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Pyrylium Salts. Part VIII.* Derivatives of 5,13:6,12-Bisepoxydibenzo[*a*,*f*]cyclodecenes

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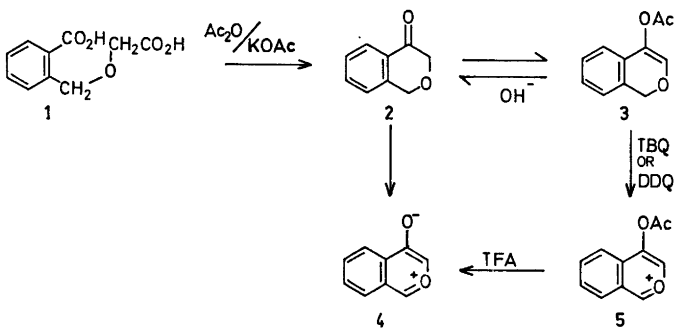
In the reaction between 4-acetoxyisochromene and TBQ or DDQ adducts were formed between the reduced quinone and the generated 4-acetoxy-2-benzopyrylium ion. The adducts in TFA yielded the *syn*- and *anti*-isomers of 5,6,12,13-tetrahydro-5,13:6,12-bisepoxydibenzo[*a*,*f*]-cyclodecene-7,14-dione; NMR showed the presence of intermediate 2-benzopyrylium-4-olate, which was dimerised.

In a recent paper we have described a synthesis of 1a,6a-dihydroindeno[1,2-*b*]azirin-6(1*H*)-ones and their photolytic rearrangements to isoquinolinium derivatives.[2] The oxygen hetero-analogue 2,3-epoxyindanone, however, was rearranged to isocoumarin on photolysis rather than to the analogous 2-benzopyrylium-4-olate.[3] The failure to form the pyrylium salt may be due to insufficient aromatic stabilisation of the pyrylium betaine (*4*). On added stabilisation from phenyl substituents, however, equilibria exist between the pyrylium and the epoxide valence isomers; the equilibrium position is dependent on conditions but is in favour of the epoxide structure.[4,5] In this work we describe a synthesis of the 2-benzopyrylium-4-olate system which is related to the method used in the synthesis of 2-benzothiopyrylium-4-olates.[1,6] The latter were readily dimerised. The oxygen analogue (*4*) was anticipated to be even more reactive in view of the relative stabilities of the thiopyrylium and pyrylium cations.[7]

The synthesis of *4* (Scheme 1) is based on hydride abstraction from isochroman-4-one (*2*). The latter is sensitive to acid as it is a benzyl ether, and it could not be satisfactorily prepared by acid catalysed cyclisation of benzyloxyacetic acid,[8] whereas the thioether analogue can be cyclised to isothiochroman-4-one in acid media.[9] Isochroman-4-one was instead prepared by cyclisation of *o*-carboxybenzyloxyacetic acid (*1*) by means of potassium acetate in acetic anhydride. The optimum yield of cyclic product (50 %) was reached by the use of four equivalents of potassium acetate in which case the major cyclic product was

* Part VII; see Ref. 1.



Scheme 1.

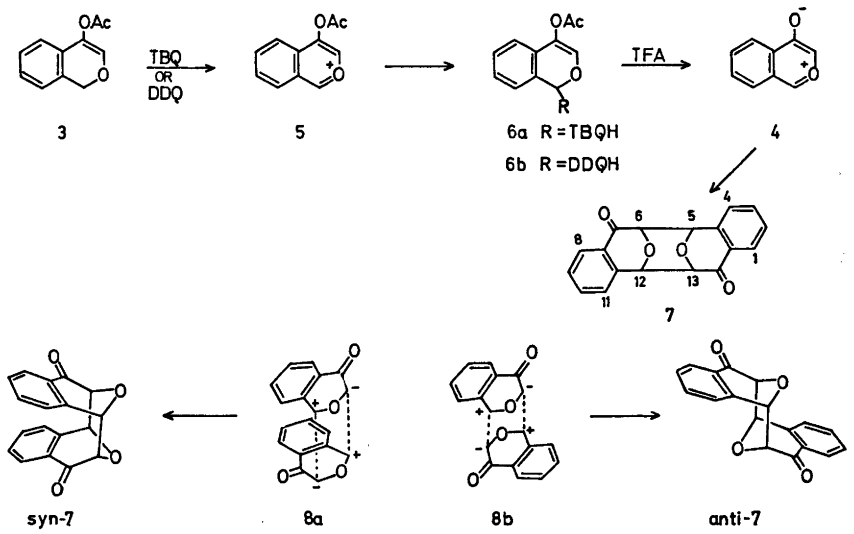
the enol acetate *3*; the latter can be converted to the ketone *2* by mild alkaline hydrolysis.

