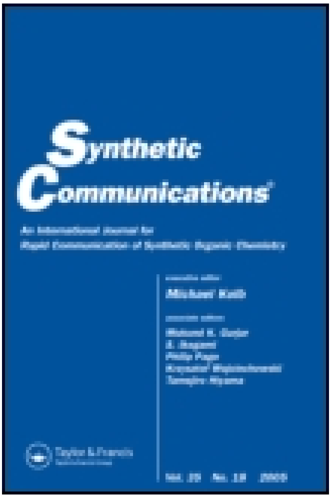

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Novel High Yielding Syntheses of Benzodifuranone Dyes Bearing Nitrogen Substituents at the 4-Position of a Pendent Phenyl Ring

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NOVEL HIGH YIELDING SYNTHESES OF BENZODIFURANONE DYES BEARING NITROGEN SUBSTITUENTS AT THE 4-POSITION OF A PENDENT PHENYL RING

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ABSTRACT

Otherwise inaccessible nitro benzodifuranone (BZDF) dyes are formed in good yield by treatment of 5-hydroxy-2-oxo-3-phenyl-2,3-dihydrobenzofuran either with $4NO_2$-3-R-$C_6H_3CBrClCO_2CH_3$ (R = H, alkyl, aryl or CO_2CH_3) in acetic acid. High yielding reduction of the nitro to the amino BZDF is accomplished by catalytic hydrogenation over Pd or by $NaBH_4$ / $SnCl_2$.

INTRODUCTION

Asymmetrically substituted benzodifuranone dyes (BZDF) (III) (Ar = Ar') combine high tinctorial strength and supreme colour fastness properties[1]. They are usually accessible by sequential addition to hydroquinone of two different ring substituted mandelic acids followed by oxidation of the resulting leuco compound (II) (Scheme 1)[2].

We needed a series of compounds (III) in which one of the pendent aryls was a phenyl ring substituted with either a nitro or an amino group at position 4 and an organic group at position 3. The sequence of Scheme 1 was not suitable for our purposes both because the requisite mandelic acids were difficult to make and because they combined with (I) in poor yield. An alternative synthesis[3], employing 4'-aminotartronic acids, needed expensive alloxan[4] as a starting material and was unsuitable for scale-up.

High yielding alternative methods using only inexpensive precursors have been devised.

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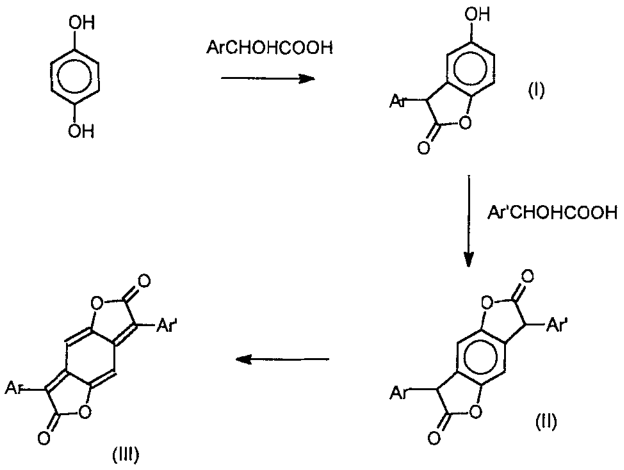
SCHEME 1



RESULTS AND DISCUSSION

Complementary syntheses of key intermediates (V) and (VII) (Schemes 2 and 3) have been reported[5,6]. Thus, conjugative addition of Grignard reagents to (IV) is high yielding when the group R is primary or secondary alkyl[5], while vicarious nucleophilic substitution (VNS) of (VIII) occurs most readily when the hydrocarbon residue R lacks a benzylic hydrogen[6]. Interconversion of the nitro (IIIa) and the amino (IIIb) BZDF dyes appeared likely to be straightforward, so it remained necesssary to find conditions for forming (III) from (I) with (V) and (VII).

