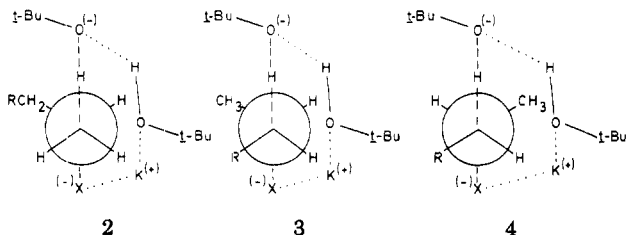


attacking dissociated base from phenoxide to bulky 2,6-di-*tert*-butylphenoxide.

Recent kinetic studies by Závada and Pánková<sup>9,10</sup> have demonstrated that the steric properties of associated and dissociated *t*-BuOK are very similar for eliminations conducted in *t*-BuOH. The Czech workers propose<sup>10</sup> that the positional orientation control produced by associated *t*-BuOK base in eliminations from RCH<sub>2</sub>CH(X)CH<sub>3</sub> may be rationalized by considering transition-state structures 2-4.



In these transition states, the base species is the homo-hydrogen-bonded *t*-BuOK ion pair which provides electrostatic interactions of the base counterion with the leaving group. These attractive interactions are stronger in transition states forming 1-alkene, 2, and *cis*-2-alkene, 3, than in that leading to *trans*-2-alkene, 4, because of the disruptive  $\alpha$ -methyl group in 4. In going from dissociated to associated base, the repression of *trans*-2-alkene formation results in proportional increases in the production of 1-alkene and *cis*-2-alkene. This leads to the observed enhancement of 1-alkene proportion and a decrease in the *trans*-2-alkene-*cis*-2-alkene ratio (Table I).

The observed inability of even highly ramified dissociated bases to produce the positional orientation control exhibited by *t*-BuOK-*t*-BuOH lends support to the Závada and Pánková model.

### Experimental Section

**Reagents.** The 2-halobutanes were distilled commercial products. 2-Butyl tosylate,<sup>11</sup> 4-methyl-2-pentyl iodide,<sup>11</sup> and *cis*-2,6-di-*tert*-butylpiperidine<sup>4</sup> were available from previous investigations. The *t*-BuOK (Aldrich) was used as received. Reagent-grade Me<sub>2</sub>SO was kept over molecular sieves. Diglyme was distilled from lithium aluminum hydride.

**Base-solvent solutions of *t*-BuOK in Me<sub>2</sub>SO** were prepared by dissolving the base powder in the solvent. Solutions of 1 in diglyme were prepared by treating solutions of *cis*-2,6-di-*tert*-butylpiperidine in diglyme with stoichiometric amounts of *n*-BuLi in hexane (Aldrich) under nitrogen followed by removal of the hexane by sweeping with nitrogen gas at 50 °C.

**Procedure.** The nitrogen gas sweep procedure and gas chromatographic analysis of olefinic products were the same as previously described.<sup>11</sup> A 10-min reaction period was employed.

**Control Experiments.** The absence of concomitant solvolysis was demonstrated as before.<sup>11</sup> That no isomerization of butene products occurred under the highly basic reaction conditions was demonstrated by injecting solutions of 1-butene, *trans*-2-butene, and *cis*-2-butene mixtures into the base-solvent combinations of *t*-BuOK-diglyme, 1-diglyme, and 1-diglyme in the presence of 12-crown-4. In all cases, the trapped butenes had the same isomeric distribution as the original solution.

**Acknowledgment** is made to the Graduate School of Texas Tech University for the award of a Graduate School Summer Research Fellowship to B.R.C.

**Registry No.** 2-Iodobutane, 513-48-4; 2-bromobutane, 78-76-2; lithium *cis*-2,6-di-*tert*-butylpiperidide, 74465-46-6; *t*-BuOK, 865-47-4; 1-butene, 106-98-9; *trans*-2-butene, 624-64-6; *cis*-2-butene, 590-18-1.

(9) Pánková, M.; Závada, J. *Collect. Czech. Chem. Commun.* 1977, 42, 3439.

(10) Pánková, M.; Závada, J. *Collect. Czech. Chem. Commun.*, in press.

(11) Bartsch, R. A.; Read, R. A.; Larsen, D. T.; Roberts, D. K.; Scott, K. J.; Cho, B. R. *J. Am. Chem. Soc.* 1979, 101, 1176.