Triphenylmethyl perchlorate is a useful reagent for hydride abstraction in pyrylium synthesis;[10] it has been applied with success in hydride abstraction from isothiochroman-4-one.[6] No reaction occurred, however, between the trityl salt and the ketone *2* or its enol acetate *3* in liquid SO_2. Triphenylmethane was formed on heating the reagents together in acetonitrile or a mixture of acetic anhydride and acetic acid, but the desired products were largely polymerised. Activated quinones are alternative reagents in hydride abstractions.[11] The reactions are acid catalysed.[11,12] Fortunately the reaction between the acid sensitive 4-acetoxyisochromene (*3*) and tetrachloro-1,2-benzoquinone (TBQ)[12] proceeded readily in cold benzene solution without acid catalyst. Isochroman-4-one (*2*), however, did not react under these conditions. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) could also be used in the hydride abstraction from *3*. The products obtained in the reactions between *3* and TBQ or DDQ are assigned structure *6* which arise by bond formation between the phenolate oxygen atom in the hydroquinone formed and the highly electrophilic pyrylium carbon atom C-1.

The NMR spectra of both adducts in trifluoroacetic acid (TFA) were the same with H-1 at δ 10.4 and H-3 at 9.6; an initial paramagnetic shift for the acetyl protons from δ 2.3 to 2.6 was followed by a gradual diamagnetic shift to δ 2.3. The chemical shifts are similar to those observed for 4-acetoxy-2-benzothiopyrylium perchlorate.[6] The NMR data show that the adduct formation *6* is reversible in acids such as TFA and the diamagnetic shift of the acetyl protons is due to deacetylation of the 4-acetoxy-2-benzopyrylium cation. *Ca.* one equivalent of $TBQH_2$-monoacetate was isolated from the corresponding adduct *6a* in TFA. Attempts to isolate the concurrently formed 2-benzopyrylium-4-olate (*4*) as fluoroboric acid salt failed since *4* reacted further under polymerisation and dimerisation (20 – 27 % yield). The *syn* and *anti* dimeric structures *7* were assigned to the products from spectroscopic data. Only one isomer was isolated from the DDQ-adduct whereas the isomer mixture from the TBQ-adduct contained *ca.* 5 % of this isomer. Both isomers have strong carbonyl absorption at 1685 cm^{-1} (KBr). The NMR spectra contain two non-aromatic types of mutually coupled methine protons. Both products have the molecular ion in the mass spectra at *m/e* 292.

A symmetrical double layer arrangement in the transition state dimerisation is unlikely because of the same regional polarisation in the reactants which will result in charge repulsion. Charge attraction, however, will be operative if the reactants are oriented so that the carbonyl groups point in opposite directions (Scheme 2). The reactants can further be arranged in two ways illustrated by *8a* and *8b* to give a *syn*- and an *anti*-isomer. The *syn*-isomer can be regarded as a 1,4-dioxane derivative locked in the boat conformation, and the *anti*-isomer as a 1,4-dioxane derivative locked in the chair conformation. The coupling between the vicinal methine protons in the isomer from the DDQ-adduct (*6b*) was small (broad singlets at δ 4.4 and 5.3) whereas the coupling in the other isomer was 11 Hz (δ 4.9 and 5.5). The former isomer is assigned the *anti*-structure and the latter the *syn*-structure in accordance with the torsional angles between the vicinal methine protons in the respective locked 1,4-dioxane conformations. The aromatic proton *ortho* to the carbonyl group in the *anti*-isomer (δ 8.0 – 8.1) and in isochroman-4-one (δ 7.8 – 8.0 in CCl_4) is at lower field than the other aromatic protons (δ 7.5 – 7.9 and 7.0 – 7.5), respectively. The aromatic *ortho*-proton in the *syn*-isomer, however, lies above the other benzene ring and is in the aromatic shielding zone which opposes the deshielding effect from the carbonyl group; all the aromatic protons in the *syn*-isomer appear in the region δ 6.9 – 7.8 (CD_3CN). The structure assignments agree with the interpretations of the spectral data of the sulfur hetero-analogues in which case the structure of the parent *syn*-isomer was confirmed by X-ray analysis.[6,13]

