Thermal Cyclization of 3-Azido-2-phenyl-indan-1-one to 5*H*-Indeno[1,2-*b*]indol-10-one [1]

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3-Azido-2-phenylindan-1-one (**4**), which was obtained from 3-chloro-2-phenylindan-1-one (**3**), cyclizes on thermolysis to 5*H*-indeno[1,2-*b*]indol-10-one (**5**). Reaction of 3-azido-2-phenylindan-1-one (**4**) with triphenylphosphane gives 2-phenyl-3-(triphenylphosphoranylideneamino)-indan-1-one (**6**), which can be hydrolyzed to 3-amino-2-phenylindan-1-one (**7**). Attempts to perform a similar cyclization sequence with 3-chloro-2-pyridylindan-1-ones failed.

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Thermolysis of azidoarenes with *ortho*-phenyl groups offers a simple way to the interesting class of indolo-fused arenes [2]. Recently we described the synthesis of naphtho[8,1-*ab*]carbazolones from 3-azidophenalen-1-ones [3]. In this work we studied the cyclization of 3-azido-2-phenylindan-1-one (**4**) to 5*H*-indeno[1,2-*b*]-indol-10-one (**5**), a compound which has recently been found interesting because of its role in the enzyme activity of antioxidant agents [4].

The reaction sequence started from 2-phenylindane-1,3-dione (**2a**) obtained from phthalic anhydride (**1**) and phenylacetic acid with a modified literature procedure [5]. Analysis by ^{1}H nmr reveals that **2** exists predominantly in its tautomeric dioxo form **2a**; the enol form **2b** is not visible in the spectrum. As reactive intermediate for the synthesis of 3-azido-2-phenylindan-1-one (**4**), 3-chloro-2-phenylindan-1-one (**3**) was prepared from **2** with phosphorylchloride in 88% yield. A reported method from **2**, phosphorus pentoxide and gaseous hydrogen chloride is inconvenient and gives a low yield [6]. The reaction of **3** with sodium azide gave azide **4** in a rather exothermic way which needed cooling to 0 °C to avoid decomposition.

The thermolysis of azidoarenes such as **4** with *ortho*-phenyl substituents is described to lead *via* arylnitrenes in an electrocyclic reaction followed by a 1,5-hydrogen shift to indoles [2], which offers a simple pathway with high yields to this interesting class of compounds. Because the azide **4** decomposes already at rather low temperatures, we investigated the thermal reactivity of **4** by means of differential scanning calorimetry (DSC). The DSC diagram of **4** (Figure 1)

