**4-Chloro-2,6-bis(phenylthio)aniline (19) and 2,4,6-Tris(phenylthio)aniline (20).** Workup afforded a 1:1 mixture ($^1$H NMR) of **19** and **20** (6.96 g) as a dark oil. A portion (398 mg) of this material was subjected to reverse-phase MPLC (3:1 acetonitrile–water) to give first 2,6-bis(phenylthio)-4-chloroaniline (**19**) (183 mg, 0.53 mmol) as a burgundy solid followed by 2,4,6-tris(phenylthio)aniline (**20**) (179 mg, 0.43 mmol) as an off-white solid. Recrystallization (EtOAc–hexane) afforded analytical samples of each. **19**: mp 106–110 °C; $^1$H NMR $\delta$ 7.51 (s, 2), 7.30–7.03 (m, 10), 4.95 (br s, 2); $^{13}$C NMR 148.96, 137.59, 134.90, 129.22, 127.20, 126.25, 121.51, 116.71; IR 3455, 3350, 3250, 1590, 1580, 1475, 1435, 730, 720, 688 cm$^{-1}$. Anal. Calcd for $C_{18}H_{14}ClNS_2$: C, 62.87; H, 4.10; N, 4.07. Found: C, 62.49; H, 4.02; N, 4.03. **20**: mp 84–87 °C; $^1$H NMR $\delta$ 7.71 (s, 2), 7.30–7.00 (m, 15), 5.07 (br s, 2); IR 3485, 3380, 3250, 1582, 1478, 1440, 735, 688 cm$^{-1}$. Anal. Calcd for $C_{24}H_{19}NS_3$: C, 69.03; H, 4.59; N, 3.35. Found: C, 69.00; H, 4.57; N, 3.35.

**3,4,5-Tris(phenylthio)aniline (22).** The scale was 0.5-fold less than that described in the general procedure. Workup gave a partially crystalline mass (2.96 g) which was triturated with hot MeOH (250 mL), giving **22** (1.04 g, 2.48 mmol, 26%) as an off-white solid. Recrystallization (EtOAc–cyclohexane) provided an analytical sample: mp 158–160 °C; $^1$H NMR $\delta$ 7.50 (m, 4), 7.39 (m, 6), 7.31–7.24 (m, 2), 7.22–7.10 (m, 3), 5.84 (s, 2), 3.53 (br s, 2); IR 3475, 3380, 3060, 1618, 1570, 1535, 1480, 1440, 1415, 1290, 1025, 830, 795, 758, 750, 738, 705, 690 cm$^{-1}$. Anal. Calcd for $C_{24}H_{19}NS_3$: C, 69.03; H, 4.59; N, 3.35. Found: C, 69.17; H, 4.61; N, 3.40.

**4-(Phenylthio)-1,3-phenylenediamine (24).** The reaction was carried out on the hemisulfate of 4-chloro-1,3-phenylenediamine (**23**). Workup afforded crude **24** as a brown solid (1.97 g). Recrystallization (MeOH) afforded analytically pure material (997 mg, 4.61 mmol, 24%): mp 103–104.5 °C; $^1$H NMR $\delta$ 7.24–7.15 (m, 2), 7.23 (d, 1, $J$ = 8.1), 7.09–7.02 (m, 3), 6.10 (dd, 1, $J$ = 2.3, 8.1), 6.07 (d, 1, $J$ = 2.3), 4.20 (br s, 2), 3.72 (br s, 2); IR 3430, 3380, 1610, 1490, 1475, 1440, 1325, 1260, 855, 735 cm$^{-1}$. Anal. Calcd for $C_{12}H_{12}N_2S$: C, 66.63; H, 5.59; N, 12.95. Found: C, 66.62; H, 5.59; N, 12.95.

**Supplementary Material Available:** Structure, crystal data, atomic cooridnates, bond lengths and angles, anisotropic displacement coefficients, and H atom coordinates for **12** (11 pages). Ordering information is given on any current masthead page.

