

Behaviour of 1,2,3-Indantrione Towards Wittig-Horner Reagents

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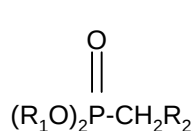
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Abstract: reagents **1a,b** react with 1,2,3-indantrione (**2**) to give the dimeric adducts **3a** and **3b**, respectively. Moreover, **2** reacts with tert-butyl diethylphosphonoacetate (**1c**) yielding the ethylenic compound **4**. On the other hand, **2** reacts with **1d** to yield the phosphonate adduct **5**. Mechanisms accounting for the formation of the new products are discussed and the probable structures of the products are presented based on compatible analytical and spectral data.

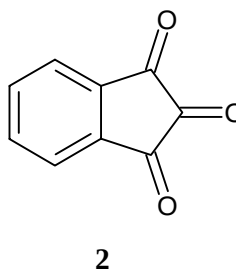
Keywords: Indantrione, Wittig-Horner reagents, phosphonate, spiroadduct.

Introduction

In previous publications [1-3], we have examined the reactions of Wittig-Horner reagents **1** with o-quinones, p-quinones and quinoneimines. The present work extends the former work by studying the behaviour of 1,2,3-indantrione (**2**) toward the same reagents **1**.



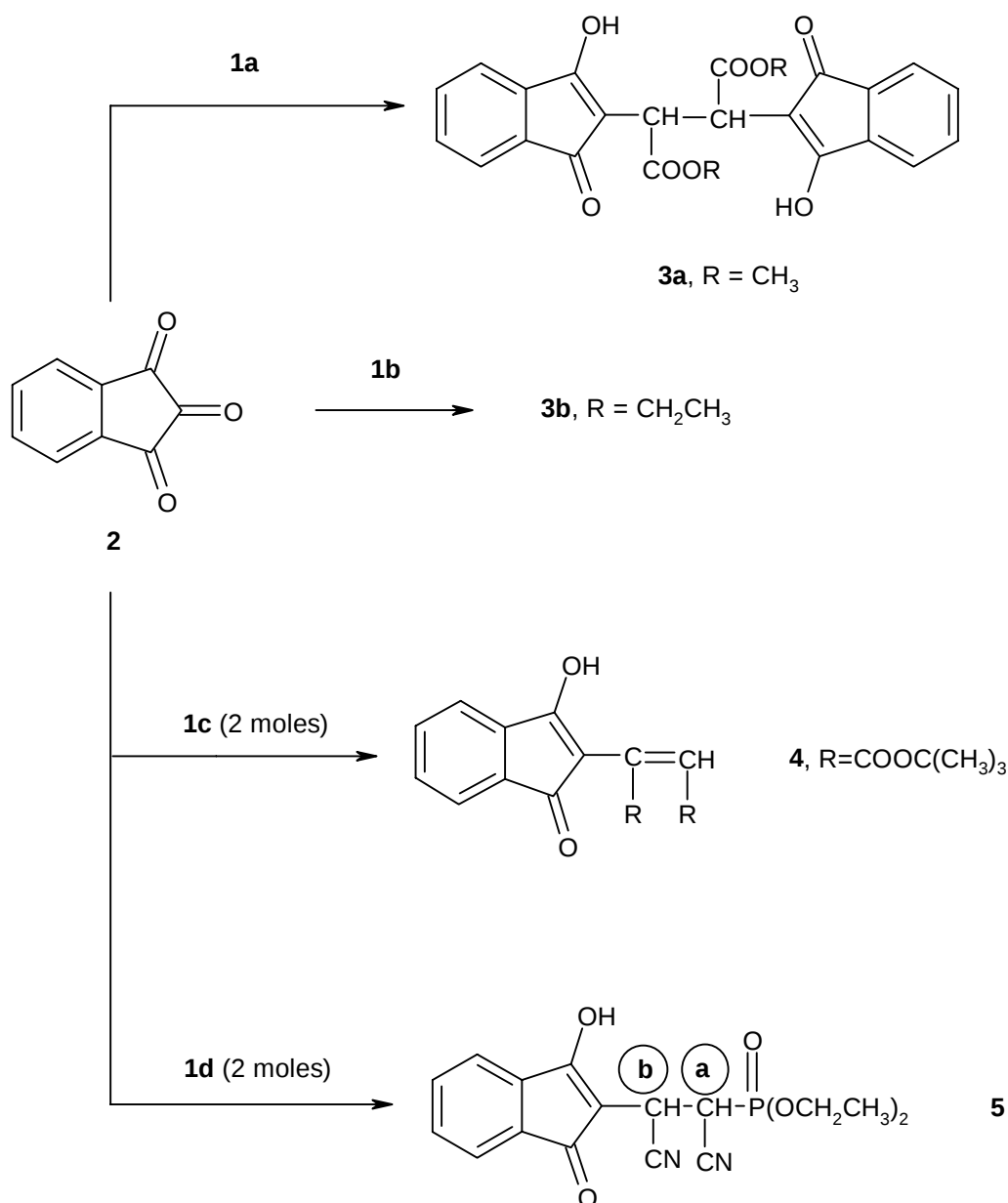
- 1a** $\text{R}_1 = \text{C}_2\text{H}_5$ $\text{R}_2 = \text{COOCH}_3$
b $\text{R}_1 = \text{C}_2\text{H}_5$ $\text{R}_2 = \text{COOC}_2\text{H}_5$
c $\text{R}_1 = \text{C}_2\text{H}_5$ $\text{R}_2 = \text{COOC}(\text{CH}_3)_3$
d $\text{R}_1 = \text{C}_2\text{H}_5$ $\text{R}_2 = \text{CN}$



