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Synthesis of Dixanthones and Poly(dixanthone)s by Cyclization of 2-Aryloxybenzonitriles in Trifluoromethanesulfonic Acid

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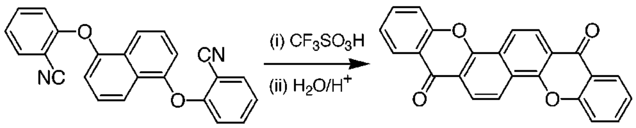
ABSTRACT



Condensation of 2-fluorobenzonitriles with phenoxides affords 2-aryloxybenzonitriles that cyclize cleanly in trifluoromethanesulfonic acid at room temperature to give xanthone-iminium triflates. The C=N bond in these compounds is remarkably resistant to hydrolysis, but prolonged reaction with strong aqueous acid under vigorous conditions affords xanthones in good yield. The synthesis is exemplified for a novel series of polynuclear dixanthones and for a high molar mass polyxanthone derived from the previously unreported monomer 3,3′-difluoro-4,4′-biphenyldicarbonitrile.

The xanthone nucleus displays very good thermo-oxidative and hydrolytic stabilty and would appear to have considerable potential as a structural motif in high-performance polymer chemistry. Very many different routes to xanthones are known,[1] including cyclodehydration of 2,2′-dihydroxybenzophenones,[2] electrophilic cycliacylation of 2-aryloxybenzoic acids,[3] and oxidative cyclization of 2-phenoxybenzaldehydes,[4] but few such reactions have been investigated in the context of polymer synthesis.[5] Here we report a new synthetic approach to xanthone-based molecules and macromolecules, in which nucleophilic condensation of a bisphenol with 2-fluorobenzonitrile or 3,3′-difluoro-4,4′-biphenyldicarbonitrile is followed by superacid-promoted Houben−Hoesch cyclization. A related route to a substituted *thio*xanthone, involving cyclization of 2-chloro-6-(phenylthio)benzonitrile at high temperature in polyphosphoric acid, has been reported.[6]

To investigate the feasibility of the proposed chemistry, 2-fluorobenzonitrile was reacted with the bisphenols 1,5-dihydroxy-naphthalene, 4,4′-dihydroxybiphenyl, and 4,4′-hexafluoroisopropylidene-diphenol, in the presence of potassium carbonate as base, giving dinitriles **1**, **2**, and **3**,

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(1) (a) Wawzonek, S. In *Heterocyclic Compounds*; Elderfield, R. C., Ed.; Wiley: New York, 1950; Vol. 2, pp 419−444. (b) Hepworth, J. D. In *Comprehensive Heterocyclic Chemistry*; Boulton A. J., McKillop, A., Eds.; Pergamon: Oxford, 1984; Vol. 3, pp 835−840.
(2) Bichan, D. J.; Yates, P. *Can. J. Chem*. **1975**, *53*, 2054−2063.
(3) Olah, G. A.; Mathew, T.; Farnia, M.; Prakash, G. K. S. *Synlett* **1999**, 1067−1068 and references therein.
(4) Okogun, J. I.; Okwute, K. S. *J. Chem. Soc., Chem. Commun*. **1975**, 8.
(5) For a serendipitous synthesis of a polyxanthone, see: Kricheldorf, H. R.; Adebahr, T. *Makromol. Chem*. **1993**, *194*, 2103−2115.
(6) Laidlaw, G. M.; Collins, J. C.; Archer, S.; Rosi, D.; Schulenberg, J. W. *J. Org. Chem*. **1973**, *38*, 1743−1746.

