SHORT PAPER

J. Chem. Research (S), 2001, 430–432

Cation radical mechanisms — α, β, γ - tribenzoyloxylation of 2-allyl-1,4,5-trimethoxybenzene†

Yu Zhao, Wei Li and Chengxue Zhao*

Department of Chemistry, Shanghai Jiaotong University, 800 Dongchuan Road, Minhang, Shanghai 200240, China

Threo- and erythro-1-(2,4,5,-trimethoxyphenyl-1,2,3-tri(4-nitro) benzoyloxypropanes were formed in a one-electron transfer reaction between 2-allyl-1,4,5-trimethoxybenzene and 4-nitrobenzoyl peroxide and a mechanism is proposed for this very unusual, subtle reaction.

Keywords: α, β, γ-tribenzoylation, 2-allyl-1,4,5-trimethoxybenzene

The important radical pathways of radical cations include deprotonation, ring-substitution, fragmentation, dimerisation, oxidation and reduction.[1-4] Olefin radical cations are of particular interest since they undergo a variety of reactions. For instance, styrene radical cations generated by photo-induced electron transfer (PET) are subjected to intensive study both on product analysis and kinetics. Their addition to a precursor olefin to give a dimer radical cation and their intermolecular as well as intramolecular additions are well known.[5-7] The additions of anionic and neutral nucleophiles to these olefinic radical cations gave *α, β,* -addition products and their rates were measured by time resolved spectrometers.[8]

Previously, we have reported that by using diacyl peroxides [$(C_6F_5CO_2)_2$, $(ArCO_2)_2$ or $(R_fCO_2)_2$] as one-electron oxidants of methoxybenzenes, the corresponding arene radical cation was generated with a nucleophile ($C_6F_5COO^-$, $ArCOO^-$ or R_fCOO^-) and a radical ($C_6F_5COO^{\cdot}$, $ArCOO^{\cdot}$ or $R_fCOO^{\cdot}$/ $R_f^{\cdot}$) in the original solvent cage[9,10] and many mechanistic details of the methoxybenzene radical cations have been disclosed.[11,12] We wondered whether the olefinic radical cations of variously ring-substituted styrenes could be readily generated or not in their reactions with diacyl peroxides. Our preliminary results showed that in the oxidation of 2-propenyl-1,4-dimethoxybenzene and 2-propenyl-1,4,5-trimethoxybenzene by 4-nitrobenzoyl peroxide, while the former underwent preferably ring-benzoyloxylation, the latter (with one more ring-substituted methoxy group) gave only an *α, β,* -dibenzoyloxylation product. Nevertheless, we believe, the similar olefinic radical cation intermediates must be involved in the reactions.[13]

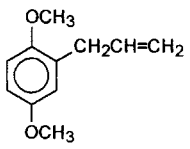
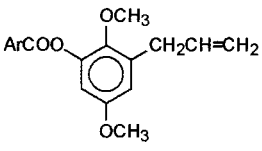
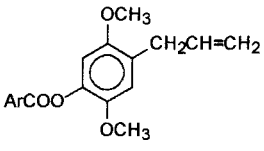
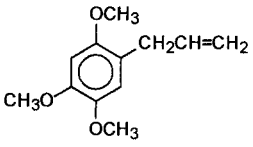
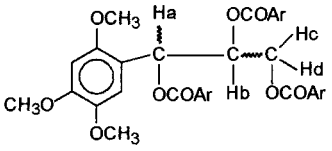
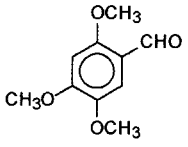
In the present work, 2-allyl-1,4-dimethoxybenzene (**1**) and 2-allyl-1,4,5-trimethoxy-benzene (**2**) were prepared as the

Table 1 Decomposition rate constants of 4-nitrobenzoyl peroxide **3**[a] in the presence of substates **1** or **2** in CH_3CN

Substrate	Initial concentration	$T \pm 0.1$/°C	$k_1 \times 10^4$/s^{-1}	$t_{1/2}$/min
None[b]	–	80	0.507	228
1	0.25 M	44.4	2.81	41
2	0.05 M	14.3	5.23	22