Results and Discussion

We have found that the reaction of 1,2,3-indantrione (**2**) with 1 mol equivalent of methyl diethylphosphonoacetate (**1a**), in the presence of alcoholic sodium ethoxide solution, proceeds at room temperature to give a chromatographically pure adduct formulated as dimethyl 2,3-bis(3-hydroxy-1-oxoinden-2-yl)butane-1,4-dioate (**3a**) (Scheme 1).

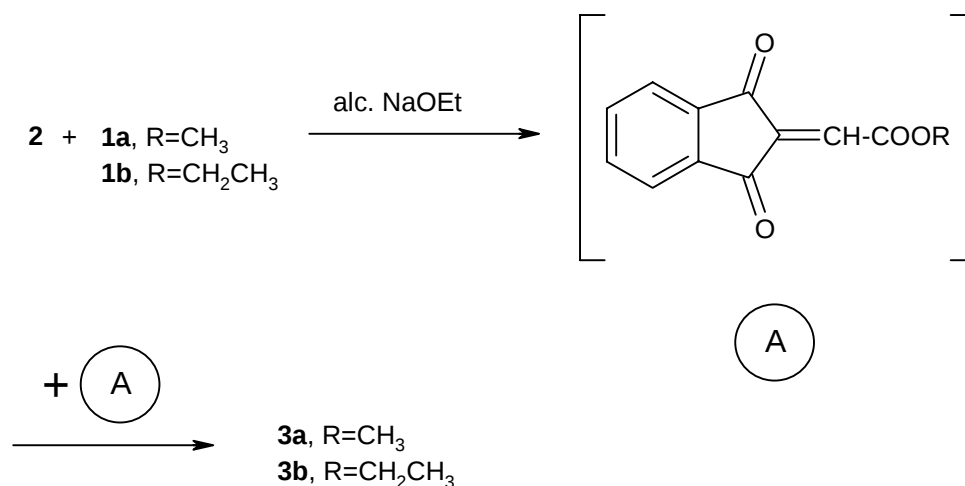
Scheme 1



The structure of **3a** was confirmed by its satisfactory IR, ¹H-NMR and MS and elemental analyses (cf. Experimental). The ¹H-NMR spectrum of **3a** showed two proton doublets centered at 4.30 and 4.33 ppm, with ³J_{H-H} = 16 Hz that suggested a trans configuration for the adduct [4]. Similarly, triethylphosphonoacetate (**1b**) reacted with 1,2,3-indantrione (**2**) in the presence of alcoholic sodium ethoxide solution at room temperature for 6 hours to give a crystalline product that was assigned