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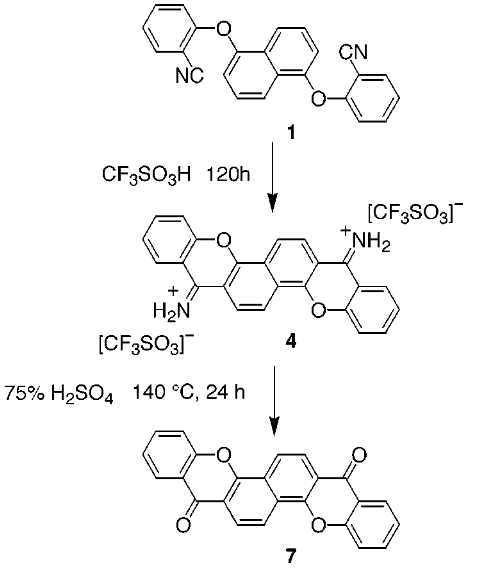
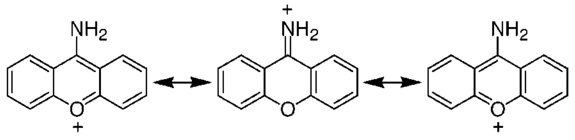
respectively, in high yields. Dissolution of these dinitriles in anhydrous trifluoromethanesulfonic acid at room temperature led to Houben−Hoesch cyclization (e.g., Scheme 1) and gave bisxanthone-iminium triflates **4**, **5**, and **6** in high yield. Nitrile cyclotrimerization, reported to be a significant side reaction in related *inter*molecular Houben−Hoesch reactions in strong-acid media,[7] was not evident in these reactions (though it have relevance for polymer-analogous chemistry; see below).

Scheme 1. Synthesis of the Fused-Ring Dixanthone **7**



The cations of **4**−**6**, which represent the first reported examples of xanthone-iminium ions, are readily deprotonated by weak aqueous base to afford neutral di-imines. Hydrolysis to the dixanthones **7**−**9**, however, requires very vigorous conditions (50−75% sulfuric acid at reflux for 24 h). The hydrolytic stability of xanthone-iminium ions contrasts sharply with that of conventional ketiminium ions (which generally hydrolyze merely on standing in air), perhaps reflecting stabilization of the electronic structure by resonance forms based on the 9-aminoxanthenylium ion (Scheme 2).

Scheme 2. Resonance Forms of the Xanthone-Iminium Ion



Dixanthones **7**−**9** were isolated in good yields and high purities and were characterized by spectroscopic methods and by elemental analysis. The substitution pattern of the naphthalene-based, fused-ring oligomer **7** was determined by single-crystal X-ray diffraction methods.[8]

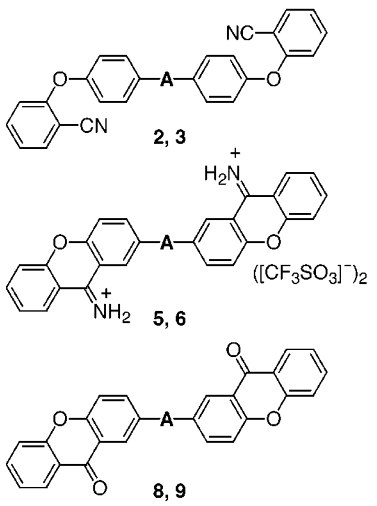


Figure 1. Dixanthones and intermediates (**A** = a direct bond for **2**, **5**, and **8** or a $C(CF_3)_2$ linkage for **3**, **6**, and **9**).

Compound **7** contains a centrosymmetric 1,2,5,6-substituted naphthalene residue (Figure 2) rather than the possible alternative having 1,4,5,8-substitution. The molecule is planar with a maximum deviation from coplanarity of 0.05 Å [for C(1)]. Molecules of **7** pack to form slightly offset π/π-stacks, with a mean interplanar separation of ca. 3.42 Å, and adjacent stacks are arranged to form a herringbone pattern (Figure 5).

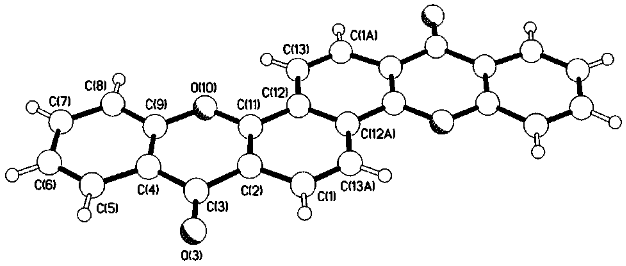


Figure 2. Crystal structure of dixanthone **7**.