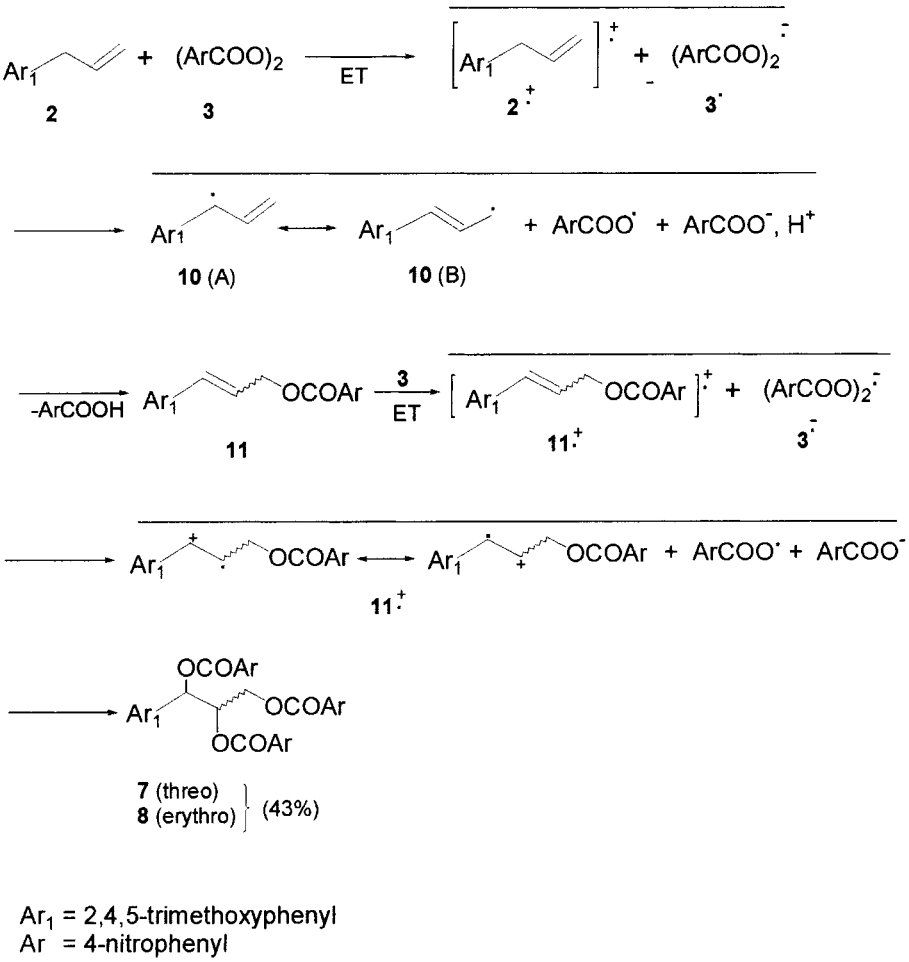
[a]Initial concentration of **3**, 0.01M.
[b]Initial concentration of **3**, 0.02M (ref. 9)

Table 2 Products and their distribution of reactions of **1** or **2**[a] with $(ArCOO)_2$ **3**[b] in CH_3CN[c]

Substrate	Product			T/°C
			ArCOOH	40
1	**4** (43%)	**5** (51%)	**6** (95%)	
			ArCOOH	25
2	**7**(threo-) + **8**(erythro-) (43%)	**9** (3%)	(55%)	

[a] 45% **2** was recovered.
[b] Molar ratio **1** (or **2**): **3** = 1:1.
[c] Ar stands for 4-$O_2NC_6H_4$-.

* To receive any correspondence. E-mail: kmlrai@yahoo.com.
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*



Scheme 1

representative substrates in the mechanistic study on their one-electron oxidation by 4-nitrobenzoyl peroxide **3**. The pseudo-first order rate constants for thermal decomposition of peroxide **3** (0.01 M in CH_3CN) in the presence of **1** (0.25M) or **2** (0.05M) are found to be 2.81×10^{-4} s^{-1} at 44.4 °C ($t_{1/2}$ = 41 min) and $5.23\times 10^{-4}s^{-1}$ at 14.3 °C ($t_{1/2}$ = 22 min), respectively (see Table 1).

