Pergamon

Tetrahedron Letters, Vol. 38, No. 12, pp. 2191-2194, 1997
© 1997 Elsevier Science Ltd
All rights reserved. Printed in Great Britain
0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)00279-7

Novel Cerium(IV) Ammonium Nitrate Induced Dimerization of Methoxystyrenes

Vijay Nair*[a], Jessy Mathew[a], Puthuparampil P. Kanakamma[a], Sreeletha B. Panicker[a], V. Sheeba[a], S. Zeena[a] and Guenter K. Eigendorf[b]

[a]Organic Chemistry Division, Regional Research Laboratory(CSIR), Trivandrum-695 019
[b]Department of Chemistry, University of British Columbia, Vancouver, Canada, V6 T 1ZI

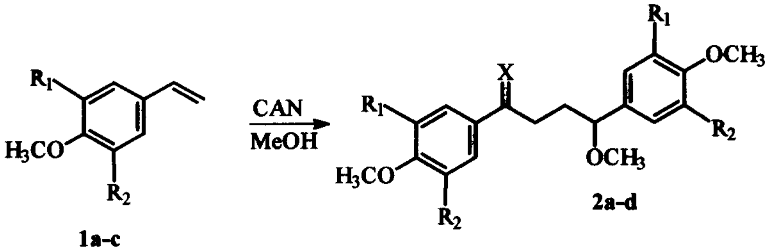
Abstract: *Methoxystyrenes undergo facile dimerization when treated with Cerium (IV) ammonium nitrate in methanol; cyclized products are obtained in acetonitrile.* © 1997 Elsevier Science Ltd.

Electron transfer induced C-C bond forming reactions have been widely accepted in organic synthesis[1]. Of the different methods available for electron transfer, electrochemical reactions and photosensitized electron transfer (PET) have received considerable attention. In contrast, however, chemical electron transfer (CET) reactions have come to the fore only recently. The CET mediated dimerization of N-vinylcarbazoles[2] and the recent work on C-C bond forming reactions involving cation radicals generated from alkoxy arenes[3-5] and bicyclo[2.1.0]pentanes[6], are examples of investigations[1] in this area.

Although there has been substantial amount of work on oxidative addition reactions mediated by Cerium (IV) Ammonium Nitrate[7-10], there is only scant information available on C-C bond forming reactions involving cation radicals generated by Ce(IV)[11-13]. We have initiated some investigations in this area and our preliminary resusits on CAN induced dimerization of methoxystyrenes, presumably *via* cation radicals[14] and the further transformations of the dimeric species are reported here.

4-Methoxystyrene on treatment with CAN in methanol afforded the products **2a** and **2d** in 40% and 34% yields respectively. Similar results were obtained with 4,5-dimethoxy and 3,4,5-trimethoxystyrenes, when the reaction was carried out in methanol (Scheme 1). The reaction of 4-methoxystyrene with CAN in acetonitrile took a different course leading to the cyclized products **3a**[15] and **4**[16] (Figure 1)[16]. 4,5-Dimethoxystyrene and 3,4,5-trimethoxystyrene under similar conditions afforded exclusively the tetralin derivatives **3b** and **3c** respectively.

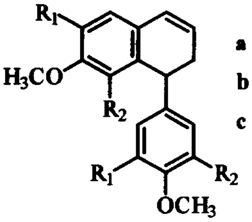
The formation of **2a** and **2d** may be rationalized as follows. Methoxystyrene gets oxidised by CAN to the cation radical **5** which then adds to another molecule of methoxystyrene leading to the intermediate **6**. Methanol addition to **6**, oxidation of the resulting radical **7** to the cation **8** and subsequent trapping of **8** by methanol would furnish **2a** (scheme 2). Dimerization of cation radical **5** followed by trapping of the dication