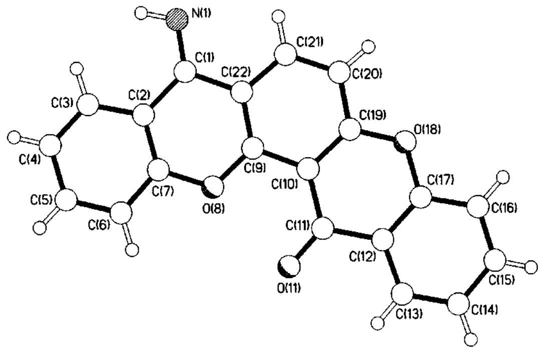


Figure 3. Crystal structure of the imino-xanthone **11**.

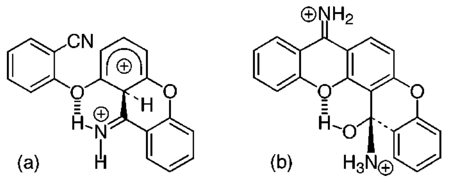
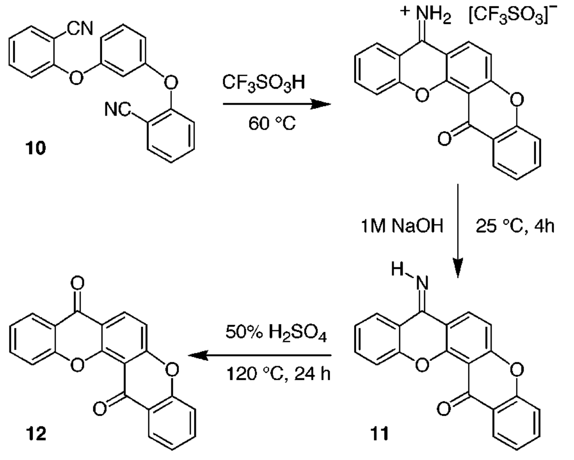


Figure 4. Hydrogen-bond stabilization of intermediates in (a) acid-catalyzed cyclization of dinitrile **10** and (b) acid hydrolysis of the di-imininium precursor to imino-xanthone **11**.

Scheme 3. Synthesis of Dixanthone **12** via the Intermediate Imino-Xanthone **11**



Cyclization of the resorcinol-derived dinitrile **10** required more forcing conditions than those described above, and after the product was treated with dilute sodium hydroxide at room temperature, the imino-xanthone **11** was obtained (Scheme 3) rather than the expected di-imine. Analysis of the intermediate iminium triflate by FAB-MS indicated that the hydrolysis had occurred during cyclization rather than on contact with the aqueous base.

The structure of **11** was established by single-crystal X-ray analysis.[9] The unit cell contains two independent molecules with identical regiochemistry, the relative positions of the imine and carbonyl groups being unambiguously determined from both the location of the imino hydrogen atom and the lengths of the C═N and C═O bonds (Figure 3). The C═N double bond is bent significantly away from one of its adjacent hydrogens as a consequence of repulsion between the aromatic and imino hydrogen atoms [C(2)−C(1)−N(1) = 127°]. The molecules form hydrogen-bonded tapes that π-stack with their centrosymmetrically related counterparts.

The dixanthone **12** was obtained by hydrolysis of **11** with 50% sulfuric acid at high temperature (Scheme 3). The regioselectivity of cyclization onto the resorcinol residue (1,2,3,4- rather than 1,3,4,6-substitution) may result from stabilization of the Wheland intermediate by intramolecular hydrogen bonding [Figure 4a] and a similar explanation, in terms of hydrogen-bond stabilization of the intermediate, could account for the enhanced susceptibility of the *endo*-imino group toward hydrolysis [Figure 4b].