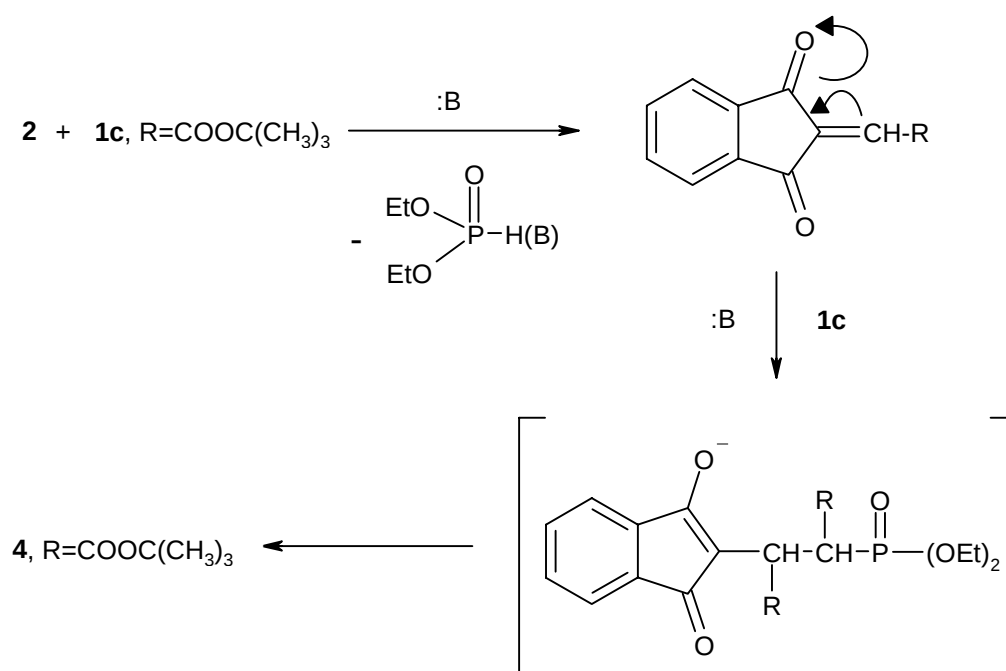
structure **3b** (Scheme 1), on the basis of its IR, $^1\text{H-NMR}$, MS and elemental analyses (cf. Experimental). Formation of compounds **3a** and **3b** can be explained in terms of carbonyl olefination of **2** by the Wittig-Horner reagents **1a,b** to give the reactive intermediate (A). Dimerization of the unstable reactive intermediate (A) results in the formation of the stable dimeric products **3a,b** (Scheme 2).

Scheme 2



We have also investigated the reaction of compound **2** with *tert*-butyl diethylphosphonoacetate (**1c**). The reaction of **2** with **1c** was performed in alcoholic sodium ethoxide solution in 1:2 molar ratio to give the olefinic product **4** (Scheme 3).