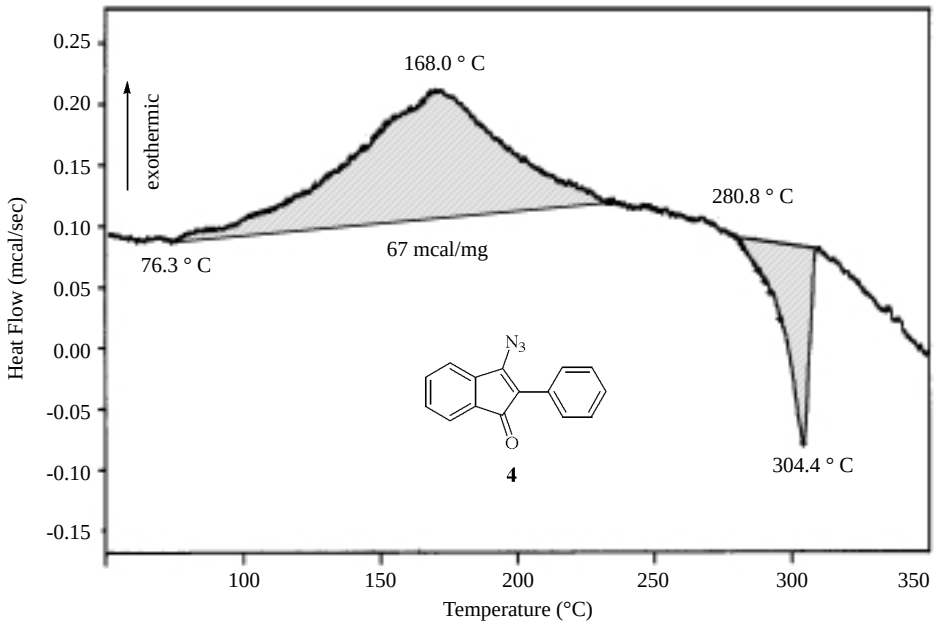
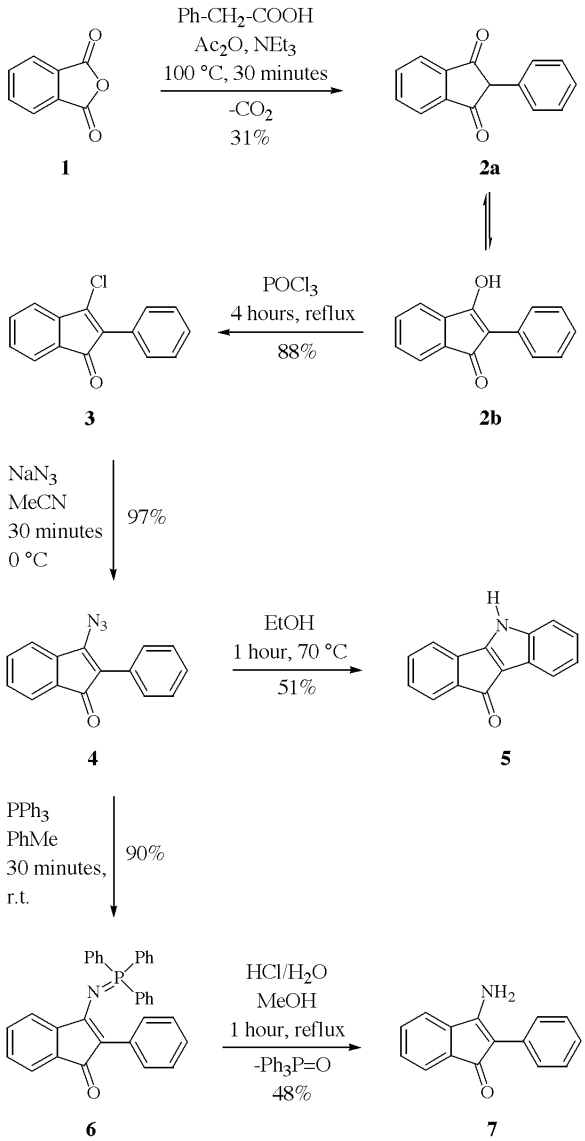


Figure 1. Differential scanning calorimetriy diagram of 3-azido-2-phenylindan-1-one (**4**).

reveals that **4** gives an exothermic reaction (ΔH = -70 mcal/mg) with an onset at about 75 °C and a maximum at 168 °C. After the reaction area, a melting point of about 304 °C is observed, which derives from the cyclization product **5** (mp of pure **5**: 331 °C). From this data we performed the thermal decomposition of **4** at 60-70 °C. After nitrogen evolution has stopped (about 1 hour), the pure cyclization product, 5*H*-indeno[1,2-*b*]indol-10-one (**5**) crystallizes on cooling in good yields from the reaction solvent.

Azides are reported to react with phosphanes by a Staudinger reaction to phosphazenes [7], which then can be hydrolyzed to amines. This offers a good and mild synthesis of amines, especially when the catalytic reduction of azides or direct amination gives by-products. 3-Azido-2-phenylindan-1-one (**4**) affords 2-phenyl-3-(triphenylphosphoranylideneamino)-indan-1-one (**6**) in excellent yields by reaction with triphenylphosphane at room temperature for 30 hours. Acid catalyzed hydrolysis of the phosphazene **6** leads by cleavage of triphenylphosphanoxide to 3-amino-2-phenylindan-1-one (**7**). However **7** is only obtained in moderate yields because the separation of the second reaction product, triphenylphosphanoxide, causes loss of the yield.

