz, T. *J. Org. Chem.* **2010**, *75*, 2955.
5. Singh, D.; Deota, P. T. *Tetrahedron Lett.* **2012**, *53*, 6527.
6. (a) Nemoto, T.; Ishige, Y.; Yoshida, M.; Kohno, Y.; Kanematsu, M.; Hamada, Y. *Org. Lett.* **2010**, *12*, 5021; (b) Zbiral, E.; Wessely, F.; Lahrmann, E. *Mh. Chem.* **1960**, *91*, 331; (c) Barton, D. H. R.; Brewster, A. G.; Ley, S. V.; Reed, C. M.; Rosenfeld, M. N. *J. Chem. Soc., Perkin Trans. 1* **1977**, 567; (d) Drutu, I.; Njardarson, J. T.; Wood, J. L. *Org. Lett.* **2002**, *4*, 493; (e) Singh, V.; Lahiri, S.; Kane, V. K.; Stey, T.; Stalke, D. *Org. Lett.* **2003**, *5*, 2199.
7. Deota, P. T.; Parmar, H. S.; Valodkar, V. B.; Upadhaya, P. R.; Sahoo, S. P. *Synth. Commun.* **2006**, *36*, 673.
8. Singh, D.; Deota, P. T. *Synth. Comm.* **2013**, *43*, 292.
9. Deota, P. T.; Upadhyay, P. R.; Parmar, H. S. *Synth. Commun.* **2005**, *35*, 1715.
10. (a) Adler, E.; Holmberg, K. *Acta Chem. Scand.* **1974**, *28B*, 465; (b) Adler, E.; Junghahn, L.; Lindberg, U.; Berggren, B.; Westin, G. *Acta Chem. Scand.* **1960**, *14*, 1261; (c) Adler, E.; Brasen, S.; Miyake, H. *Acta Chem. Scand.* **1971**, *25*, 2055; (d) Adler, E.; Dahlen, J.; Westin, G. *Acta Chem. Scand.* **1960**, *14*, 1580; (e) Adler, E.; Falkehag, I.; Smith, B. *Acta Chem. Scand.* **1962**, *16*, 529.
11. (a) Corey, E. J.; Dittami, J. P. *J. Am. Chem. Soc.* **1985**, *107*, 256; (b) Cabal, M. P.; Coleman, R. S.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1990**, *112*, 3253.
12. *Typical experimental procedure for the syntheses of diacetates of bisphenol (**10**–**14**)*: To a stirred solution of bisphenol (0.004 mol) in acetic anhydride (10 ml) was added sodium metaperiodate (1.28 g, 0.006 mol) in portions over a period of 15 min. Stirring was further continued for an appropriate time period (Table 1) while maintaining the reaction temperature at 75 °C. The reaction mixture was allowed to cool down to room temperature and then poured into a saturated solution of sodium bicarbonate (75 ml). The aqueous layer was then extracted with ethyl acetate (25 ml × 3) and organic extracts were washed with water (20 ml), brine (20 ml) and dried over anhydrous sodium sulphate. The solvent was removed under reduced pressure to give the crude product as a dark brown residue, which was chromatographed over a column of silica gel using a mixture of light petroleum/ethyl acetate furnished white solid as acylated product. (Scheme 2, Table 1) The structures of the products were confirmed by their analytical and spectral data that are given below.
*4-[1-(4-Acetoxy-3,5-dimethyl-phenyl)-ethyl]-2,6-dimethyl-phenyl ester (**10**)*: mp 112 °C. IR: (KBr): 3049, 1762, 1408, 1253 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.88 (4H, s, aromatic), 3.96 (1H, q, J = 2.6 Hz, CH), 2.31 (6H, s, $OCOCH_3$), 2.12 (12H, s, $4CH_3$), 1.54 (3H, d, J = 7.2 Hz, CH_3). MS (EI) m/z: Calcd for $C_{22}H_{26}O_4$ 354.18. Found: 354.08 (M^+).
*4-[1-(4-Acetoxy-3,5-dimethyl-phenyl)-propyl]-2,6-dimethyl-phenyl ester (**11**)*: mp 96 °C. IR: (KBr): 3140, 2985, 1774, 1190 cm^{-1}. ^1H (400 MHz, $CDCl_3$): δ 6.88 (4H, s, aromatic), 3.50 (1H, t, J = 7.6 Hz, CH), 2.30 (6H, s, $OCOCH_3$), 2.10 (12H, s, $4CH_3$), 1.97 (2H, m, CH_2), 0.82 (3H, t, J = 7.2 Hz, CH_3). MS (EI) m/z: Calcd for $C_{23}H_{26}O_4$ 368.47. Found: 368.11 (M^+).
*4-[1-(4-Acetoxy-3,5-dimethyl-phenyl)-butyl]-2,6-dimethyl-phenyl ester (**12**)*: mp 118 °C. IR: (KBr): 3045, 2852, 1762, 1240 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.89 (4H, s, aromatic), 3.71 (1H, t, J = 7.8 Hz, CH), 2.29 (6H, s, $OCOCH_3$), 2.10 (12H, s, $4CH_3$), 1.92 (2H, m, CH_2),1.25 (2H, m, CH_2), 0.90 (3H, t, J = 7.4 Hz, CH_3). MS (EI) m/z: Calcd for $C_{24}H_{28}O_4$ 382.49. Found: 382.12 (M^+).
*4-[1-(4-Acetoxy-3,5-dimethyl-phenyl)-1-methyl-ethyl]-2,6-dimethyl-phenyl ester (**13**)*: mp 138 °C. IR: (KBr): 3028, 1764, 1402 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.89 (4H, s, aromatic), 2.31 (6H, s, $OCOCH_3$), 2.09 (12H, s, $4CH_3$), 1.59 (6H, s, $2CH_3$). MS (EI) m/z: Calcd for $C_{23}H_{28}O_4$ 368.2. Found: 368.10 (M^+).
*4-[1-(4-Acetoxy-3,5-dimethyl-phenyl)-1-cyclopentyl]-2,6-dimethyl-phenyl ester (**14**)*: mp 160 °C. IR: (KBr): 3028, 1764, 1402 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.49 (4H, s, aromatic), 2.34 (6H, s, $OCOCH_3$), 2.14 (12H, s, $4CH_3$), 1.84 (4H, m, CH_2), 1.61 (4H, m, CH_2). MS (EI) m/z: Calcd for $C_{25}H_{30}O_4$ 394.5. Found: 394.21 (M^+).