To extend this chemistry to macromolecular systems, we next developed a route to the new biphenyl-based monomer **13**. Initial studies involving nickel-catalyzed coupling of 4-bromo-2-fluorobenzonitrile, in the presence of $[Ni(PPh_3)_4]$ and zinc powder,[10] yielded complex mixtures of products that proved very difficult to separate, but a clean, high-yielding synthesis of **13** was eventually developed using [Ni-(1,5-cyclooctadiene)$_2$] as a stoichiometric coupling agent (Scheme 4).[11]

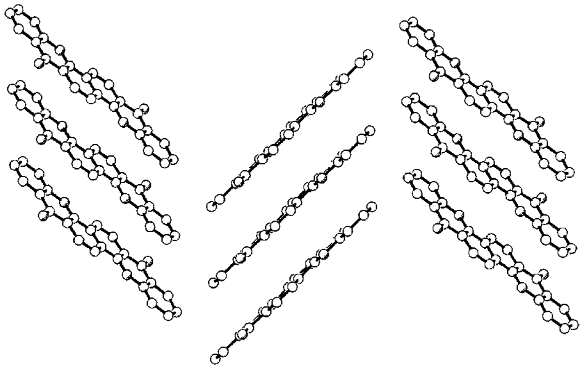
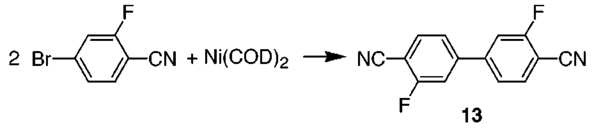


Figure 5. Crystal packing in dixanthone **7**.

Scheme 4. Synthesis of Monomer **13**



Polycondensation of **13** with 1,5-dihydroxynaphthalene and with 4,4′-dihydroxydiphenyl gave rather insoluble, crystalline polymers of very low molecular weight, but the polyethernitrile **14**, from condensation of **13** with 4,4′-hexafluoroisopropylidene-diphenol (Scheme 5), proved to be

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(7) Booth, B. L.; Noori, G. F. M. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2894−2900.

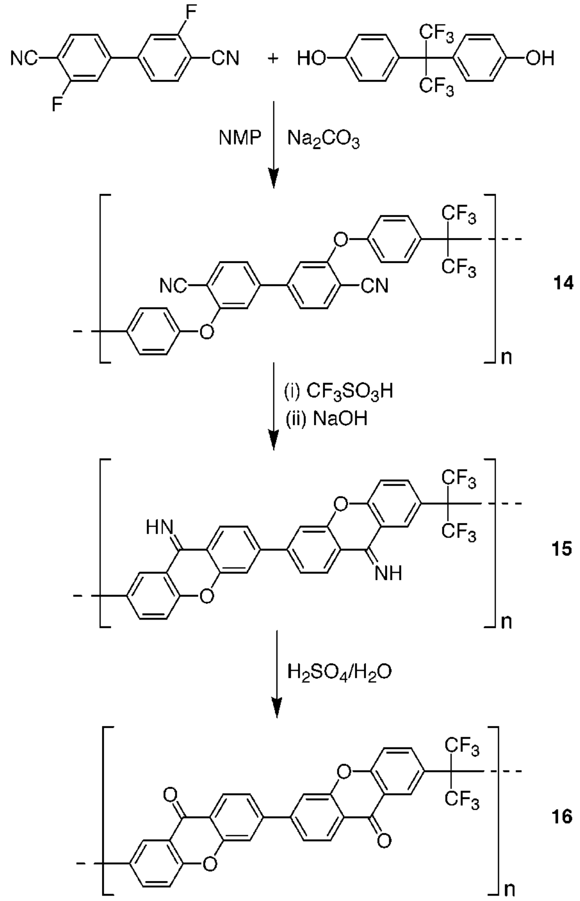
(8) **Crystal data for 7:** $C_{42}H_{12}O_4$, $M = 364.34$, monoclinic, space group $P2_1/n$, $a = 7.4211(12)$, $b = 4.7907(5)$, $c = 23.106(2)$ Å, $\beta = 95.728\ (7)°$, $V = 817.4(2)$ Å^3, $T = 296$ K, $Z = 2$, $D_c = 1.480$ g cm^{-3}, μ(Cu Kα) = 8.27 cm^{-1}, $F(000) = 376$; 1284 independent reflections, $R_1 = 0.060$, $wR_2 = 0.149$ for 887 independent observed reflections [$2\theta \leq 128°$, $F_o > 4\sigma(F_o)$]. Crystal dimensions 0.03 × 0.05 × 0.50 mm^3. Data were measured on a Siemens P4/RA diffractometer with graphite-monochromated Cu Kα radiation using ω-scans. The structure was solved by direct methods, and non−hydrogen atoms were refined anisotropically using F^2 data and the SHELXTL program package version 5.03.