Scheme 1

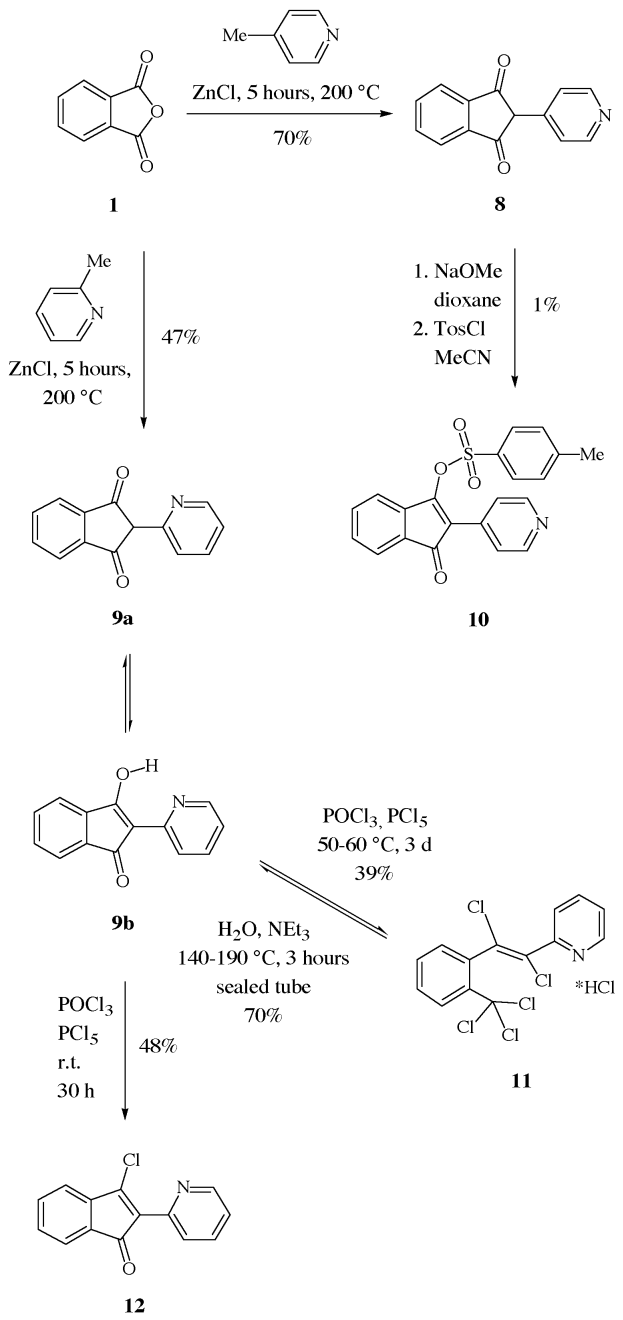


Recently we showed that the cyclization of arylazides with *ortho*-pyridyl-substituents gives an interesting type of new heterocycle, namely zwitterionic 8-azaindoles [3], by direction of the cyclization to the more basic α–nitrogen of the pyridyl substituent. 2-(2-Pyridyl)-indandione (**9**) [8] should serve as a good starting material for such a ring closure reaction. We prepared **9** from phthalic anhydride (**1**) and 2-methylpyridine using zinc chloride as catalyst by adopting a literature method [9], and obtained **9** in moderate yields. The ^{1}H nmr spectrum reveals that **9** exists mainly as the enolized tautomer, 3-hydroxy-2-(2-pyridyl)-indan-1-one (**9b**), with the OH signal at δ = 14.20 ppm, and no signal was observed for the aliphatic proton at C-2 of the indane ring, in contrast to **2**, which shows in the nmr data no enol tautomer. The reason is probably a hydrogen bond between the hydroxy group and the nitrogen at position 2 of the pyridine ring. In a similar way, 2-(4-pyridyl)-indane-1,3-dione (**8**) was obtained from phthalic anhydride (**1**) and 4-methylpyridine in excellent yields; for **8** the ^{1}H nmr spectrum shows signals corresponding to a mixture of tautomers.

The conversion of **9** to a reactive chloro intermediate with phosphorylchloride, as occurred for **2** to give the chloro compound **3** failed. A reaction sequence described in the literature at 160 °C gave only tarry material [10]. Addition of triethylamine to destroy the hydrogen bond gave a reaction product in low yields. However, with a mixture of phosphoryl chloride and phosphorous pentachloride at room temperature for 30 hours, **9** was converted into 3-chloro-2-(2-pyridyl)-indan-1-one (**12**) though in moderate yields. By increasing the reaction time (3 days) and the temperature (50-60 °C) a new product was isolated to which the structure of 1,2-dichloro-1-(2-trichloromethyl)phenyl-2-(2-pyridyl)-ethene-hydrochloride (**11**) was assigned on the basis of analytical and spectral data (see experimental part). Unexpectedly, attempts to hydrolyze **11** in aqueous triethylamine in a sealed tube at 190 °C led to the isolation of starting **9** in good yields.

A further planned reaction step was the nucleophilic exchange of the chloro substituent of **12** against the azido group, but was unsuccessful. The isomer 2-(4-pyridyl)-indane-1,3-dione (**8**) gave no chlorination product similar to **12**; as an alternative, 3-(4-methylphenyl)sulfonyloxy-2-(4-pyridyl)-indan-1-one (**10**) was prepared from **8** with toluenesulfonylchloride, however it was obtained in too low yields for further reactions.