$R_1 = R_2 = H$
$R_1 = OCH_3$; $R_2 = H$
$R_1 = R_2 = OCH_3$

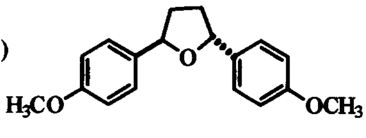
a $R_1 = R_2 = H$ X =H, OCH_3 (40%)
b $R_1 = OCH_3$; $R_2 = H$, X =H, OCH_3 (74%)
c $R_1 = R_2 = OCH_3$, X =H, OCH_3 (45%)
d $R_1 = R_2 = H$, X= O (34%)
e $R_1 = OCH_3$; $R_2 = H$, X = O (5%)

Scheme 1



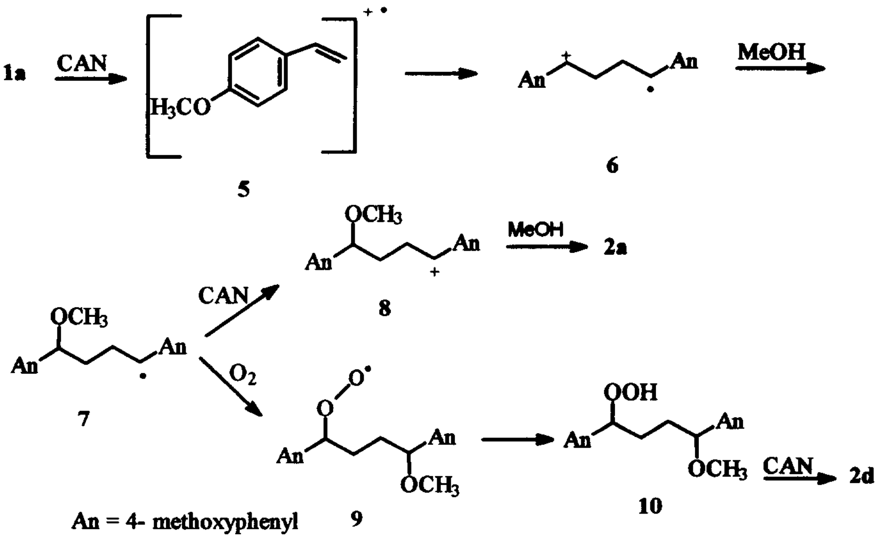
3a-c

a $R_1 = R_2 = H$ (22%)
b $R_1 = OCH_3$; $R_2 = H$ (34%)
c $R_1 = R_2 = OCH_3$ (54%)



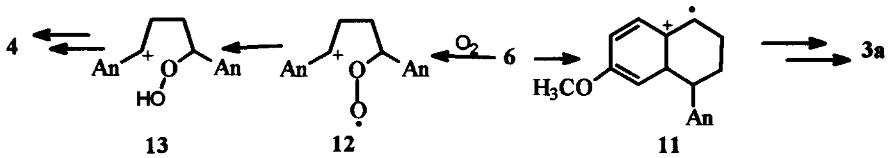
4 (41%)

Figure 1



An = 4- methoxyphenyl

Scheme 2



Scheme 3

by methanol is also a valid possibility. Alternately radical **7** may be trapped by molecular oxygen[17,18] to give the peroxyl radical **9** which will be easily converted to the hydroperoxide **10**. The latter on oxidative fragmentation would produce **2d**.

While the mechanistic details for the formation of **3a** and **4** remain obscure, rationalizations along the following lines may be made (scheme 3). The intermediate **6** can add on to aromatic system leading to **11**, loss of a proton followed by further oxidation would give **3a**. Trapping of **6** by molecular oxygen leading *via* **12** to the hydroperoxy species **13** and further transformation of the latter can conceivably give rise to **4**.

In conclusion, it appears from this study that the CAN mediated dimerization of methoxystyrenes is an attractive C-C bond forming process; the experimental simplicity and mild reaction conditions are noteworthy. It is anticipated that this method will find wide applications in organic synthesis especially in the synthesis of lignans and other polycyclic natural products.

