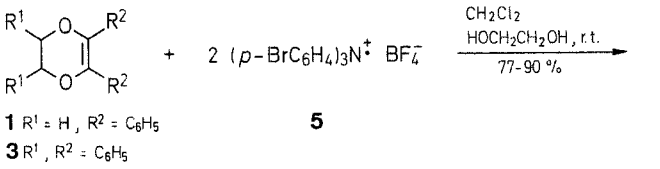
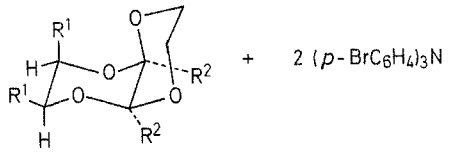



1 $R^1$ = H, $R^2$ = $C_6H_5$
3 $R^1$, $R^2$ = $C_6H_5$




2 $R^1$ = H, $R^2$ = $C_6H_5$
7 $R^1$, $R^2$ = $C_6H_5$

## A New Synthesis of *cis*-1,6-Diphenyl-2,5,7,10-tetraoxabicyclo[4.4.0]decane and Related Six Membered Cyclic Oxido Compounds

Luigi Lopez,*[a] Vincenzo Calò,[a] Francesca Stasi[b]

[a] Centro di Studio sulle Metodologie Innovative di Sintesi Organiche, Dipartimento di Chimica, Università di Bari, via Amendola 173, I-70126 Bari, Italy
[b] Centro Interdipartimentale di Cristallografia, c/o Dipartimento di Geomineralogia Università di Bari, I-70126 Bari, Italy

The synthesis of *cis*-tetraoxabicyclo decanes **2** and **7** have been performed by treatment of 2,3-diphenyl-5,6-dihydro-1,4-dioxin **(1)** or *cis*-2,3,5,6-tetraphenyl-5,6-dihydro-1,4-dioxin **(3)** with two equivalents of tris (*p*-bromophenyl)ammonium tetrafluoroborate in a dichloromethane/ethylene glycol mixture. The structural and conformational assignments have been made on the basis of spectroscopical and single crystal X-ray diffraction data. Similar reaction of 2,3,5,6-tetraphenyl-*p*-dioxin **(4)** with the same one electron oxidizing agent in dichloromethane/alcohol mixtures afford *trans*-2,3-dialkoxy derivatives **8** and **9**.

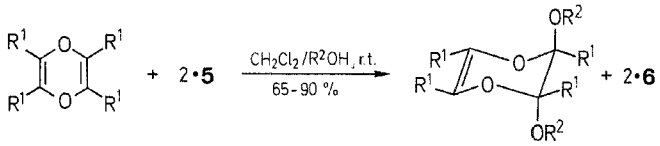
Recently, we have reinvestigated the bromination of 2,3-diphenyl-5,6-dihydro-1,4-dioxin **(1)** with molecular bromine and/or 2,4,4,6-tetrabromocyclohexa-2,5-dien-1-one (TBCHD) in carbon tetrachloride/ethylene glycol mixture, obtaining, for the first time and in high yields, the *cis*-1,6-diphenyl-2,5,7,10-tetraoxabicyclo[4.4.0]decane **(2)**.[1] The well documented interest in synthetic, structural and conformational problems of similar compounds,[2] induced us to explore novel and convenient reaction pathways affording **2** and related six membered cyclic oxido derivatives.

We wish to report herein the results of our continuing studies[3] on one electron-transfer oxidation of **1**, *cis*-2,3,5,6-tetraphenyl-5,6-diphenyl-5,6-dihydro-1,4-dioxin **(3)** and 2,3,5,6-tetraphenyl-1,4-dioxin **(4)** by tris(*p*-bromophenyl)ammonium tetrafluoroborate **(5)**. The latter is a useful triaryl ammonium salt[4] with a suitable oxidizing power,[5] and good thermal stability[6] affording a neutral by-product, tris(*p*-bromophenyl)amine **(6)**, which is sparingly soluble in many organic solvents and therefore easy to separate from the product mixture.

Treatment of a dry dichloromethane/ethylene glycol mixture of **1** and **3**, respectively, with one equivalent of **5**, at room temperature gave dark red solutions which faded within a few minutes. GC and TLC analyses of the colorless reaction mixture revealed **6**, unreacted starting materials **1** and **3** together with the reaction products **2** and **7**, respectively. Complete conversion of **1** and **3** into **2** and **7**, respectively, required two equivalents of **5**.