Scheme 2



EXPERIMENTAL

Melting points were determined on a Gallenkamp Melting Point Apparatus, Model MFB-595 in open capillary tubes. Calorimetric data were obtained on a Rheometric Scientific DSC-Plus instrument with the differential scanning calorimetry software V5.42 or Orchestrator V6.2.2. The differential scanning calorimetry plots were recorded between 25-500 °C, with a heating rate of 2-10 °C/minute, and 1.5-3 mg compound in sealed aluminium crucibles (11 bar). Infrared spectra were taken as potassium bromide pellets on a Perkin-Elmer 298 spectrophotometer. The ^{1}H nmr spectra were recorded on a Varian Gemini 200 (200 MHz) or a Bruker AM 360 instrument (360 MHz); ^{13}C nmr spectra were recorded on a Bruker AM 360 instrument (90 MHz). Chemical shifts are reported in ppm from internal tetramethylsilane standard and are given in δ-units. The solvent for NMR spectra was deuteriodimethylsulfoxide unless otherwise stated. Microanalyses were performed on a Fisons elemental analyzer, Mod. EA1108, and are within ±0.4 of the theoretical percentages. All reactions were monitored by thin layer chromatography, carried out on 0.2 mm silica gel 60 F-254 (Merck) plates using uv light (254 and 366 nm) for detection. Common reagent-grade chemicals are either commercially available and were used without further purification or prepared by standard literature procedures.

2-Phenylindane-1,3-dione (**2**).

A mixture of acetic anhydride (153 g, 1.5 mol), phenylacetic acid (27.2 g, 0.2 mol) and phthalic anhydride (30.0 g, 0.2 mol) was heated on a water bath until a clear solution was obtained. Then triethylamine (84 mL, 0.6 mol) was added dropwise which formed a dark red solution and carbon dioxide was evolved. After 30 minutes stirring, the mixture was poured onto a mixture of ice (200 g) and concentrated hydrochloric acid (100 mL), which gave at first an oily product that solidified after stirring for some hours. The precipitate was filtered by suction, washed with water and recrystallized from ethanol. The yield was 14.0 g (31%), orange prisms, mp 140-141 °C (ethanol); lit. mp 143-150 °C [5,11]; ir: 1750 m, 1705 s, 1580 m, 1500 w cm^{-1}; ^{1}H nmr: δ 4.25 (s, 1 H, H-2), 7.25 (s, 5 H, Ph-H), 7.90-8.00 (m, 4 H, Ar-H).

3-Chloro-2-phenylindan-1-one (**3**).

A suspension of 2-phenylindane-1,3-dione (**2**) (10.0 g, 45 mmol) in phosphoroxychloride (30 mL) was heated under reflux for 4 hours. After cooling to room temperature the mixture was poured slowly under permanent stirring onto ice/water (300 g) and brought to pH = 5-6 with concentrated sodium hydroxide solution. The precipitate was stirred for 12 hours at room temperature and then filtered by suction and dried. The yield was 9.51 g (88%), yellowish prisms, mp 90-92 °C (methanol); lit. mp [6] 93-94 °C; ir: 1740 s, 1580 w cm^{-1}.

3-Azido-2-phenylindan-1-one (**4**).

A solution of 3-chloro-2-phenylindan-1-one (**2**) (2.00 g, 8.3 mmol) in dry acetonitrile (30 mL) was cooled to 0 °C with ice/water, then sodium azide (1.64 g, 25 mmol) was added and the suspension stirred at this temperature for 30 minutes. The mixture was then poured into ice/water (100 mL) and an orange precipitate was formed. After standing for 1 hour, the solid was isolated by suction filtration and dried at room temperature. The yield was 2.05 g (97%), brownish prisms, mp 320.2-321.7 °C (acetone/water); ir: 2130 s (N_3), 1700 s, 1600 m, 1570 m cm^{-1}; calorimetric data: reaction onset 76.3 °C, reaction peak maximum 168.0 °C (ΔH = - 70 mcal/mg), mp onset 280.8 °C, mp peak maximum 304.4 °C (18 mcal/mg).

No satisfactory analytical data of **4** could be obtained because of the ease of decomposition.

5*H*-Indeno[1,2-*b*]indol-10-one (**5**).