The reported unimolecular decomposition rate of **3** in dilute acetonitrile solution (~0.02M) at 80 °C is $5.07\times 10^{-5}s^{-1}$ ($t_{1/2}$ = 228 min).[9] Therefore, such a significant acceleration of peroxide decomposition should be taken as an indication of a bimolecular election-transfer process between the donor (**1** or **2**) and peroxide **3**.

Notably, donor **2** bearing one more electron releasing methoxy substituent on the ring compared with donor **1**, reacted at a rate of nearly twice of that of **1** at much lower temperature and smaller molar ratio. The only reason for such a rate difference is the lower oxidation potential of donor **2** than **1**. This is a good example to show that the oxidation potential of the substrate is really a main factor in affecting the rate of electron transfer process.

For the products, at first we expected that both the radical cations $\mathbf{1}^{+\cdot}$ and $\mathbf{2}^{+\cdot}$ generated in an electron transfer step may deprotonate from the α-carbons and lead to α-benzoyloxylation. However, deprotonation did not take place in the reaction of donor **1**. No benzoyloxylation product was found but ring-substitution products (**4** + **5**) were formed with a yield of 94%. For the reaction of **2**, very unusual α, β, γ-tribenzoyloxylated products, namely, *threo*-1-(2,4,5-trimethoxy)phenyl-1,2,3-tri (4-nitro) benzoyloxypropane **7** and *erythro*-1-(2,4,5-trimethoxy) phenyl-1,2,3-tri(4-nitro) benzoyloxypropane **8** were formed with almost one-half (45%) of the substrate recovered (see Table 2). By column chromatography on silica gel, **7** (*threo*) and **8** (*erythro*) were isolated and characterised. Their molar ratio (1:1) was determined by ^{1}H NMR integrations in the reaction mixture. The doublet at δ 6.87 ppm is reasonably assigned to **H**a (see Table 2) in the *threo* isomer **7** for its bigger coupling constant (J = 8.5Hz) and the chemical shift of **H**a in *erythro* isomer **8** appeared at δ 6.83 ppm with a smaller coupling constant (J = 4.7Hz). The two methylene protons at $\mathbf{C}_\gamma$ (**H**c and **H**d) of both diastereomers are unequivalent and show AB type doublets of doublets with very similar coupling constants ($J_{gem} \approx 12$ Hz).

A reasonable mechanism can be proposed for the reaction of **1**: since no significant steric hindrance is felt at C_5 and C_6 of the phenyl ring, the ring-substitution has an advantage over the deprotonation[13] and thus the side C=C bond remains unreacted. For reaction of **2**, much mechanistic details can be told based on the very unusual main products and interesting stochiometry. The formation of **7** and **8** may involve several elementary steps: caged radical-ion pair $\mathbf{2}^{+\cdot}$ / $\mathbf{3}^{-\cdot}$ is generated via electron transfer from **2** to **3.** After separation of such a radical-ion pair, radical anion $\mathbf{3}^{-\cdot}$ collapses into 4-$O_2NC_6H_4COO^-$ and 4- $O_2NC_6H_4COO^{\cdot}$, and radical cation $\mathbf{2}^{+\cdot}$ deprotonates to give radical **10**. Benzoyloxylation of radical **10** takes place and generates a neutral intermediate substrate **11**. After fast diffusion from cage, **11** is oxidised by **3** in the second ET process generating a new radical cation $\mathbf{11}^{+\cdot}$. Then

both radical benzoyloxylation and nucleophilic benzoyloxylation take place and finally lead to the formation of two α, β, γ, -tribenzoyloxylated diastereomers **7** and **8** (molar ratio, 1:1).The aldehyde **9** is formed in a small amount via C_α–C_β cleavage of the corresponding radical cation. A tentative mechanism is proposed in Scheme 1.