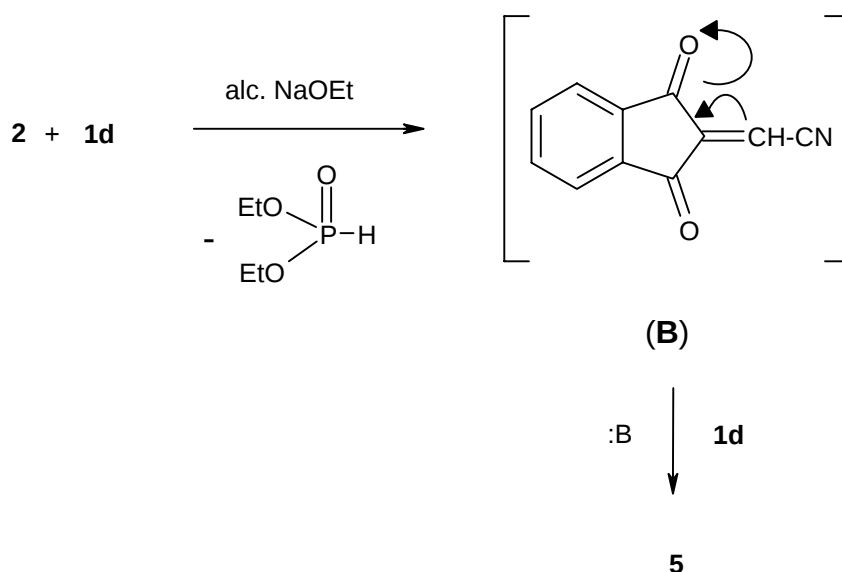
Scheme 3



Compound **4** was obtained in a sharp-melting chromatographically pure form. Its elemental and mass spectral analyses corresponded to a molecular formula of $C_{21}H_{24}O_6$, and the structure of the adduct was further confirmed by its IR, 1H -NMR and mass spectral data (cf. Experimental). A possible explanation of the course of the reaction of *tert*-butyl diethylphosphonoacetate (**1c**) with 1,2,3-indantrione (**2**) is shown in Scheme 3. In the presence of NaOEt solution trione **2** reacts with two moles of *tert*-butyl diethylphosphonoacetate (**1c**) to give the stable olefinic compound **4**. Next, when 1,2,3-indantrione (**2**) was treated with one mole equivalent of diethyl(cyanomethyl)phosphonate (**1d**) in the presence of alcoholic sodium ethoxide solution at room temperature for 10 hours, adduct **5** together with some unchanged trione **2** were isolated. Carrying out the reaction using two moles of **1d** instead of one led to the formation of adduct **5** in a good yield (Scheme 1). The proposed structure of compound **5** was confirmed by correct elemental analyses, molecular weight determination by MS, IR spectrum, ^{31}P NMR spectrum which indicates a phosphonate structure [6-8] and 1H NMR spectrum.

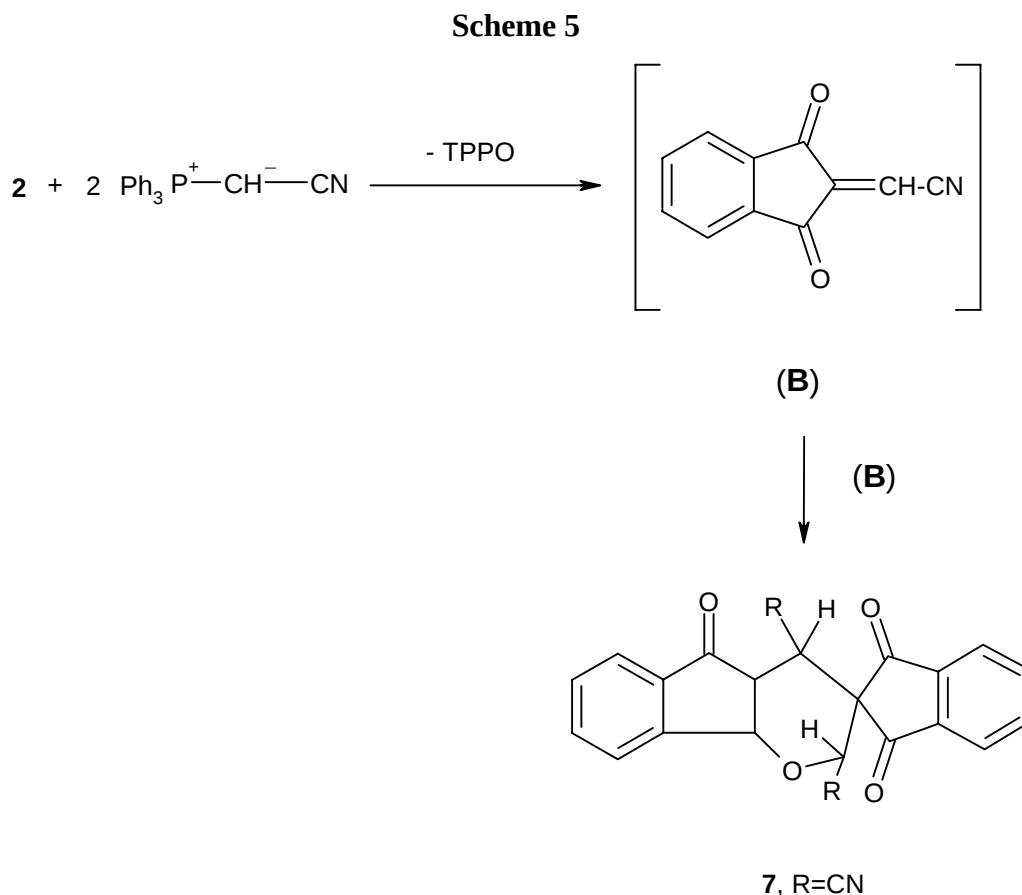
Apparently compound **2** reacts with one mole equivalent of diethyl (cyanomethyl)phosphonate (**1d**) in the presence of sodium ethoxide solution to give the unstable olefinic intermediate (B) which then reacts with another mole of **1d**, in the presence of NaOEt solution, to give the stable phosphonate adduct **5** (Scheme 4).