The mass spectra of the dimers are similar but differ slightly in relative fragment intensities. The molecular ion (*m/e* 292) intensities were 42 and 10 % (*m/e* 133 base peak) for the *anti*- and *syn*-isomers, respectively. The high intensity (*ca.* 80 %) of the *m/e* 146 species



Scheme 2.

roused our interest since this mass number corresponds to the molecular weight of the betaine *4*; the latter could have arisen by thermal dissociation of the dimer *7* in the mass spectrometer prior to ionisation. The appearance potential for the *m/e* 146 species from the *anti*-isomer was found to be 9.70 eV whereas the ionisation potential of *anti-7* was 8.75 eV. The values are to be compared with the ionisation potentials of 2,3-epoxyindan-1-one (9.10 eV) and *N*-benzylisoquinolinium-4-olate (7.10 eV)[14] The ionisation potential of 2-benzopyrylium-4-olate (*4*) is expected to be no higher than that of the mesoionic *N*-benzylisoquinolinium-4-olate which excludes thermal generation of the former in the mass spectrometer. The appearance and ionisation potential data also exclude transient formation of *4* followed by thermally induced valence isomerisation to 2,3-epoxyindan-1-one; the *m/e* 146 species is formed through electron-impact induced fragmentation routes from the molecular ion of *7*.

1,3-Diphenyl-2-benzopyrylium-4-olate is the minor component in equilibrium mixtures with its valence isomer 2,3-diphenyl-2,3-epoxyindan-1-one.[4,5] A dimeric molecule is formed by the reaction of the former as a 1,3-dipolar reactant with the carbonyl group of the latter.[5] 2-Methyl-3-phenyl-2,3-epoxyindan-1-one on photolysis yielded mainly the corresponding isocoumarin, but the product also contained 6 % of a dimeric material. The latter was assigned the same cyclic skeleton as in *7* but its stereochemistry was not discussed.[15] In the dimerisation of 2-benzothiopyrylium-4-olate there is a clear preference for the *syn*-isomer,[6] and this is the preferential stereochemical course in Diels-Alder reactions and in 1,3-cycloaddition reactions,[16] whereas introduction of a methyl group into the 1-position of the heterocycle resulted in formation of the *anti*-dimer.[1] In the present work only the *anti*-isomer *7* was isolated after dissociation of the DDQ-adduct *6b* whereas *syn-7* was the major isomer formed from the TBQ-adduct.

EXPERIMENTAL

NMR spectra were recorded with a Varian A-60 or A-100 instrument, UV spectra with a Cary 14 spectrophotometer, and mass spectra with an AEI-902 spectrometer. Ionisation and appearance potential values were determined as previously described by semilog plot interpretation of the ionisation efficiency curves.[14] The ionisation and appearance potential values are the average of three determinations, the deviation being ± 0.05 eV.

4-Acetoxyisochromene (3). A solution of *o*-carboxybenzyloxyacetic acid[17] (10.0 g, 0.048 mol) and potassium acetate (20.0 g, 0.211 mol) in acetic anhydride was heated under reflux

for 3 h. The solution was then evaporated at reduced pressure, water was added, and the mixture was extracted with ether. The ether extracts were dried, evaporated and the residue was distilled; the collected material had b.p. 94–96 °C at 0.01–0.05 Torr (5.5 g) and was the title compound admixed with isochroman-4-one. The title compound was isolated by fractional crystallisation from dilute ethanol as the less soluble material and was obtained in 49 % yield (4.4 g), m.p. 48–49 °C (Lit.[8] 49 °C); δ ($CDCl_3$) 2.3 (MeCO), 5.2 (2 H-1), 6.9 (H-3), 7.0–7.5 (4 H-arom); λ_{max} (MeCN) 244 (log ε 3.91), 280 nm (3.77).

Isochroman-4-one (2). 4-Acetoxyisochromene (4.0 g, 0.021 mol) was dissolved in ethanol (20 ml) and 2 N NaOH added dropwise until the base was no longer consumed. The solution was then diluted with water and left in the cold. The title compound was precipitated in 70 % yield (2.2 g), m.p. 53 °C [Lit.[8] 53 °C]; δ (CCl_4) 4.2 (2 H-3), 4.8 (2 H-1), 7.8–8.0 (H-5), 7.0–7.5 (3 H-arom); λ_{max} (MeCN) 245 (log ε 4.01), 288 cm (3.18).