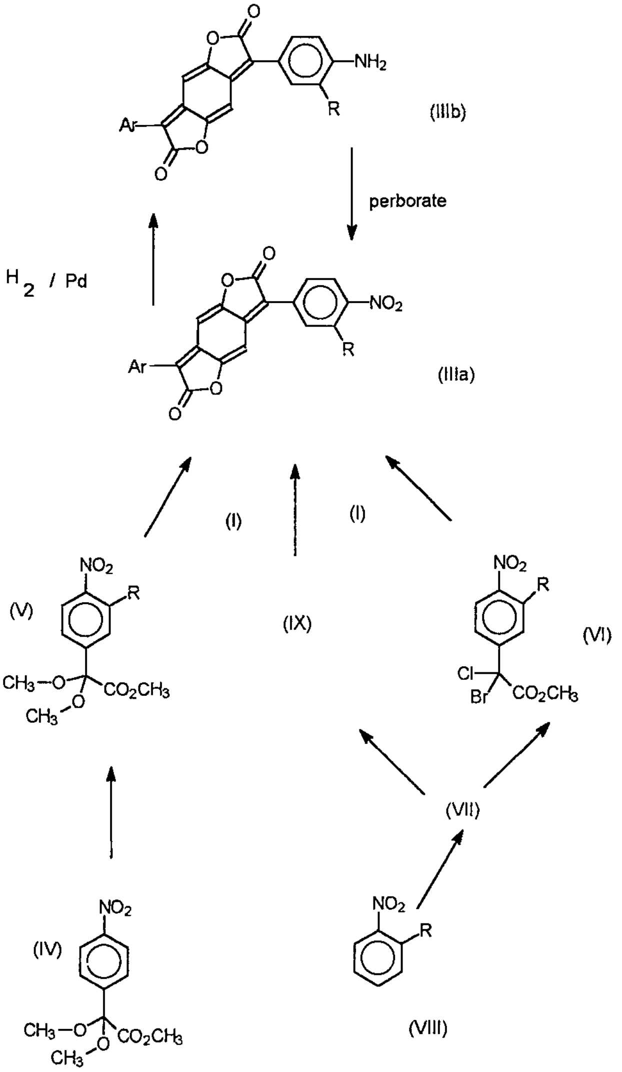
Reactions of (V) and (IX) with (I)

Although treatment of (I) with many mandelic acids under acidic conditions affords moderate yields of (II)[2], application of most of these methods to (V), (IX) and (VII) was unsuccessful. Surprisingly, both (V) and (IX) reacted with (I) in methane sulphonic acid at room temperature to give (IIIa) in moderate yield (Exp 1). Because both these reactions occurred under essentially anhydrous conditions, it is unlikely that they involved a common carbocation intermediate.

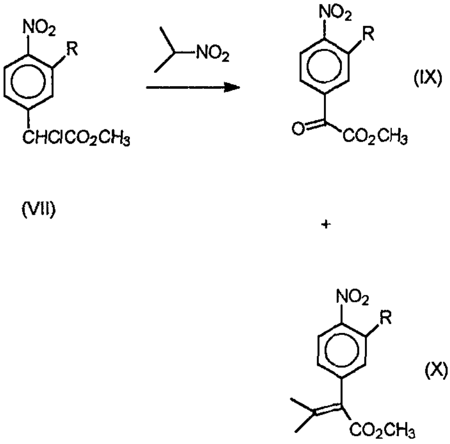
Reactions of (VII)

In contrast to (V), which requires a costly starting material (IV), the generation of (VII) needs only inexpensive reactants[6]. The unexpected discovery that VNS could be applied even to such highly unsuitable substrates as 2-nitrotoluene increased our desire to effect the conversion of (VII) into (IIIa).

SCHEME 2


NH2
R
(IIIb)
perborate
H2 / Pd
Ar
O
NO2
(IIIa)
(I)
(I)
(V)
NO2
R
CH3–O
CO2CH3
CH3
(IX)
(VI)
Cl
Br
(VII)
(IV)
(VIII)

SCHEME 3



Numerous attempts to condense (VII) with (I) were unsuccessful so the conversion of (VII) into (IX) was tried. Use of sodium azide[7] and of amine oxides[8] was rejected on grounds of cost and hazard. The less expensive oxidant 2-nitropropane[9] gave (IX) (40%) together with unacceptable amounts of (X) (Scheme 3) (Exp 2).

Following an alternative approach, bromination of (VII), under controlled conditions which integrate well with VNS, afforded (VI) (80%) (Exp 3). Treatment of (I) with (VI) in the presence of of various Lewis acids gave (IIIa) in poor yields (ca 10%). Most surprisingly, (IIIa) was formed in high yield (90%) and purity merely upon heating (I) with (VI) in acetic acid (Exp 4). Thus, various (IIIa) were accessible in only three steps in overall yield > 50% from (VIII).