# Synthesis of 2-Cyano-1,3-dibenzoyl-2,3-dihydrobenzimidazole: A Novel Reissert Compound from Benzimidazole[1]

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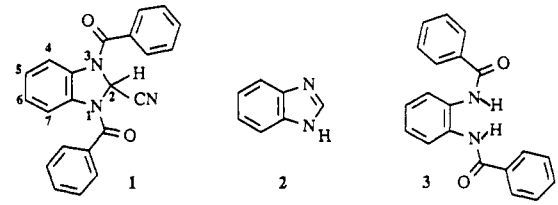
## Introduction

Since their discovery by Arnold Reissert,[2a] Reissert compounds, $\alpha$-acylaminonitriles, have proven useful as intermediates in the synthesis of various heterocyclic compounds, such as derivatives of isoquinoline, quinoline, quinazoline, etc., including alkaloids and other biologically active compounds.[2] During the course of synthetic studies for the preparation of specialty heterocyclic polymers,[3] we had the occasion to investigate methods of incorporating heterocycles via Reissert chemistry.

One of the requirements for polymer synthesis is the presence of difunctionality in the starting materials. Benzimidazoles are difunctional in the sense that via Reissert compound formation two amide linkages can be formed, e.g., as in **1**. Further, benzimidazoles are inexpensive, commercially available materials. This potential has led us to investigate the scope and limitations of the Reissert reaction of benzimidazoles with the expectation that this process could serve as a simple and expedient method for the synthesis of polybenzimidazoles.

However, little is known about benzimidazole Reissert compounds, although a carbamate analog was reported by Uff et al.[4] In the two phase (dichloromethane–water) system, the Reissert reaction of benzoyl chloride and KCN with benzimidazole (**2**), with or without phase-transfer catalyst, is reported to yield *o*-phenylenedibenzamide[5] (**3**). In a very recent publication, Uff et al.[6] claim the synthesis of **1**. However, we have obtained totally different results in our laboratory and report them here.




## Results and Discussion

**A. Direct Reaction of Benzimidazole.** Our first approach to the synthesis of 2-cyano-1,3-dibenzoyl-2,3-dihydrobenzimidazole (**1**) (Scheme I) was the direct Reissert reaction of benzimidazole (**2**) in a range of anhydrous solvents (dichloromethane, dioxane, *N*-methylpyrrolidinone, tetrahydrofuran) with 2 equiv of benzoyl chloride in presence of trimethylsilyl cyanide (TMSCN) and a suitable base like triethylamine or pyridine. This led mainly to 1-benzoylbenzimidazole (**4**) along with the desired product **1** in trace amounts, probably because of the similar basicities of the second nitrogen in benzimidazole and the acid acceptors used.

**B. Reactions of 1-Benzoylbenzimidazole.** To obtain a better yield of the desired product **1**, we approached the synthesis by a two-step process. In the first step, we prepared 1-benzoylbenzimidazole (**4**) from benzimidazole by reaction with benzoyl chloride in the presence of triethylamine in *N*,*N*-dimethylformamide (DMF) (80% yield).

**a. Use of Dichloromethane–Water Method.** 1-Benzoylbenzimidazole (**4**) with benzoyl chloride and KCN in dichloromethane–water yielded a new product in excellent yield. The melting point of this product (**5**) (159–60 °C) was much lower than that of *o*-phenylenedibenzamide (**3**) (lit.[7] mp 301–4 °C). The infrared spectrum of **5** showed NH as well as three carbonyl absorptions. $^1$H and $^{13}$C NMR showed one of the carbonyl groups to be a formyl function. Additional information obtained from $^1$H NMR, MS, and CHN analysis of the product conclusively proved