4-Acetoxy-1-(2-hydroxy-3,4,5,6-tetrachlorophenoxy)isochromene (6a). A solution of TBQ (6.6 g, 0.027 mol) in anhydrous benzene (75 ml) was added dropwise to a solution of 4-acetoxyisochromene (5.0 g, 0.027 mol) in anhydrous benzene (25 ml). The precipitated product was filtered off after 5 h at room temperature and the product washed with cyclohexane to remove any TBQ; yield 6.5 g (57 %). The analytical sample was recrystallised from toluene, m.p. 153 °C. (Found: C 46.97; H 2.36 Calc. for $C_{17}H_{10}Cl_4O_5$: C 47.10; H 2.31); δ (acetone-d_6) 2.3 (Ac), 6.3 (H-1), 6.7 (H-3), 7.2–7.4 (4H-arom.); λ_{max} (MeCN) 217 (log ε 4.35), 263 (4.01), 298 nm (3.44).

4-Acetoxy-1-(2,3-dichloro-5,6-dicyano-4-hydroxyphenoxy)-isochromene (6b) was prepared as above with DDQ instead of TBQ. The precipitated adduct after 3 h was slightly contaminated with DDQ and $DDQH_2$ which were difficult to remove due to low solubilities. The crude product (*ca.* 75 % yield) was used in the next reaction step without further purification. δ (acetone-d^6) 2.3 (Ac), 6.6 (H-1), 6.9 (H-3), 7.2–7.5 (4 H-arom.); λ_{max} (MeCN) 220 (log ε 4.5), 255 (4.1), 347 nm 3.8).

syn-*5,6,12,13-Tetrahydro-5,13:6,12-bisepoxydibenzo*[a,f]*cyclodecene-7,14-dione (7).* The TBQ-adduct *6a* (4.3 g, 0.01 mol) was added to anhydrous TFA (100 ml), and the mixture was stirred vigorously at room temperature for 1 h. $HBF_4 \cdot Et_2O$ (1.6 g, 0.01 mol) was added, and the stirring was continued for 48 h. After evaporation the residue was extracted with ether (3 × 75 ml), and the ether solution was washed with 2 N Na_2CO_3 to remove the acid and most of the hydroquinone. The ether solution was then evaporated and the residue dissolved in chloroform, and the solution was passed through a column of basic aluminium oxide in order to remove the residual hydroquinone. The chloroform eluate was slowly concentrated in a stream of nitrogen when most of the *anti*-isomer *7* crystallised out. The remaining solution was chromatographed on a silica gel column. The residual *anti*-isomer was eluted before the *syn*-isomer *7* with chloroform. The *syn*-isomer crystallised from the chloroform eluate on slow concentration in a stream of N_2; m.p. 172–174 °C. The total yield of the *anti*-isomer (*7*) was 1 % (20 mg), and the yield of the *syn*-isomer *7* was 19 % (270 mg). (Found: C 74.22; H 4.18. Calc. for $C_{18}H_{12}O_4$: C 73.97, H 4.11). δ (CD_3CN) 4.9 (H-6 and –13, d, $J_{5,6} = J_{12,13} = 11$ Hz), 5.5 (H-5 and H-12, d), 6.9–7.8 (8 H-arom); λ_{max} (MeCN) 250 (log ε 4.28), 296 nm (3.34); m.s. (*m/e*) 292 (10 %, M), 246 (7), 159 (13), 147 (18), 146 (77), 134 (44), 133 (100), 131 (42).

anti-*5,6,12,13-Tetrahydro-5,13:6,12-bisepoxydibenzo*[a,f]*cyclodecene-7.14-dione (7)* was prepared as above from the DDQ-adduct *6b*. Again a chloroform solution of the reaction product was passed through a column of basic aluminium oxide to remove the residual hydroquinone. The title compound was crystallised from the chloroform eluate by slow concentration of the solution under a stream of N_2; yield 27 %, m.p. 280 °C. (decomp.). (Found: C 73.55; H 4.03. Calc. for $C_{18}H_{12}O_4$: C 73.97; H 4.11). δ (DMSO-d_6) 4.4 (H-6 and H-13, broad singlet), 5.3 (H-5 and H-12, broad s), 7.5–7.9 (6 H-atom), 8.0–8.1 (H-1 and H-8); λ_{max} (MeCN) 240 (log ε 4.45), 291 nm (3.42); m.s. (*m/e*) 292 (42 %, M), 246 (8), 159 (19), 147 (13), 146 (87), 134 (35), 133 (100), 131 (30).

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