Interconversion of (IIIa) and (IIIb)

As expected, these conversions were not difficult. Hydrogenation of the nitro group of (IIIa), which occurred readily and cleanly at room temperature in ethyl acetate in the presence of 5% Pd on alumina, gave the amino compound in its leuco form (II). After removal of the catalyst by filtration, the filtrate rapidly generated (IIIb) (80% overall yield from (IIIa)) in air after the addition of a drop of triethylamine. Selective reduction of (IIIa) to (IIIb), avoiding over reduction to the leuco form, was accomplished in refluxing ethanol using sodium borohydride in the presence of stannous chloride (> 7 mol / mol BZDF)[10]. It proved possible to replace most of the stannous chloride (except for ! mol / mol BZDF) by an equivalent amount of concentrated hydrochloric acid, the addition of which accompanied that of borohydride, with only a small loss in selectivity to (IIIb) (from 80 to 70%). Oxidation of (IIIb) to (IIIa) (> 50%) proved possible using perborate[11].

EXPERIMENTAL

Exp. 1. Formation of BZDF (IIIa) from (I) and esters (V) and (IX)

(I)(Ar = Ph) (1.0g, 4.4 mmol) was stirred with (V)(R = sec-butyl) (1.0g, 3.9 mmol) in methane sulphonic acid (10 ml) at room temperature for three days. The mixture was drowned into water and the resulting solid filtered off, well washed and dried. There was obtained (IIIa) (R = sec-butyl, Ar = Ph) (1.18g, 60%), m / e = 441, λ_{max}= 568 nm, $w_{1/2}$ = 140 nm, ε = 29,000 mol^{-1} l cm^{-1} in CH_2Cl_2. Similar treatment of (I) (Ar = Ph) with (IX) (R = Ph), formed by oxidation of (VII) (R = Ph) with pyridine N-oxide[8], gave (IIIa) (R = Ph) (55%), m /e = 461, λ_{max} = 462 nm, $w_{1/2}$ = 83 nm, ε = 28, 000 mol^{-1} l cm^{-1} in CH_2Cl_2. In the same way, there was made (IIIa) (R = CO_2CH_3), m / e = 443, λ_{max} = 462 nm, $w_{1/2}$ = 84 nm, ε = 35,000 mol^{-1} l cm^{-1} in CH_2Cl_2.

Exp. 2. Reaction of the VNS adduct (VII) with 2-nitropropane

(VII) (R = CH_3) (5g, 15.5 mmol) and 2-nitropropane (5g) in DMF (50 ml) were stirred at 5°. There was added dropwise over 10 min 0.54 M methanolic $NaOCH_3$ (38 ml). GC on CPSIL5CB at 100 to 250° showed that there had been formed (IX) (R = CH_3) (40%), m / e = 223 together with (X) (R = CH_3) (ca 20%), m / e = 249.

Exp. 3. Bromination of VNS adduct (VII)

Reagent solutions were (a) bromine ((4.3 g) in methanol (60 ml), and (b) $NaOCH_3$ (5 ml of 5.4 M diluted to 60 ml in methanol). These reagents were added dropwise at equal rates to a stirred solution of (VII) (R = CH_3) (6.0 g, 24.6 mmol) in methanol (20 ml). The reaction was rapid and could be followed by transient colour changes as alternative drops of (a) (brown) and (b) (purple anion of (VII)) were added. The additions were stopped when (b) no longer generated a purple colour. Methanol was removed at the pump and the residue was recrystallised from ethanol to give (VI) (5.0 g, 75%). ^{1}HNMR in $CDCl_3$ δ 2.65 s (3.0 H), 3.9 s (2.9 H), 7.7 m (1.9H), 8.0 d (1.0 H), ^{13}CNMR in $CDCl_3$ 20.61, 55.27, 70.11, 124.73, 125.9, 131.62, 133.82, 143.57, 149.38, 165.97 ppm, m / e = 322 (1Cl, 1 Br). $C_{10}H_9NBrClO_4$ needs C (37.2), H (2.8), N (4.3), found C (37.8), H (2.9), N (4.5).

Exp. 4. BZDF (IIIa) formation from (I) and (VI)

A mixture of (I) (Ar = Ph) (1.0 g) and (VI) (R = CH_3) (1.0 g) and acetic acid (10 g) was stirred at room temperature for 15 min, at 50° for 90 min and at 115° for 16 hr. The mixture was cooled to 20°, poured into 10% w /w hydrochloric acid (100 g), stirred for 15 min and the resulting solid filtered off, washed and dried to give (IIIa) (R = CH_3) (1.24 g, 90%), λ_{max} = 463 nm, ε = 50,000 mol^{-1} l cm^{-1} in THF.

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