A solution of 3-azido-2-phenylindan-1-one (**4**) (2.00 g, 8 mmol) in ethanol (75 mL) was heated to 60-70 °C until the evolution of nitrogen had stopped and a clear solution was formed (about 1 hour). Then the mixture was cooled to room temperature and the formed precipitate isolated by suction filtration. The yield was 0.90 g (51%), reddish prisms, mp 331 °C (ethanol); lit. mp 326 °C [12] ir: 3220 br, 1730 w, 1670 s, 1610 s, 1580 w cm^{-1}; ^1H nmr: δ 7.10-7.64 (m, 8 H, Ar-H), 10.00 (s, broad, 1 H, NH).

Anal. Calcd. for $C_{15}H_9NO$ (219.3): C, 82.18; H, 4.14; N, 6.39. Found: C, 81.97; H, 4.28; N, 6.28.

2-Phenyl-3-(triphenylphosphoranylideneamino)-indan-1-one (**6**).

A solution of 3-azido-2-phenylindan-1-one (**4**) (5.00 g, 20 mmol) in toluene (100 mL) was mixed with triphenylphosphane (5.80 g, 22 mmol) and the mixture stirred for 30 hours at room temperature. The solvent was removed under reduced pressure, the red-orange residue heated with hexane to remove soluble impurities and the solid was isolated by filtration and dried. The yield was 8.97 g (90%), red-orange prisms, mp 168-169 °C (toluene/hexane); ir: 1665 s, 1600 w, 1570 w cm^{-1}.

Anal. Calcd. for $C_{33}H_{24}NOP$ (481.5): C, 82.31; H, 5.02; N, 2.91. Found C, 82.30; H 5.07; N 2.93.

3-Amino-2-phenylindan-1-one (**7**).

A suspension of 2-phenyl-3-(triphenylphosphoranylideneamino)-indan-1-one (**6**) (4.00 g, 8 mmol) in hydrochloric acid (0.5 mol/L, 80 mL) and methanol (5 mL) was heated under reflux for 1 hour. After cooling to room temperature, triphenylphosphanoxide formed during the reaction was removed by filtration. The oily residue was triturated several times with toluene and the formed solid isolated by suction filtration. The yield was 0.89 g (48%), brownish prisms, mp 264-268 °C (toluene); lit. mp 260-275 °C [9,11]; ir: 3460 w, 3320 w, 3160 br, 1640 s, 1610 m, 1580 w cm^{-1}; ^1H nmr: δ 7.30-7.90 (m, 9 H, Ar-H), 8.19 (s, 2 H, NH_2).

2-(4-Pyridyl)-indane-1,3-dione (**8**).

A mixture of phthalic anhydride (**1**) (20.0 g, 0.14 mol), 4-methylpyridine (13.33 mL, 0.14 mol), and fresh melted zinc chloride (1.80 g, 13 mmol) was heated to 200 °C for 5 hours. Then, the reaction cake was extracted several times with boiling water, isolated by suction filtration and dried. The yield was 21.1 g (70%), orange prisms, mp 313-316 °C (ethanol/water); lit. mp 325 °C [13]; ir (KBr): 3240 br, 1670 m, 1615 s, 1590 w cm^{-1}; ^1H nmr: δ 4.70 (s, 1 H, H-2), 7.20-7.35 (m, 1 H, Ar-H), 7.48-7.53 (m, 4 H, Ar-H), 7.79-7.95 (m, 1 H, Ar-H), 8.50-8.60 (m, 2 H, Ar-H), 13.90 (s, 1 H, OH).

3-Hydroxy-2-(2-pyridyl)-indan-1-one (**9**).

Method A.

A mixture of phthalic anhydride (**1**) (20.0 g, 0.14 mol), 4-methylpyridine (12.57 g, 0.14 mol), and fresh melted zinc chloride (1.80 g, 13 mmol) was reacted and worked up as described for **8**. The yield was 14.25 g (47%), orange prisms, mp. 280-284 °C (ethanol/water); lit. mp 292 °C [13].

Method B.

A suspension of 1,2-dichloro-1-(2-trichloromethyl)phenyl-2-(2-pyridyl)-ethene-hydrochloride (**11**) in water (70 mL) and triethylamine (4 mL) was heated in a sealed tube to 190 °C (pressure 10-15 bar) and kept at this temperature under stirring for 3 hours. The yield was 1.48 g (70%), mp, tlc and ir was identical with the product obtained by method A; ir: 1730 w, 1665 s, 1620 s, 1600 m, 1570 s cm^{-1}; ^1H nmr: δ 7.16 (t, J = 8 Hz, 1 H, Ar-H), 7.53-7.56 (m, 4 H, Ar-H), 8.06 (t, J = 8 Hz, 1 H, Ar-H), 8.30 (s, 1 H, Ar-H), 8.50-8.54 (d, J = 8 Hz, 1 H, Ar-H), 14.20 (s, 1 H, OH).