Scheme 4



Finally, this study has been extended to include the reaction of **2** with cyanomethylene-triphenylphosphorane ($Ph_3P^+ - ^-CHCN$) (**6**) to establish whether it would behave in a similar manner. Thus, 1,2,3-indantrione (**2**) was treated with two mole equivalents of phosphonium ylide **6** in dry benzene at room temperature for 5 hours.

The reaction mixture was separated by column chromatography on silica gel, whereby, triphenylphosphine oxide, as well as a crystalline product **7** were isolated (Scheme 5). Compound **7** was obtained as colourless crystals (60% yield) and was formulated as 2,4-dihydrospiro(indan-2,3-(2H)indeno{[1,2-b]pyran}-1,3,5(4H)-trione dicyanate.



The structure of the new spiro compound **7** was established from its elemental analyses and spectral properties (cf. Experimental). Adduct **7** can be obtained via carbonyl olefination with one molecule of ylide **6** to give the reactive intermediate (B), with expulsion of triphenylphosphine oxide. Dimerization of (B) by a Diels-Alder type reaction [10], afforded the final product (Scheme 5). From the above results, it is evident that 1,2,3-indantrione (**2**) behaves toward cyanomethylene-triphenylphosphorane **6** in a manner quite similar to that previously reported for the reaction of 1,2,3-indantrione with alkoxycarbonylmethylenetriphenylphosphoranes which produce the spiro compound **7** (R = COOCH₃ or COOC₂H₅) almost exclusively (Scheme 5) [10].

Conclusions

Although 1,2,3-indantrione (**2**) has been reported [10] to react with resonance-stabilized Wittig reagents to give the spiro adducts **7** (R = COOCH₃, COOC₂H₅), a different behaviour is observed in the reaction of this trione **2** with Wittig-Horner reagents **1** (Scheme 1). From the results of the present

investigation, it can be concluded that the reaction of 1,2,3-indantrione (**2**) with Wittig-Horner reagents **1** leads to different products, depending on the nature of the phosphonate anion used as well as on the stability of the addition products [11]. The finding of the present investigation is of particular interest since it represents a novel synthetic application of Wittig-Horner reagents.

Experimental

General

All melting points are uncorrected. Wittig-Horner reagents **1a-d** were prepared by the Michaelis-Arbuzov reaction [12,13]. Cyanomethylenetriphenylphosphorane was prepared by a published procedure [14]. The IR spectra were measured in KBr disks with a Perkin Elmer Infracord Model 157 Grating Spectrophotometer. The ^1H -NMR spectra were run on Varian Spectrophotometer at 200 MHz, using TMS as an internal reference. The ^{31}P -NMR spectra were recorded in CDCl_3 (vs., 85% H_3PO_4 as an external standard) with a JNM-PS-100Fa Spectrometer. The mass spectra were run at 70 eV with Kratos MS equipment and/or a Varian MAT 311 A Spectrometer.

*Reaction of 1,2,3-indantrione (**2**) with methyl diethylphosphonoacetate (**1a**): Preparation of dimethyl 2,3-bis(3-hydroxy-1-oxoinden-2-yl)butane-1,4-dioate (**3a**).*