According to the mechanism proposed, the reaction involves two electron-transfer steps. The donor involved in the second ET process, $Ar_1CH{=}CHCH_2OCOAr$ (**11**), is conceivably the product generated in the first ET-reaction. This assumption is well rationalised by the interesting stochiometry of the overall reaction. Since unimolecular decomposition of peroxide **3** at room temperature is negligible, the disappearance of the peroxide should be a consequence of its electron transfer reaction with the donor. The reaction started at a molar ratio of **2**:**3** = 1:1 and was completed with almost one half (45%) of donor **2** recovered. The recovery of the donor is a strong indication of the involvement of the second ET step with a greater reaction rate. As mentioned above, an ET reaction exhibits a faster rate toward the donor with lower oxidation potential. For intermediate $Ar_1CH{=}CHCH_2OCOAr$ (**11**), with the expanded conjugation system and hence lower oxidation potential than donor **1**, oxidation by peroxide **3** should take place much faster than oxidation of the starting material **1**. Besides, these two ET steps occur at much lower rates than other elementary steps: deprotonation, radical recombination and nucleophilic addition.

Furthermore, the yield of 4-nitrobenzoic acid of the overall reaction is 55%. This is because the nucleophile, 4-nitrobenzoate generated in ET-steps, is consumed partly in the nucleophilic addition to the olefinic radical cation and partly by neutralisation by the proton released in the deprotonation of radical cation $\mathbf{2}^{+\cdot}$.

Experimental

IR spectra were taken on a Perkin Elmer Joel 983 spectrometer. ^{1}H NMR spectra were recorded in $CDCl_3$ solutions on a Bruker AM 300 spectrometer with Me_4Si as the internal standard. The quantitative product analyses were conducted on the same NMR apparatus [using $(CD_3)_2SO$ as solvent] and on a Model 102 gas chromatograph (Shanghai Analytical Instrument Works). MS spectra were recorded on a HP 5989 A instrument and elemental analyses were determined using a Hitachi analyser.

4-Nitrobenzoyl peroxide (**3**) was prepared from the corresponding acid chloride by the procedure described previously[14] and recrystallised from toluene (purity > 99% by iodometry). Donor substrate 2-allyl-1,4-dimethoxybenzene (**1**) was prepared by two operations: Claisen rearrangement of 4-methoxyphenyl allyl ether, followed with methylation by using CH_3I and purification by column chromatography on silica gel. 2-Allyl-1,4,5-trimethoxybenzene (**2**) was prepared by following the reported procedure.[15]

The determination of decomposition rates of **3** in the presence of **1** or **2** in acetonitrile, was carried out by standard iodometry: each of eight degassed sealed vials [containing 2.0ml CH_3CN solution of **1** (or **2**) + **3**] maintained in a thermostat (for **1** + **3** at 44.4 ± 0.1°C), molar ratio, 25:1; for **2** + **3** at 14.3 ± 0.1 °C, molar ratio 5:1) was taken out at each time interval and the remaining peroxide **3** was determined by iodometry. The pseudo-first order rate constants were obtained by linear regression.

The reactions of substrates (0.4 mmol) with peroxide **3** (0.4 mmol) were completed in 10ml of acetonitrile overnight at 40 ± 2 °C (for **1)** and 25 ± 2 °C (for **2)**. Then the solvent was removed and the residue was isolated by column chromatography on silica gel (petroleum ether/dichloromethane as binary eluent) and the pure compounds were characterised .

1-Allyl-2,4,5-trimethoxybenzene (**2**): m.p. 25 °C; ^{1}H NMR: 6.61 (s, 1H, aromatic), 6.43 (s, 1H, aromatic), 5.92-5.81 (d × d × t, *J* = 15.9 Hz, 11 Hz, 6.5 Hz, 1H, -C**H** =), 4.99–4.92 (m, *J* = 15.9 Hz, 11 Hz, 1.5 Hz, 2H, = C$\mathbf{H}_2$), 3.79 (s, 3H, OC$\mathbf{H}_3$), 3.74 (s, 3H, OC$\mathbf{H}_3$), 3.71 (s, 3H, OC$\mathbf{H}_3$), 3.24 (d × d, *J* = 6.5 Hz, 1.5 Hz, 2H, benzylic).

