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# ELECTROCHEMICAL REDUCTION OF PHTHALYL CHLORIDE. A NEW ROUTE FOR THE SYNTHESIS OF 3-SUBSTITUTED PHTHALIDES

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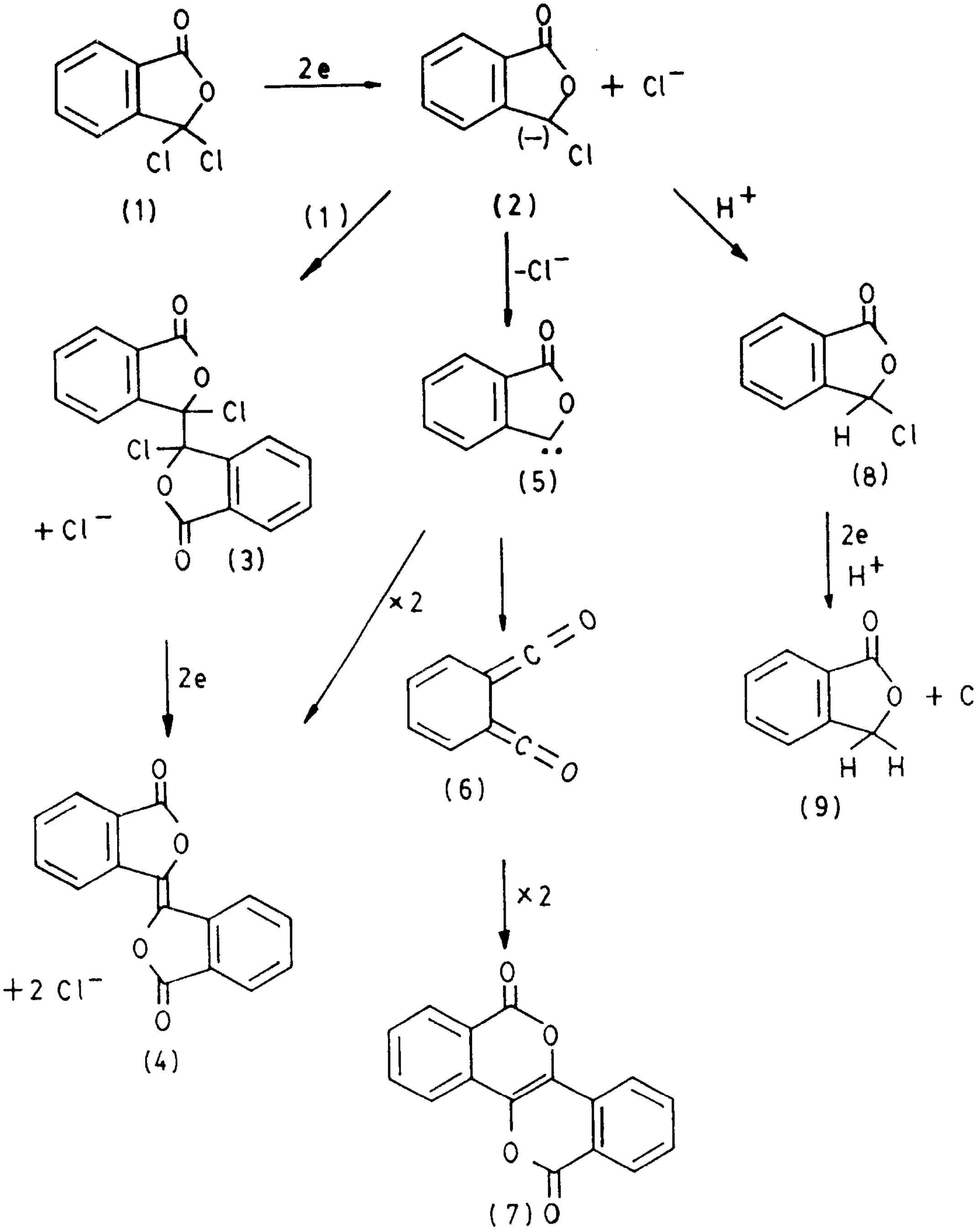
Abstract: The cathodic reduction, under various conditions, of phthalyl chloride enables efficient synthesis of (E)-[1,1']biisobenzofuranyliden-3,3'-dion (4), [2]-benzopyrano [4,3-c]-[2]benzopyrano-6,12-dione (7), 3-chlorophthalide (8), phtalide (9), or (E)-3[α-(benzoyloxy) benzylidene] phthalide (12); the structure of the latter compound was confirmed by X-ray crystallography.