A solution of 1 mol of sodium ethoxide in absolute ethanol was treated with an equimolar amount of phosphonate **1a** (0.21 g, 0.001 mol). After 5 min. 1 mol of trione **2** was added and the resulting mixture was stirred at room temperature for 6 hr. The reaction mixture was poured onto a small amount of water, extracted with ethyl acetate, dried, and the extracts were evaporated under vacuum. The residue was purified on a silica gel column using 40-60°C pet. ether- ethyl acetate (v:v) as eluent to give compound **3a**, which was recrystallized from benzene (yield 78%); m.p. 182-183°C; Analysis Calcd. for $\text{C}_{24}\text{H}_{18}\text{O}_8$ (434.408), C, 66.36; H, 4.18; Found, C, 66.45; H, 4.22; Mol. wt (MS) = 434 (M^+ , 75%); IR (cm^{-1}): 1720, 1675; ^1H -NMR (ppm): 3.30 (3H, s, OCH_3); 3.50 (3H, s, OCH_3), 8.20 (s, 1H, D_2O exchangeable, OH) and 8.35 ppm (s, 1H, D_2O exchangeable, OH); signals at 4.30 ppm (d, 2H, $^3J_{\text{HH}} = 16$ Hz) and 4.33 ppm (d, 2H, $^3J_{\text{HH}} = 16$ Hz) suggest the trans configuration of adduct **3a** [4]; 6.80-8.05 (complex m, 8H, aromatic protons).

*Reaction of 1,2,3-indantrione (**2**) with triethylphosphonoacetate (**1b**): Preparation of diethyl 2,3-bis-(3-hydroxy-1-oxoinden-2-yl)butane-1,4-dioate (**3b**).*

A solution of 1 mol of sodium ethoxide in absolute ethanol was treated with an equimolar amount of phosphonate **1b** (0.22 g, 0.001 mol), After 5 min. 1 mol of trione **2** was added and the resulting mixture was stirred at room temperature for 4 hr. The reaction mixture was poured onto a small amount of water, extracted with ethyl acetate and the filtered extracts were evaporated under vacuum after drying over anhydrous sodium sulfate. The residual material was purified on a silica gel column using 40/60°C pet. ether - ethyl acetate (v:v) as an eluent to give **3b** as pale orange crystals (yield

80%); m.p. 159-160°C from benzene; Analysis Calcd. for $C_{26}H_{22}O_8$ (462.462): C, 67.53; H, 4.80; Found, C, 67.6; H, 4.83; Mol. wt (MS) = 462. (M^+ , 65%); IR (cm^{-1}): 3500 (OH), 1740 (C=O, ester), 1680 cm^{-1} (C=O, indene); 1H -NMR (δ): 0.6 (t, 3H, ethoxy-CH₃), 1.25 (t, 3H, ethoxy-CH₃), 3.45 (q, 2H, ethoxy-CH₂), 3.7 (q, 2H, ethoxy-CH₂), 4.5 (2H, t, $^2J_{HH} = 16$ Hz, CH-CH) and 6.8-8 (m, 8H, Ar), . 8.2 (s, 1H, D₂O exchangeable proton, OH), 8.35 (s, 1H, D₂O exchangeable proton, OH),

Reaction of tert-butyl diethylphosphonoacetate (1c) with 1,2,3-indantrione (2): Preparation of di-tert-butyl (Z)-2-(3-hydroxy-1-oxoinden-2-yl)but-2-ene-1,4-dioate (4).

The reaction of phosphonate **1c** (0.002 mol) with trione **2** (0.001 mol) was carried out in alcoholic sodium ethoxide solution (0.002 mol of Na in 20 mL C₂H₅OH). The mixture was maintained under stirring at room temperature over night. The reaction mixture was poured onto water and extracted with chloroform. The extracts were evaporated under vacuum after drying. The residue was purified on a silica gel column using 40/60°C pet. ether - ethyl acetate (v:v) as an eluent to give compound **4** (yield 76%); M.p. 98-100°C (from cyclohexane); Analysis, Calcd. for $C_{21}H_{24}O_6$ (372.423): C, 67.73; H, 6.50; Found, C, 67.65; H, 6.55; mol. wt. (MS) = 372. (M^+ , 70%); IR (cm^{-1}): 1715 (C=O, indene), 1740 (C=O, ester) and 3524 (OH); 1H -NMR: 1.85 ppm (s, 9H, C (CH₃)₃) and 1.90 ppm (s, 9H, C(CH₃)₃), 6.95 (s, 1H, methine), 7.35-7.60 (m, 4H, Ar) and 9.40 (s, 1H, D₂O exchangeable proton, OH),

Reaction of diethyl(cyanomethyl)phosphonate (1d) with 1,2,3-indantrione (2): Preparation of [1,2-dicyano-2-(3-hydroxy-1-oxo-1H-inden-2-yl)-ethyl]-phosphonic acid diethyl ester (5).