3-Allyl-2,5-dimethoxyphenyl 4-nitrobenzoate (**4**): m.p. 77–77.5°C; ^{1}H NMR 8.42 and 8.38 (AA′BB′ system, *J* = 6.8 Hz, 4H, aromatic), 6.70 (d, *J* = 3.0Hz, 1H, aromatic), 6.65 (d, *J* = 3.0Hz, 1H, aromatic), 6.07-5.93 (d × d × t, *J* = 16.6Hz, 10.4Hz, 6.5Hz, 1H, -C**H**=), 5.14–5.09 (m, *J* = 16.6Hz, 10.4Hz, 1.5Hz, 2H, = C$\mathbf{H}_2$), 3.77 (s, 3H, OC$\mathbf{H}_3$), 3.70 (s, 3H, OC$\mathbf{H}_3$), 3.45 (d, *J* = 6.5Hz, 2H, benzylic); MS (EI): 344, 343 (M^+), 193, 150 (base), 104, 92, 76; IR (KBr), *v*: 1743, 1606, 1527, 1432, 1347, 1266, 1219, 876, 858; Anal. Calcd for $C_{18}H_{17}NO_6$: C, 62.97; H, 4.99; N, 4.08; Found: C, 62.96; H, 4.87; N, 3.90.

*4-Allyl-2,5-dimethoxyphenyl 4-nitrobenzoat***e** (**5**): m.p. 105.5–106.5°C; ^{1}H NMR: 8.39 and 8.33 (AA′BB′ system, *J* = 6.9Hz, 4H, aromatic), 6.86 (s, 1H, aromatic), 6.74 (s, 1H, aromatic), 6.06–5.92 (d × d × t, *J* = 16.7Hz, 10.5Hz, 6.6 Hz, 1H, -C**H** =), 5.12–5.07 (m, *J* = 16.7Hz, 10.5Hz, 1.5Hz, 2H, =C$\mathbf{H}_2$), 3.79 (s, 3H, OC$\mathbf{H}_3$), 3.77 (s, 3H, OC$\mathbf{H}_3$), 3.40 (d, *J* = 6.6Hz, 2H, benzylic); MS (EI): 344, 343 (M^+), 193, 150 (base), 104, 92, 76; IR (KBr), *v*: 1744, 1636, 1606, 1510,1454, 1408, 1348, 1264, 1220, 922, 878, 860; Anal. Calcd for $C_{18}H_{17}NO_6$: C, 62.97; H, 4.99; N, 4.08; Found: C, 63.20; H, 5.08; N, 4.02.

Threo-*1-(2,4,5-trimethoxy)phenyl-1,2,3-tri(4-nitro)benzoyloxypropane* (**7**): m.p. 167–168°C**;** ^{1}H NMR: 8.40–8.07 (m, 12H, aromatic), 6.98 (s, 1H, aromatic), 6.87 (d, *J* = 8.5 Hz, 1H, **H**a), 6.55 (s, 1H, aromatic), 6.16-6.12 (m, 1H, **H**b), 4.61 (d × d, *J* = 12.3Hz, 3.4Hz, 1H, **H**c), 4.53 (d × d, *J* = 12.3Hz, 6.1Hz, 1H, **H**d), 3.90 (s, 3H, OC$\mathbf{H}_3$), 3.87 (s, 3H, OC$\mathbf{H}_3$), 3.79 (s, 3H, OC$\mathbf{H}_3$); MS (EI): 705 (M^+), 538, 388, 167, 150 (base), 104, 76; IR (KBr), *v*: 1726, 1610, 1520, 1466, 1352, 1269, 1236. The structural assignment of **7** is tentative but expected to be correct in view of the structural data and the presence of the *erythro* isomer.