Similar reactions, carried out without ethylene glycol, afforded benzil together with by-products, such as *meso*-stilbenediol, as previously reported.[3] The stoichiometric requirement of two equivalents of the one electron-oxidizing agent **5**, together with the peculiar features of substrates **1**, **3** and **4** are evinced by cyclic voltammetric experiments, two oxidation waves with the second one irreversible.[7] They point out that, under our experimental conditions, the radical cations intermediates $(\mathbf{1}, \mathbf{3})^+$ could disproportionate[3,8] to give neutral parent compounds **1** and **3**, respectively, and the corresponding doubly charged ions, easily trapped by ethylene glycol to afford **2** and **7**, respectively.

The disproportionation during ion radical reactions appears limited to those substrates whose corresponding ion radicals are long lived.[9] Structural factors are important in determining the first and second oxidation potentials, as well as their disproportionation equilibrium constant.[8,9]




4 $R^1$ = $C_6H_5$

8 $R^2$ = $(CH_2)_2OH$
9 $R^2$ = $CH_3$

Although both the radical cation species mentioned above are highly reactive entities so that, a chain mechanism *via* radical cation could lead to the same reaction products, we believe that this latter mechanism does not affect appreciably the reaction. In fact GC control on reactions carried out with equimolecular amounts of the reactants show unchanging ratios, after long reaction time, among the products.

The problems of the structural and conformational assignements was solved respectively by $^1$H-, $^{13}$C-NMR, mass spectroscopy, elemental analyses (see experimental section) and by single crystal X-ray diffraction. The reported crystal data for **2** is as follows: $C_{18}H_{18}O_4$, $M_r = 298.432$, monoclinic, $P2_1/n$, $a = 7.966$, $b = 33.04$, $c = 11.416$ Å, $\beta = 93.05°$, $V = 3000.40$ Å$^3$, $Z = 8$, $D_x = 1.32$ Mg m$^{-3}$, $F(000) = 12.64$ MoK radiation, $\lambda = 0.71069$ Å.

Details of the crystallographic analysis will be submitted in the near future for publication.[10]

The exclusive formation of the *cis*-isomers of these bicyclic systems could be interpreted as being due mainly to a destabilizing double chair form with all the C–O bonds equatorial, as opposed to the pairwise axial-equatorial arrangement in **2** and **7**. The elusiveness of the *trans*-derivative has been fully rationalized,[11] even in the case of the unsubstituted bicyclodecane. In fact both isomers have similar COCCOC interactions, but they differ in the anomeric geometry in the COCOC acetal fragments from two *anti, anti*-moieties in the *trans*-isomer, and to two *anti*.

*gauche*-moieties in the *cis*-isomer.[12] The corresponding energy difference,[13] ranging over 3.79–3.75 kcal/mol substantiates the exclusive formation of the *cis*-isomers.

A similar reaction of **4** does not afford the corresponding bicyclic derivative but it yields the more thermodynamically stable 2,3-bis(2-hydroxyethoxy)-2,3,5,6-tetraphenyl-2,3-dihydro-1,4-dioxin **(8)**.

Although, the large phenyl groups should have a powerful influence in determining the configuration and stability of the intermediate due to the tendency for the large groups to assume equatorial positions leading to the axial addition of the alkoxy groups, we found the spectral data inconclusive in determining the *trans*-and/or *cis*-structure of **8**.

The preferred *trans*-configuration was demonstrated by synthesizing 2,3-dimethoxy-2,3,5,6-tetraphenyl-2,3-dihydro-1,4-dioxin **(9)**, by a similar reaction starting from **4**, but in the presence of methanol. The melting point and spectral data of **9** are consistent with the *trans*-isomer prepared as reported.[14] In conclusion, both the anomeric effect of the alkoxy groups and the steric interactions of axial phenyl groups operate in these reactions, affording the *trans*-diaxial alkoxy isomers, also favoured by two anomeric effects over the symmetric trans diequatorial ones.[2,15]

Further work on the reaction of several dioxins in the presence of different nucleophiles are in progress.

Melting point were taken on an electrothermal apparatus and are uncorrected. $^1$H- and $^{13}$C-NMR spectra were recorded on Varian EM 90 and XL-200 MHz instruments. IR and MS spectra were performed on a Perkin-Elmer 681 spectrometer and on a Kratos MS-80 instruments respectively. GC analyses were carried out on an Hewlett-Packard gas chromatograph, model 5750 B, on columns (1/4" × 15 feet) packed with SP 2100 (5% on Supelcoport 100/120); TLC were performed on silica gel sheets with fluorescent indicator (Stratocrem SIF-Carlo Erba). Column chromatography was carried out by using 70–230 mesh silica gel from Merck. $CH_2Cl_2$ was purified by distillation and stored over molecular sieves. Compounds **3**,[14] **4**,[14] and **5**[9] were prepared according to literature procedures.