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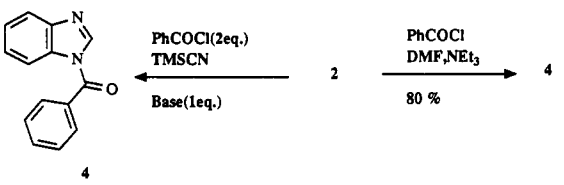
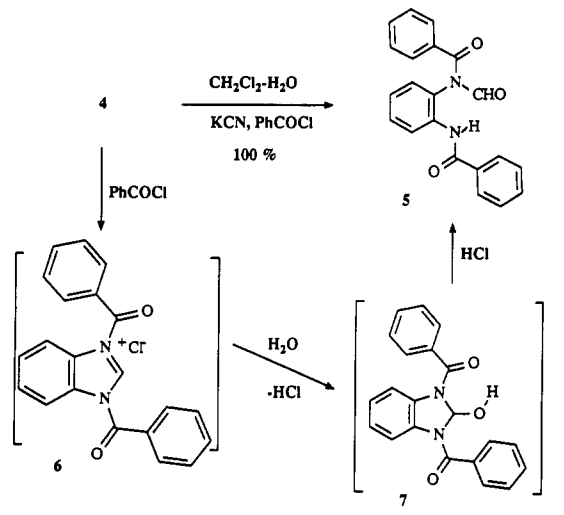
**Scheme I**




**Scheme II**




the structure to be *N*-formyl-*N*,*N*'-dibenzoyl-*o*-phenylenediamine (**5**). This arises probably by the initial formation of the acylium ion (**6**), followed by the nucleophilic attack of water at C-2 leading to the formation of an intermediate **7**, which upon in situ hydrolysis yields compound **5** as shown in Scheme II. The above reaction was repeated without KCN, and we obtained the same results. (We appreciate the suggestion of the reviewer to do this experiment.) This is in agreement with the proposed mechanism of formation of compound **5**.

To avoid the hydrolysis of the intermediate **6**, we used a base to abstract the HCl generated in the reaction. Interestingly, it changed the reaction dramatically. Thus, reaction of **2** or **4** with benzoyl chloride (2 equiv) in persence of a base (triethylamine, 2.2 equiv) and KCN (3 equiv) in a two-phase system (dichloromethane–water) led to several other ring opened products (not **3** or **5**). The Reissert reaction on **4** with benzoyl chloride and (a) KCN/18-crown-6 in DMF or (b) LiCN with a catalytic amount of $AlCl_3$ in DMF also led to several ring-opened products. However, we recovered starting material from the reaction of **4** with benzoyl chloride in DMF in the presence of LiCl and KCN.

**b. Use of Single-Phase Method with TMSCN.** Finally, the Reissert reaction of **4** with benzoyl chloride/TMSCN in dichloromethane went very smoothly to give the stable, expected product **1** (96%). The IR (KBr) spectrum showed amide carbonyls at 1677 and 1664 $cm^{-1}$. As is the case with most of the Reissert compounds, nitrile absorption in the IR spectrum was not observed. All benzimidazole protons shifted distinctly upfield in the proton NMR spectrum (Figure 1). The broadness of the peak of $H_4$ and $H_7$ at $\delta$ 6.65–6.25 is attributable to amide isomerism (**1**, **1a**, **1b**) coupled with the anisotropic effect of the amide carbonyl. The structure of **1** was further supported by elemental analysis and $^{13}C$ NMR. When the same reaction was carried out in anhydrous tetrahydrofuran, we obtained **1** in nearly quantitative yield. However, in the case of anhydrous *N*-methylpyrrolidinone as a solvent, we could isolate **1** only to the extent of 27%. Generation of Reissert anion of **1** and its reactions will be published elsewhere.[1]