Phthalide may be deprotonated by strong bases at C-3 to give a carbanion which may react with electrophiles[1]. However severe experimental conditions for carbanion formation may be an obstacle in using sensitive reagents and may additionally cause degradation of the products. 3-cyano and 3-phenylsulphonyl phthalides have been employed to form more stable carbanions, which have improved utility in synthesis.[2]

We herein report a new system to generate carbanions at C-3, via electrochemical reduction of phthalyl chloride (1), which is easily obtained from phthalic acid in high yield[3]. Its electrochemical induced umpolung reactivity, under mild conditions, provides a valuable synthetic method for products in which the lactone ring is retained.

The controlled potential cathodic reduction of (1), 10 mmol, in dry DMF-$NaClO_4$, 0.4M (40ml), at a mercury pool cathode, at -0.8V vs SCE, gave (E)-[1,1'] biisobenzofuranyliden-3,3'-dion[4] (4), (trans-biphthalyl) in high yield (84%) with [2]-benzopyrano[4,3-c]-[2]benzopyrano-6,12-dione[4] (7), (10%). When similar electrolysis was carried out adding the substance (1) to the cell slowly, during the time of electrolysis, (4) was obtained in 28% yield and (7) in 31%. At -0.7V vs SCE reduction in DMF-AcOH-$NaClO_4$ gave 3-chlorophthalide[4] (8), yield 83% and in the same electrolyte but at -1.2V vs SCE, phthalide[4] (9) was the major product of the cathodic reduction, yield 78%. The reductions giving (8), (4) and (7) consumed $2F.mol^{-1}$ whereas that giving (9) consumed $4F.\ mol^{-1}$.

This is consistent with the initial electrogeneration of the 3-chlorophthalid-3-ide intermediate (2) with subsequent reactions according to Scheme 1; competition between the three routes depends crucially on the experimental conditions.



Scheme 1

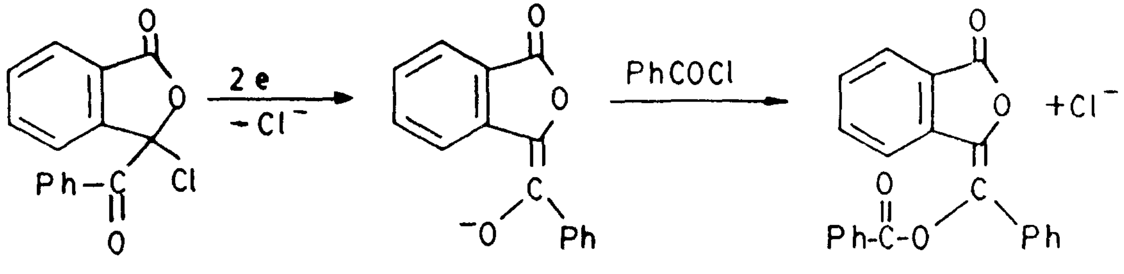
Carbanion (2) is probably long lived because no dimeric products are formed in aprotic conditions and electrophilic attack appears to be faster than α-elimination of chloride to give (5). The dependence of the ratio of the products (4) and (7) on the concentration of (1) is in agreement with the rate-limiting step being bimolecular formation of (4); this implies the intermediancy of 3,3'-dichlorobiphthalidyl[5] (3) rather than dimerisation of carbene (5).

Compound (7) may plausibly be formed via unimolecular elimination of chloride from (2) to give the carbene (5) with subsequent rearrangement to the o-quinonoide bisketene species (6) and dimerisation to (7).

Attempts at trapping (5), with cyclohexene present during the reduction, failed, but the bisketene intermediate (6) was trapped when the electrolysis was carried out in the presence of a dienophile, acetylenedicarboxylic acid diethyl ester. Compound (7) was not formed and the major products were the cis and trans isomers from reduction of the corresponding Diels-Alder adduct: diethyl 2,3-dihydro-1,4-naphthoquinone-2,3-dicarboxylate[6].