(9) **Crystal data for 11:** $C_{20}H_{11}NO_3$, $M = 313.30$, triclinic, space group $P\bar{1}$, $a = 7.2454(9)$, $b = 13.7838(12)$, $c = 14.205(2)$ Å, $\alpha = 87.375(5)°$, $\beta = 85.609(8)°$, $\gamma = 83.879(7)°$, $V = 1407.2(3)$ Å^3, $T = 293$ K, $Z = 4$, $D_c = 1.479$ g cm^{-3}, μ(Cu Kα) = 8.22 cm^{-1}, $F(000) = 648$; 4182 independent reflections, $R_1 = 0.071$, $wR_2 = 0.156$ for 2466 independent observed reflections [$2\theta \leq 120°$, $F_o > 4\sigma(F_o)$]. Crystal dimensions 0.40 × 0.06 × 0.03 mm^3. Data collection and structure solution as for compound **7**.

(10) Colon, I.; Kelsey, D. *J. Org. Chem.* **1986**, *51*, 2627−2637.

(11) Semmelhack, M. F.; Helquist, P. M.; Jones, L. D. *J. Am. Chem. Soc.* **1971**, *93*, 5908−5910.

Scheme 5. Synthesis of Polymer **16**



noncrystalline, of high molecular weight (inherent viscosity in NMP = 0.42 dL g^{-1}), and readily soluble in organic solvents such as dichloromethane.

Successful cyclization of polymer **14** to a soluble poly(xanthone-iminium) salt required dissolution of **14** in dichloromethane, followed by slow addition of trifluoro-methanesulfonic acid. Direct contact between polymer **14** and the superacid resulted in cross-linking and insolubilization, possibly as a result of nitrile cyclotrimerization.[7]

After treatment with mild base the neutral, soluble polyxanthone-imine **15** was isolated and shown by ^{13}C NMR to have undergone essentially quantitative cyclization. Finally, the target polyxanthone **16** was obtained by acid hydrolysis of **15** at elevated temperatures. This amorphous polymer has a glass transition temperature of 372 °C and is insoluble in conventional organic solvents, though it dissolves readily and without degradation in strong acid solvents such as dichloro- and trifluoroacetic acids and 98% H_2SO_4. Its inherent viscosity in sulfuric acid was 0.69 dL g^{-1}. Transparent, free-standing films could be obtained by evaporation of solutions in dichloroacetic acid, and these remained strong and flexible at 300 °C.

In many ways, the properties of polymer **16** resemble those of aromatic polyimides (amorphous but insoluble in organic solvents, and with very good temperature resistance). However, the xanthone-based polymer has the considerable advantage that it (very evidently) does not suffer the problems of hydrolytic sensitivity at high or low pH that are inherent in any imide-based structure.

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Supporting Information Available: Experimental procedures and characterization data for compounds **1**−**3** and **7**−**13** and for polymers **14** and **16**. Crystallographic data for compounds **7** and **11**. This material is available free of charge via the Internet at http://pubs.acs.org.

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