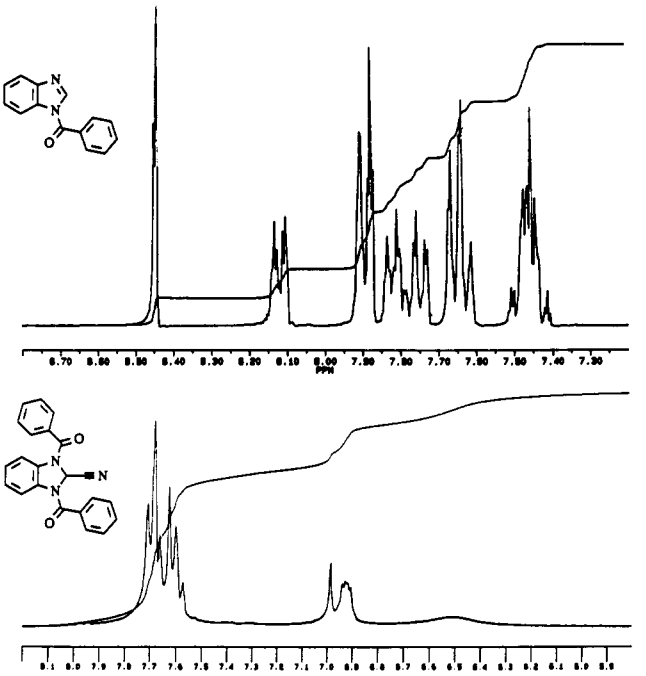
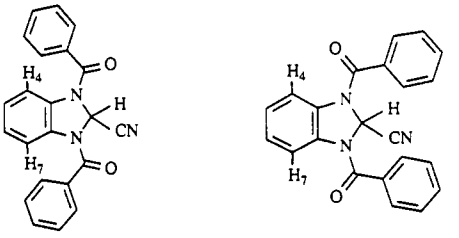


**Figure 1.** Proton NMR spectra of 1-benzoylbenzimidazole and 2-cyano-1,3-dibenzoyl-2,3-dihydrobenzimidazole in DMSO-$d_6$.




**1a** **1b**

**C. Comparisons to Uff Report.** When 1 equiv of benzimidazole (**2**) was refluxed along with 1 equiv of KCN, 2 equiv of benzoyl chloride, and a catalytic amount of tetrabutylammonium bromide [TBAB] (0.1 equiv) in anhydrous dichloromethane, a method reported by Uff et al.,[6] we obtained *o*-phenylenedibenzamide (**3**) (87%). Similarly, compound **4** with benzoyl chloride (1 equiv), KCN (1 equiv), and TBAB (0.1 equiv) yielded 94% of *o*-phenylenedibenzamide (**3**) in our hands. Uff et al.[6] report that these methods both produce **1** with mp 132–4 °C in 57% and 61% yield, respectively. Surprisingly, Uff et al.[6] also obtained the same compound with mp 132–4 °C (28% yield) when 1-benzoylbenzimidazole (**4**) was reacted with benzoyl chloride and TMSCN whereas under the same reaction conditions, we obtained compound **1** with mp 188–9 °C (96% yield).

## Conclusions

A new, novel benzimidazole Reissert compound (**1**) has been synthesized and characterized.

## Experimental Section

All melting points were determined on a Haake-Buchler melting point apparatus and are corrected. $^1H$ and $^{13}C$ NMR (DMSO-$d_6$) spectra were recorded on a Bruker 270-MHz instrument and a Hewlett-Packard 7550A graphics plotter. FTIR (KBr) spectra were recorded on a Nicolet MX-1. Mass spectra were measured with a VGA 7070E analytical mass spectrometer. Elemental

analyses were performed by Atlantic Microlab, Norcross, GA.

**1-Benzoylbenzimidazole (4).** To a solution of benzimidazole (2) (0.2 mol, 23.6 g, recrystallized from water) and triethylamine (0.22 mol, 22.36 g or 30.66 mL) in DMF (200 mL) cooled in an ice-water bath under dry conditions ($N_2$) was added benzoyl chloride (0.22 mol, 30.92 g or 25.6 mL) with stirring during a 1-h period. Stirring was continued overnight at 25 °C. The reaction mixture was poured into water (2 L) and stirred for 6 h. The solid obtained by filtration was stirred in water (1 L) for 1 h, filtered, and dried. The product obtained was treated once with Norit and recrystallized from ethyl acetate and hexane: white needlelike crystals; 35.58 g (80%); mp 91-2 °C (lit.[8] mp 91-2 °C); $^1$H NMR (DMSO-$d_6$) $\delta$ 8.46 (s, 1 H, $H_2$), 8.17-8.08 (m, 1 H, $H_7$), 7.94-7.85 (m, 2 H), 7.85-7.72 (m, 2 H), 7.70-7.60 (m, 2 H), 7.53-7.4 (m, 2 H).