The carbanion (2) also reacted with benzoyl chloride. In this case the electrolysis of (1), 10 mmol, was carried out in dry dicloromethane-tetrabutylammonium tetrafluoroborate 0.2M, and the product, previously unknown, was (E)-3[α -benzoyloxy) benzylidene ]phthalide[7], m.p. 147-8 °C, yield 74%.

Formation of (12) corresponds to a $4F.mol^{-1}$ reaction; (2) is generated at a lower potential than that required for reduction of benzoyl chloride which therefore acts as an acylating agent for electrogenerated nucleophile. It is proposed that initial acylation gives the α-chloroketone (10) which will reduced more easily than (1). Acylation of the resulting (E)-enolate anion by a second molecule of benzoyl chloride gives (12). No examples of this class of compound have previously been reported.



(10) (11) (12)

Unequivocal determination of the configuration of (12) was achieved by X-ray structural analysis . The molecular structure found is illustrated in Figure 1.

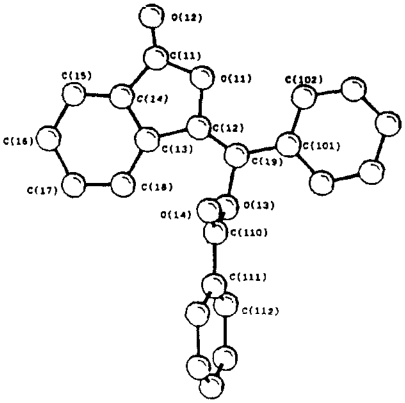


Figure 1. Molecular Structure of (12).

Crystal data: $C_{22}H_{14}O_4$, M= 342.33, orthorhombic, a=18.963(6), b=5.579(1), c=31.658(6)Å, U=3349.2Å$^3$, space group Pna$2_1$, $D_c$=1.36gcm$^{-3}$, Z=8. Data were collected on a CAD4 diffractometer using Ni-filtered Cu-K$\alpha$ radiation ( $\lambda$ = 1.5418Å) via the $\omega/2\theta$ scan mode width 2.0 $\leqslant \theta \leqslant$ 60.0°, giving 2391 data of which 1536 were unique $I > 1.5\sigma(I)$. Structure solved via direct methods (SHELX84S) and refined using full matrix least squares, but with each of two independent molecules contained in separated blocks. Phenyl rings treated as regular hexagons, all atoms anisotropic but no hydrogen included, in view of the small no. of observed data. Final R=0.066 (unit weights). The unit cell contains two crystallographically independent molecules of identical structure, which are related by a pseudo centre of symmetry at 0.8711, 0.7131, 0.3650. Full crystallographic data have been deposited with the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, England.

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4). Product (4) was characterised by comparison with an authentic sample obtained by an electrochemical synthetic method of enediol diesters[8] applied to phthaloyl chloride[9]. (7) was characterised by comparison with an authentic sample obtained by isomerisation of (4) in Concentrated sulphuric acid[10]. (8) and (9) were characterised by their coincident m.p. with the reported, and agreements of microanalyses and spectral data with those expected from their structures.
5). (3) was not detected probably because vicinal halides are more easily reduced than comparable gem halides[11].
6). both isomers show identical retention times in g.l.c. in capillary column, and coincident mass spectra as those obtained by condensation of diethyl phthalate with diethyl succinate.
7).spectral data for (12): I.R. (KBr) two carbonyl bands at 1734 and 1780 cm$^{-1}$; MS 70eV m/z (rel. intensity) 342 ($M^+$, 13), 209(8), 106(8), 105(100), 77(26), 51(6); HRMS calcd for $C_{22}H_{14}O_4$ m/z 342.0892, found m/z 342.0894; $^1$H NMR($CDCl_3$ 80 MHz) very complex signals between $\delta$ 7.32-8.40; $^{13}$C NMR ($CDCl_3$/63MHz) $\delta$ : 123.17, 123.90, 125.80, 127.32, 128.48, 128.63, 129.14, 129.39, 129.90, 130.38, 131.98, 133.92, 134.43, 134.95, 138.13, 139.62, 164.45, 166.09.
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