General experimental procedure:

A solution of CAN (1.32 g, 2.27mmol) in methanol (15mL) was added dropwise to an ice cold solution of 4-methoxystyrene **1a** (0.25g, 1.86 mmol) in methanol (10 mL) and stirred for 30 min. The reaction mixture was diluted with water (100 mL) and extracted with CH_2Cl_2. (3x60 mL). The combined extracts were washed with water, brine, dried over Na_2SO_4 and evaporated. . The residue on column chromatography using ethyl acetate in hexane as eluent afforded **2a** (colourless solid, 0.125g, 40%) and **2d** (pale yellow solid, 0.1g, 34%). Recrystallization from hexane-ethyl acetate mixture gave colourless crystals of **2a** (mp. 98-100°C) and pale yellow crystals of **2d** (mp. 107-108°C).

1,4-bis (methoxy-4'-methoxy phenyl) butane **(2a)**- IR (KBr) ν_{max} 2961, 1615, 1160 cm^{-1}; ^1H NMR (300 MHz) δ 7.04 (d, J = 8.6 Hz, 4 H, ArH), 6.74 (d, J = 8.6 Hz, 4 H, ArH), 3.89-3.86 (m, 2 H, $-C\underline{H}-OCH_3$), 3.69 (s, 6 H, $-OCH_3$), 3.03 (s, 6 H, $-OCH_3$), 1.62-1.60 (m, 4 H, $-CH_2$); ^{13}C NMR (75.5 MHz) δ : 159.28, 134.53, 128.12, 128.05, 113.99, 113.95, 83.83, 56.59, 55.47, 34.83; GC-MS *m/z*, 298 (M^+-OCH_3-1, 5), 266 (4), 227 (5), 166 (25), 151 (100), 135 (15). Anal calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.64; H, 8.15.

1,4-bis (4'-methoxyphenyl)-4-methoxy-butan-1-one **(2d)**. IR (KBr) ν_{max} 2954, 1676, 1604, 1258 cm^{-1}; ^1H NMR (300 MHz) δ 7.85-7.82 (m, 2 H, ArH), 7.18-7.14 (m, 2 H, ArH), 6.85-6.79 (m, 4 H, ArH), 4.10 (dd, J = 7.7, 5.5 Hz, 1 H, $-CHOCH_3$), 3.12 (s, 3 H, $-OCH_3$), 2.89 (t, J = 7.2 Hz, 2 H, $-CH_2$), 2,10-2.01 (m, 2 H, $-CH_2$); ^{13}C NMR (75.5 MHz) δ 198.83, 163.60, 159.39, 134.14, 130.52, 130.47, 128.06, 114.09, 113.89, 82.74, 56.68, 55.66, 55.49, 34.55, 32.82 Anal. Calcd for $C_{19}H_{22}O_4$: C, 72.59; H7.05. Found: C, 72.38; H, 7.02.

A solution of CAN (1.23 g, 2.23 mmol) dissolved in acetonitrile (15 mL) was added dropwise to a solution of 4-methoxystryene (0.250 g, 1.86 mmol) at 0°C and stirred for 30 min. The reaction mixture was worked up as described above. The residue on column chromatography using ethyl acetate in hexane afforded **3a**

(colourless oil,0.03g,12%) and 4 (colourless solid, 0.112g, 42%). 4 on crystallization from hexane-ethyl acetate mixture furnished colourless needles, mp. 79-80°C. Spectral data of 4: IR (KBr) ν_{max} 2937, 2869, 1515, 1248, 1035 cm^{-1}. ^1H NMR (90MHz) δ 7.57.25 (m,2H), 7.0-6.8 (m,2H), 5.3-4.8 (m,2H), 3.75 (s,6H), 2.55-1.80 (m,4H); ^{13}C NMR (22.4MHz) δ 158.84,135.71,135.06,127.27, 126.28, 113.73, 80.85, 55.22, 35.53, 34.34; HRMS exact mass calcd for $C_{18}H_{20}O_3$: 284.1412; Found: 284.1408.

Acknowledgemets

Financial support by CSIR (J.M) and American Cynamid Co., USA (V.S.) is gratefully acknowledged. We also thank Prof. Abhijit Mitra, Manhattan College, New York for high resolution NMR spectra.