***N*-Formyl-*N*,*N*'-dibenzoyl-*o*-phenylenediamine (5): Method A.** To a well-stirring mixture of 4 (0.005 mol, 1.12 g), KCN (0.015 mol, 0.977 g), dichloromethane (10 mL), and water (5 mL) was added benzoyl chloride (0.01 mol, 1.4 g) dropwise, and stirring was continued for an additional 5 h. The reaction mixture was then diluted with water (100 mL) and extracted with dichloromethane (3 × 10 mL). Organic layers were pooled, washed consecutively with aqueous saturated sodium bicarbonate (3 × 50 mL), aqueous 8% HCl (3 × 50 mL), and water (3 × 50 mL), dried over anhydrous sodium sulfate, and concentrated to get crude product (1.73 g, 100%). Pure product was obtained by recrystallization from ethyl acetate to get white crystals: mp 159-160 °C; MS-EI *m/e* 344 ($M^+$), 316, 298, 222, 194, 105, 77; MS-CI *m/e* 345 [$(M + 1)^+$], 317, 299, 223, 195, 105, 91; IR (KBr) 3264 (NH), 1721, 1678, 1655 (N-CO-), 1600, 1580 (aromatic), 1497, 1482, 1453, 1310, 1297, 1272 cm$^{-1}$; $^1$H NMR (DMSO-$d_6$) $\delta$ 10.02 (s, 1 H, $D_2O$ exchangeable, NH), 9.19 (s, 1 H, CHO), 7.9-7.2 (m, 14 H, Ar-H); $^{13}$C NMR (DMSO-$d_6$) 170.89, 165.55 (NHCO), 163.2 (CHO, showed a doublet in the undecoupled experiment) and 14 other peaks from 136 to 124 ppm (aromatic). Anal. Calcd for $C_{21}H_{16}N_2O_3$: C, 73.24; H, 4.68; N, 8.14. Found: C, 73.33; H, 4.72; N, 8.07.

**Method B.** To a well-stirring mixture of 4 (0.005 mol, 1.12 g), dichloromethane (10 mL), and water (5 mL) was added benzoyl chloride (0.01 mol, 1.4 g) dropwise, and stirring was continued for an additional 5 h. The reaction mixture was then diluted with water (100 mL) and extracted with dichloromethane (3 × 50 mL). Organic layers were pooled, washed consecutively with aqueous saturated sodium bicarbonate (3 × 50 mL), aqueous 8% HCl (3 × 50 mL), and water (3 × 50 mL), dried over anhydrous sodium sulfate, and concentrated to get crude product (1.73 g, 100%). Pure product was obtained by recrystallization from ethyl acetate to get white crystals, mp 159-159.5 °C. The melting point, IR, and NMR data of this product were identical with those of compound prepared in method A.

**2-Cyano-1,3-dibenzoyl-2,3-dihydrobenzimidazole (1).** To a well-stirring solution of 4 (0.05 mol, 11.2 g) in $CH_2Cl_2$ (100 mL) were added benzoyl chloride (0.05 mol, 7.0 g) and TMSCN (0.052 mol, 5.46 g). The reaction mixture was stirred for 5 days at 25 °C and quenched by pouring into water (1 L). This solution was extracted with dichloromethane (3 × 150 mL). The organic layer was washed with 8% HCl (3 × 150 mL), aqueous saturated bicarbonate (3 × 150 mL), and water (3 × 150 mL) and dried over $MgSO_4$. Solvent evaporation yielded the product (17.1 g, 96%). Pure product was obtained by treating once with Norit and recrystallizing from ethyl acetate and hexane to get white crystals; mp 188-9 °C; IR (KBr) 1677, 1664, 1658, 1644, 1632, 1601, 1494, 1475, 1450, 1390, 1378, 1355, 1342, 1333, 1321, and 1302 cm$^{-1}$; $^1$H NMR (DMSO-$d_6$) $\delta$ 7.75-7.55 (m, 10 H, $COC_6H_5$), 6.99 (s, 1 H, $H_2$), 6.98-6.85 (m, 2 H, $H_5$ and $H_6$), and 6.7-6.3 (br s, 2 H, $H_4$ and $H_7$); $^{13}$C NMR (DMSO-$d_6$) 166.40, 133.58, 132.09, 131.39, 129.12, 127.64, 124.51, 115.53, 114.67 (CN), and 66.14 (C-2, showed a doublet in undecoupled experiment) ppm. Anal. Calcd for $C_{22}H_{15}N_3O_2$: C, 74.77; H, 4.28; N, 11.89. Found: C, 74.64; H, 4.33; N, 11.83.