**cis-1,6-Diphenyl-2,5,7,10-tetraoxabicyclo[4.4.0]decane(2); Typical Procedure:**

To a stirred solution of 2,3-diphenyl-5,6-dihydro-1,4-dioxin (**1**; 0.059 g 0.25 mmol) in $CH_2Cl_2$ (25 mL) is added ethylene glycol (2.5 mL) and then one equivalent of tris (*p*-bromophenyl)ammonium tetrafluoroborate (**5**; 0.184 g, 0.25 mmol). The dark red solution fades within a few minutes and the GC analysis shows unreacted starting material **1** together with tris-(*p*-bromophenyl)amine **(6)** and the reaction product **2**. To the colourless solution is added a second equivalent of **5** and the complete conversion of **1** into the reaction product is monitored by GC. The mixture is poured into water (200 mL), the organic phase is separated, dried ($Na_2SO_4$) and the solvent is removed under vacuum. The residue, adsorbed on silica gel, is chromatographed with hexane/ether (5:1) as eluent to give **2**; yield: 0.066 g (90%). Recrystallization from ethanol affords white crystals, m.p. 145–146°C (Lit.[1] m.p. 145–146°C).

IR (KBr): $\nu$ = 1480, 1445, 1268, 760, 697 cm$^{-1}$.

$^1$H-NMR ($CDCl_3$): $\delta$ = 3.7–4.33 (AA'BB' system, m, 8H); 7.06–7.73 (m, 10H).

$^{13}$C-NMR ($CDCl_3$): $\delta$ = 60.1 (t), 93.8, 126.2, 127.1, 127.3, 137.2.

MS: (m/e, %) = 149 (47), 105 (100), 77 (41).

*cis-1,3,4,6-Tetraphenyl-2,5,7,10-tetraoxabicyclo[4.4.0]decane* **(7)**; yield: 77%; m.p. 202–203°C (white crystals from EtOH).

| | | | |
|---|---|---|---|
| $C_{30}H_{26}O_4$ | calc. | C 79.9 | H 5.81 |
| (450.5) | found | 79.6 | 5.88 |

IR (KBr): $\nu$ = 1495, 1450, 1268, 705 cm$^{-1}$.

$^1$H-NMR ($CDCl_3$): $\delta$ = 3.6–4.23 (AA'BB' system, m, 4H); 5.34 (s, 2H); 7.0–7.7 (m, 20H).

$^{13}$C-NMR ($CDCl_3$): $\delta$ = (60.9 (t); 74.5, 96.3, 126.8, 127.1, 127.4, 128, 128.1, 128.5, 138.3, 138.8.

MS: (m/e, %) = 238 (13), 180 (100), 165 (11), 105 (63), 77 (27).

*2,3-bis(2-hydroxyethoxy)-2,3,5,6-tetraphenyl-2,3-dihydro-1,4-dioxan* **(8)**; yield: 65%; m.p. 280–282°C (EtOH).

| | | | |
|---|---|---|---|
| $C_{32}H_{30}O_6$ | calc. | C 75.2 | H 5.87 |
| (510.5) | found | 74.6 | 5.74 |

IR (KBr): $\nu$ = 1662, 1498, 1452, 1270, 760 cm$^{-1}$.

$^1$H-NMR ($CDCl_3$): $\delta$ = 1.98 (br, 2H, exchangeable with $D_2O$); 3.44–3.76 (m, 8H), 7.06–7.43 (m, 20H).

$^{13}$C-NMR ($CDCl_3$): $\delta$ = 61.8 (t), 63.5 (t), 99.5, 127, 128.1, 128.6, 128.9, 129.3, 131.6, 134, 134.4.

MS: (m/e, %) = 510 (2), 178 (47), 105 (100), 77 (32).

*2,3-dimethoxy-2,3,5,6-tetraphenyl-2,3-dihydro-1,4-dioxan* **(9)**; Dry methanol is used as the solvent instead of ethylene glycol. Yield: 90%; m.p. 294–295°C (EtOH) (Lit.[13] m.p. 292–293°C).

| | | | |
|---|---|---|---|
| $C_{30}H_{26}O_4$ | calc. | C 80.2 | H 5.87 |
| (450.5) | found | 80 | 5.82 |

IR (KBr): $\nu$ = 1660, 1495, 1450, 1263, 786 cm$^{-1}$.

$^1$H-NMR ($CDCl_3$): $\delta$ = 3.2 (s, 6H), 7.0–7.7 (m, 20H).

$^{13}$C-NMR ($CDCl_3$): $\delta$ = 50.1, 100.1, 126.8, 127.5, 127.9, 128.3, 128.9, 129.6, 134.6, 134.7.

MS: (m/e, %) = 450 (7), 240 (74), 225 (43), 178 (95), 105 (100), 77 (67).

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