References

1. Reviews a). Dalko, P. I.*Tetrahedron*,**1995**, *51*, 7579 .(b) Bauld, N. L. *Tetrahedron*,**1989**, *45*, 5307 .
2. Bell, F. A.; Crellin, R. A.; Fugi, N.; Ledwith, A. *J. Chem. Soc., Chem.Commun.*, **1969**, 251.
3. Kita, Y.; Gyoten, M.; Ohtsubo, M.; Tohma, H.; Takada, T. *J. Chem. Soc., Chem. Commun.*, **1996**, 1481.
4. Pelter, A.; Ward R. S.; Abd-el-Ghani, A.*J. Chem. Soc., Perkin Trans. 1*, **1996**, 1353.
5. Brede, O.; David, F.; Steenken, S. *J.Chem. Soc., Perkin Trans 2*, **1995**, 23
6. Adam, W.; Corma, A.; Miranda, M. A.; Sabater-Picot, M. -J C. Sahin., *J. Am. Chem. Soc.*, **1996**, *118*, 2380.
7. (a) Heiba, E. I.; Dessau, R. M. *J. Am. Chem. Soc.*, **1971**, *93*, 524, 995. (b) *ibid*, **1972**, *94*, 2888.
8. Kurz, M. E.; Baru, V.; Ngugen, P. N.; *J. Org. Chem.*, **1984**, *49*, 1603.

9 (a) Baciocchi, E.; Ruzziconi, R.; Aira, D. D. *Tetrahedron Lett.*, **1986**, *27*, 2763, 1645.
(b) Baciocchi, E.; Ruzziconi, R. *J. Org. Chem.* **1986**, *51*, 1645. (c) Baciocchi, E.; Civatarese, G.; Ruzziconi, R. *Tetrahedron Lett.*, **1987**, *28*, 5357 and references cited therein.

10 (a) Nair, V.; Mathew, J. *J. Chem. Soc., Perkin Trans. 1*,**1995**, 187.
(b) Nair, V.; Mathew, J. *J. Chem. Soc., Perkin Trans. 1*, **1995**, 1881.
(c) Nair, V.; Mathew, J.; Radhakrishnan, K. V. *J. Chem. Soc., Perkin Trans. 1*,**1996**, 1487.

11 Cossy, J.; Bouzide, A.; *J. Chem. Soc., Chem. Commun.*, **1993**,1218. 31.

12. Narasaka, K.; Okauchi, T.; Tanaka, K.; Murakami, M. *Chem. Lett.*, **1992**, 2099.
13. (a) Baciocchi, E.; Casu, A.; Ruzziconi, R. *Tetrahedron Lett.*,**1989**, *30*, 3707. (b) Baciocchi, E.; Casu, A.; Ruzziconi, R. *Synlett*, 1990, 679. (c) Snider, B. B.; Kwon, T. *J. Org. Chem.*, **1990**, *55*, 4786 . (d) Paolobelli, A. B.; Latini, D.; Ruzziconi, R. *Tetrahedron Lett.*,**1993**, *34*, 721.
14. Styrenes on oxidation with CAN has been shown to give rise to cation radicals. Interestingly, however, no C-C bond formation of these cation radicals was observed. Baciocchi, E.; Rol,C.; Sebastiani G.; Zampini, A. *J. Chem. Soc.,Chem. Commun.*, **1982**, 1045
15. 4-methoxystyrene under PET conditions has been reported to give the substituted dihydronaphthalene derivative **4a** and a cyclobutane derivative. Schepp, N. P.; Johnston, L. J. *J. Am. Chem. Soc.*,**1994**, *116*, 6895. See also *ibid*, **1996**, *118*, 2872.
16. The stereochemical assignment for **4** is tentative, but based on the reasonable assumption that reaction conditions favor the formation of the trans dihydrofuran which is more stable than the *cis*.

17 Frimer, A. A. in 'Singlet Oxygen', Vol II, CRC Press,1985 p.227.

18. The absence of **3a** in experiments conducted under argon atmosphere lends credence to this argument.

(*Received in UK* 28 *January* 1997; *accepted* 7 *February* 1997)