Erythro-1-(2,4,5-trimethoxy) phenyl-1,2,3-tri(4-nitro)benzoyloxypropane (**8**): m.p. 178–179°C; ^{1}H NMR: 8.34–8.08 (m, 12H, aromatic), 6.96 (s, 1H, aromatic), 6.83 (d, *J* = 4.7Hz, 1H, **H**a), 6.54 (s, 1H, aromatic), 6.19–6.16 (m, 1H, **H**b), 4.82 (d × d, *J*=12.1Hz, 3.3Hz, 1H, **H**c), 4.62 (d × d, *J* = 12.1Hz, 6.6Hz, 1H, **H**d), 3.91 (s, 3H, OC$\mathbf{H}_3$), 3.86 (s, 3H, OC$\mathbf{H}_3$), 3.76 (s, 3H, OC$\mathbf{H}_3$); MS (EI): 705 (M^+), 538, 389, 388, 346, 150 (base), 120, 104; IR (KBr), *v*: 1730, 1608, 1528, 1457, 1322, 1296, 1264; Anal. Calcd for $C_{33}H_{27}N_3O_{15}$: C, 56.18; H, 3.85; N, 5.96; Found: C, 55.93; H, 4.06; N, 5.70.

Received 20 February 2001; accepted 3 July 2001
Paper 00/657

References

1 (a) C. Walling, C.-X. Zhao and G.M. EI-Taliwai, *J. Org. Chem.*, 1983, **48**, 4910; (b) C. Walling, G.M. EI-Taliwai and C.-X. Zhao, *J. Org. Chem.*, 1983, **48**, 4914.
2 M. Schmittel and A. Burghart, *Angrew. Chem. Int. Ed. Engl.*, 1997, **36**, 2550.
3 E. Baciocchi, M. Mattioli and R. Romano, *Acta Chem. Scand.*, 1990, **44**, 645.
4 M. Mella, M. Fagnoni, M. Freccero, E. Fasani and A. Albini, *Chem. Soc. Rev.*, 1998, **27**, 81.
5 (a) S. Toji, S. Toki and S. Takamaku, *J. Org. Chem.*, 1991, **56**, 6240; (b) P. Chyongin, *Pure Appl. Chem.*, 1986, **58**, 1249.
6 (a) C.M. Hudson, M.R. Marzabadi, K.D. Moeller and D.G. New, *J. Am. Chem. Soc.*, 1991, **113**, 7372; (b) H.E. Zimmerman and K.D. Hofferacker, *J. Org. Chem.*, 1996, **61**, 5626.
7 T. Miyashi, H. Ikeda and Y. Takahashi, *Acc. Chem. Res.***,** 1999, **32**, 815
8 (a) L.J. Johnston and N.P. Schepp, *J. Am. Chem. Soc*., 1993, **115**, 6564; (b) Ibid. *Pure Appl. Chem.*, 1995, **67**,71; (c) M.S. Workentin, N.P. Schepp, L.J. Johnston and D.D.M. Wayer, *J. Am. Chem. Soc***.,** 1994, **116**, 1141.
9 C. Walling and C.-X. Zhao, *Tetrahedron*, 1982, **38**, 1105.
10 C.-X. Zhao, G.M. EI-Taliawi and C. Walling, *J. Org. Chem.*, 1983, **48**, 4908.
11 X.-K. Jiang, C.-X. Zhao and Y.-F. Gong, *J. Phys. Org. Chem.***,** 1991, **4**, 1.
12 C.-X. Zhao, Y.-F. Gong, H.-Y. He and X.-K. Jiang, *J. Phys. Org. Chem.*, 1999, **12**, 688.
13 Y. Zhao, W.Li, C.-X.Zhao and Q.-Y.Qu, *Res. Chem. Intermed.*, accepted.
14 C.G. Swain, W.H. Stockmeyer and J.T. Clarke, *J. Am. Chem. Soc.*, 1950, **72**, 5426.
15 B.L. Chenard, M.J. Manning, P.W. Raynolds and J.S. Swenton, *J. Org. Chem.*, 1980, **45**, 383.