**Reaction of Benzimidazole (2) with KCN/TBAB.** To a well-stirring mixture of 2 (1.18 g, 0.01 mol), KCN (0.65 g, 0.01 mol), and TBAB (0.322 g, 0.001 mol) in anhydrous dichloromethane (35 mL) was added benzoyl chloride (2.82 g, 0.02 mol) over a period of 10 min. The reaction mixture was heated gently (in an oil bath maintained at 50 °C) under reflux for 10 h. It was then cooled. The organic layer was separated, washed with water (3 × 30 mL), aqueous 8% HCl (3 × 30 mL), aqueous saturated sodium bicarbonate (3 × 30 mL), and water (3 × 30 mL), and dried over sodium sulfate. Evaporation of the solvent yielded a gummy residue (2.75 g, 87%). This residue was heated in ethanol (20 mL) and cooled. The white precipitate was collected and recrystallized from ethanol to get white crystals: mp 308-310 °C (mp of *o*-phenylene dibenzamide[7] = 301-4 °C). The melting point, IR, and NMR data of this product were identical with those of *o*-phenylenedibenzamide prepared from *o*-phenylenediamine.

**Reaction of 1-Benzoylbenzimidazole (4) with KCN/TBAB.** To a well-stirring solution of 4 (2.24 g, 0.01 mol), KCN (0.65 g, 0.01 mol), and TBAB (0.322 g, 0.001 mol) in anhydrous dichloromethane (35 mL) was added benzoyl chloride (2.82 g, 0.02 mol) over 10 min. The reaction mixture was heated gently (in an oil bath maintained at 50 °C) under reflux for 2.5 h. It was then cooled, and the organic layer was separated, washed with water (3 × 30 mL), aqueous 8% HCl (3 × 30 mL), aqueous saturated sodium bicarbonate (3 × 30 mL), and water (3 × 30 mL), and dried over sodium sulfate. Evaporation of the solvent yielded a gummy residue (3.0 g, 94%). This residue was heated in ethanol (25 mL) and cooled. The white precipitate was collected and recrystallized from ethanol to get white crystals: mp 308-310 °C (mp of *o*-phenylene dibenzamide[7] = 301-4 °C). The melting point, IR, and NMR data of this product were identical with those of *o*-phenylenedibenzamide prepared from *o*-phenylenediamine.

**Acknowledgment.** This work was supported in full by AKZO America Inc., to whom we wish to express our gratitude.

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## Pentacovalent Oxaphosphorane Chemistry in Organic Synthesis: A New Route to Substituted Phosphonates

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Phosphonate-containing compounds are of biological interest as antimetabolites and enzyme active-site probes, especially of pyrophosphatases, the glycolytic pathway, lipid and glycerol-related processes.[1] They also have medicinal value as antivirals,[2] antibiotics,[3] and antiacidosis agents,[4] as well as exhibiting herbicidal and insecticidal activities.[1a,b] In connection with our interest in synthesizing biologically active compounds containing phosphonate group(s), we are investigating the carbon analogue of the Ramirez condensation of pentacovalent oxaphosphoranes with carbonyl compounds as a new method for the production of phosphonate-containing compounds.

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