A solution of two moles of sodium ethoxide in absolute ethanol was treated with equimolar amounts of phosphonate **1d** and trione **2** and the resulting mixture was stirred at room temperature for 10 hr. The reaction mixture was poured onto a small amount of water, extracted with ethyl acetate and the extract was dried over anhydrous sodium sulfate then evaporated under reduced pressure. The residual material was applied to a silica gel column chromatography using 40/60°C pet. ether – ethyl acetate (v:v) as an eluent to give **5** as pale yellow crystals in 75% yield; m.p. 176-177°C from benzene; Analysis, calcd. for $C_{17}H_{17}N_2O_5P$ (360.311): C, 56.67; H, 4.76; N, 7.77; P, 8.60%. Found: C, 54.6; H₂, 4.8; N, 7.4; P, 8.27%; mol. wt. (MS) = 360 (M^+ , 90%). IR (cm^{-1}): 3502 (OH), 1230 (P-O-bonded)[5], 1047 (P-O-C₂H₅) [5] and 2208 cm^{-1} (CN). ^{31}P -NMR: $\delta = 19.95$ ppm indicates a phosphonate structure [6-8]. 1H -NMR δ (ppm): 1.25 (6H, t) and 3.95 ppm (4H, q) (P-OCH₂CH₃) [9]; 3.70 ppm (d, 1H, with $^3J_{HP} = 12$ Hz, $J_{HH} = 7.5$ Hz) and 3.65 ppm ($^2J_{HP} = 10$ Hz, $J_{HH} = 7.5$ Hz) for the two methine protons b and a, respectively (Scheme 1); 7.35-7.64 ppm (4H, m, aromatic protons); 9.4 (s, D₂O exchangeable, OH).

Reaction of 1,2,3-indantrione (2) with cyanomethylene triphenylphosphorane (6): Preparation of 2,4-dihydrospiro(indan-2,3-(2H)indeno{[1,2-b]pyran}-1,3,5(4H)-trione dicyanate (7).

To a suspension of trione **2** (0.16g, 0.001 mol) in dry benzene (25 mL), was added a solution of the ylide **6** (0.6g, 0.002 mol) in absolute benzene (25 mL). The reaction mixture was stirred at room

temperature for 5 h, then evaporated under reduced pressure. The residual substance was dissolved in CH₂Cl₂ (100 mL) and evaporated till dryness in the presence of silica gel (5 g). The reaction mixture was then added to a column previously loaded with silica gel in petroleum ether. The column was developed with petroleum ether (60/80°C) containing increasing amounts of CHCl₃. A fraction eluted with 9:1 v/v petroleum ether/CHCl₃ gave a substance that was recrystallized from benzene to give compound **7** as colourless crystals (60% yield); m.p. 168-169°C; Anal. Calcd. for C₂₂H₁₀N₂O₄ (366.336): C, 72.13, H, 2.75; N, 7.64; Found : C, 72.3; H, 2.8; N, 7.66%; Mol. wt (MS) = 366 (M⁺, 60%); IR (cm⁻¹): 1745 (C=O, cyclopentanone), 1715 (C=O, 1,3-dicarbonyl), 2226 (CN) and 3100 (CH, aromatic). ¹H-NMR (ppm) 4.21 and 4.23 (two s, 2H, dihydropyran ring), 7.47 (dd, 1H, J_{HH} = 8.4 Hz, J_{HH} = 1.1 Hz), 7.68 (m, 1H), 7.43 (m, 1H), 8.21 (dd, 1H, J_{HH} = 8.4 Hz, J_{HH} = 1.1 Hz), 7.8 (m, 4H, Ar). A fraction eluted by petroleum ether/CHCl₃ (7:3 v/v) yielded colourless needles, shown to be triphenylphosphine oxide by m.p., mixed m.p., and comparison of the respective IR and MS spectra.

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