3-(4-Methylphenyl)sulfonyloxy-2-(4-pyridyl)-indan-1-one (**10**).

A) Sodium salt of **8**: A solution of 2-(4-pyridyl)-indane-1,3-dione (**8**) (5.96 g, 26.7 mmol) in dry, hot dioxane (80 mL) was added to sodium methoxide, prepared from sodium (0.76 g, 33 mmol) and methanol (20 mL). The sodium salt of **8** precipitated and was kept overnight at 4 °C, and then isolated by suction filtration and dried. The yield was 5.57 g (85%), light-grey powder.

B) Tosylation of **8**-sodium salt: A mixture of **8**-sodium salt (5.57 g, 22.7 mmol) and 4-toluenesulfonyl chloride (5.09 g, 26.7 mmol) in dry acetonitrile (40 mL) was heated under reflux with strirring for 1 hour. The reaction mixture was poured into ice/water (350 mL) which gave a yellow precipitate. Purification was performed using a hot extractor with cyclohexane. After 24 hours extraction, 20 mg (1%) of **10** was obtained, mp 215.5-216 °C (cyclohexane); ir: 1695 m, 1650 s, 1620 s, 1530 cm^{-1}.

Anal. Calcd. for $C_{21}H_{15}NO_4S$ (377.4): C, 66.83; H, 4.01; N, 3.71. Found: C, 66.89; H, 4.39; N, 3.76.

1,2-Dichloro-1-(2-trichloromethyl)phenyl-2-(2-pyridyl)-ethene-hydrochloride (**11**).

A mixture of 2-(2-pyridyl)-indane-1,3-dione (**9**) (8.00 g, 35 mmol) and phosphorus pentachloride (3.00 g, 14 mmol) in phosphoroxychloride (20 mL) was stirred for 3 days at 50-60 °C. Then the mixture was poured into ice/water (150 mL) and the formed precipitate kept for 2 hours at 0 °C and then isolated by suction filtration and dried *in vacuo*. The yield was 5.96 g (39%), brownish solid, mp 189-190 °C (xylene); ir: 3100-3000 br, 2780-2300 br, 2110 w, 2040 w, 1645 s, 1620 w, 1605 w, 1540 m cm^{-1}; ^1H nmr: δ 7.46-7.68 (m, 4 H, Ar-H), 7.84-7.94 (q, J = 2 Hz, 1 H, Ar-H), 7.96-8.14 (m, 2 H, Ar-H), 8.82-8.86 (d, J = 7 Hz, 1 H, Ar-H); ^{13}C nmr (DMSO-d_6): δ 83.4 (CCl_3), 121.4-122.2 (aryl C), 126.5-127.6 (aryl C), 129.0-132.1 (aryl C), 133.5 (alkene C-1), 134.9 (alkene C-2), 142.7 (α-pyridyl C), 148.5 (γ-pyridyl C).

Anal. Calcd. for $C_{14}H_9Cl_6N$ (403.9): C, 41.63; H, 2.25; N, 3.47; Cl, 52.66. Found: C, 41.24; H, 2.34; N, 3.08; Cl, 53.03.

3-Chloro-2(-2-pyridyl)-indan-1-one (**12**).

A mixture of 2-(2-pyridyl)-indane-1,3-dione (**9**) (3.00 g, 13 mmol) and phosphorus pentachloride (1.14 g, 5.4 mmol) in phosphorus oxychloride (10 mL) was stirred for 30 hours at room temperature. Then the mixture was poured into ice/water (100 mL), the formed precipitate kept at 0 °C for 2 hours and then isolated by suction filtration to give 1.1 g of unreacted starting material. The filtrate was brought to pH = 4-6, the precipitate

kept at 0 °C for 2 hours and then isolated by suction filtration. The yield was 1.57 g (48%), yellowish prisms, mp 205-6 °C (hexane); ir: 1740 sh, 1725 s, 1690 sh, 1625 w, 1590 cm^{-1}.

Anal. Calcd. for $C_{14}H_8ClNO$ (241.7): C, 69.58; H, 3.34; N, 5.80. Found: C, 69.96; H, 3.68; N, 5.85.

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