### Synthesis of Some Aromatic Diisocyanides with Trichloromethyl Chloroformate

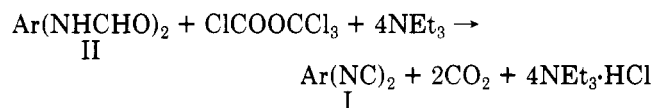
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Received March 24, 1980

Dehydration of *N*-alkyl- or *N*-arylformamides represents the method of choice for the preparation of isocyanides.<sup>1</sup> Among the dehydrating agents, application of phosgene in the presence of tertiary amines was found to be particularly effective. Though effective chemically, phosgene is a volatile toxic material whose handling, especially in large quantities, requires special precautions. Moreover, availability of phosgene outside production plants appears to be limited owing to strict transport safety regulations. A new synthetic route to isocyanides which utilizes trichloromethyl chloroformate (diphosgene) as the dehydrating agent has recently been reported<sup>2</sup> by Skorna and Ugi to afford certain monoisocyanides in excellent yields. Diphosgene is easily prepared<sup>3</sup> in significant quantities, and its handling is considerably simpler compared to phosgene. The advantages presented by the new diphosgene method, coupled with our interest in the coordination properties of certain polyisocyanides, prompted the investigation described below.

Application of diphosgene in the synthesis of the aromatic diisocyanides 1,3-diisocyanobenzene (Ia), 1,4-diisocyanobenzene (Ib), 4,4'-diisocyanobiphenyl (Ic), and 4,4'-diisocyanodiphenylmethane (Id) was investigated during the course of the current study. These diisocyanides were prepared by treating a boiling suspension of the corresponding diformylamino derivative II, in a dichloromethane-triethylamine mixture, with diphosgene dissolved in dichloromethane. Relevant information



concerning the characterization of the diisocyanides Ia-d is furnished in Tables I and II. A comparison between the phosgene and diphosgene methods reveals consistently higher yields with the former approach. In the instance of Ia, the 35% yield obtained with diphosgene compares rather unfavorably with those of 55, 74, and 83% which have previously been reported for the phosgene method.<sup>4,5</sup> Incidentally, attempts to improve the yield of Ia by performing the diphosgene reaction at lower temperatures (e.g., -20 °C) have so far been unsuccessful. The preparations of the other diisocyanides with diphosgene afford yields ( $\geq 70\%$ ), which are either within the range or slightly lower than those previously reported by the phosgene method<sup>4,5</sup> for Ib (47, 75, and 90%), Ic (79 and 94%), and Id (72 and 83%). In spite of the somewhat lower yields,

(1) I. Ugi, U. Fetzer, U. Eholzer, H. Knupfer, and K. Offermann, *Angew. Chem., Int. Ed. Engl.*, 4, 472 (1965).

(2) G. Skorna, and I. Ugi, *Angew. Chem., Int. Ed. Engl.*, 16, 259 (1977).

(3) Diphosgene is best prepared by the photochlorination of methyl chloroformate rather than methyl formate as was originally reported by H. C. Ramsperger and G. Waddington, *J. Am. Chem. Soc.*, 55, 214 (1933). A laboratory-scale preparation of diphosgene starting with methyl chloroformate is described in the experimental section.

(4) P. Hoffmann, G. Gokel, D. Marquarding, and I. Ugi in "Isonitrile Chemistry", I. Ugi, Ed., Academic Press, New York, 1971, Table I, Chapter 2, and appropriate references therein.



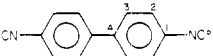
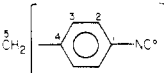
(5) R. Neidlein, *Arch. Pharm. (Weinheim)*, 297, 589 (1964).

Table I. Selected Data on Diisocyanoarenes Ia-d Prepared by the Diphosgene Method

| compd                               | yield,<br>% | mp dec,<br>°C | elemental composition, % <sup>a</sup> |                |                  | $\nu(\text{NC}), \text{cm}^{-1}$ <sup>b</sup> |
|-------------------------------------|-------------|---------------|---------------------------------------|----------------|------------------|---|
|                                     |             |               | C                                     | H              | N                |   |
| 1,3-diisocyanobenzene (Ia)          | 35          | 101-102       | 74.84<br>(74.99)                      | 3.25<br>(3.15) | 21.97<br>(21.88) | 2108 (vs), 2128 (sh), 2140 (m)                |
| 1,4-diisocyanobenzene (Ib)          | 76          | 165-166       | 75.16<br>(74.99)                      | 3.25<br>(3.15) | 21.90<br>(21.88) | 2122 (vs)                                     |
| 4,4'-diisocyanobiphenyl (Ic)        | 72          | 185-186       | 82.60<br>(82.33)                      | 4.05<br>(3.95) | 13.71<br>(13.73) | 2131 (vs)                                     |
| 4,4'-diisocyanodiphenylmethane (Id) | 70          | 134-135       | 82.58<br>(82.54)                      | 4.63<br>(4.62) | 12.61<br>(12.61) | 2133 (vs)                                     |

<sup>a</sup> Calculated values are given in parentheses. <sup>b</sup> IR spectra, taken on samples dissolved in  $\text{CH}_2\text{Cl}_2$ , were recorded on a Perkin-Elmer 467 grating infrared spectrometer; the estimated accuracy of the data is  $\pm 2 \text{ cm}^{-1}$ .

Table II. <sup>1</sup>H and <sup>13</sup>C NMR Spectra of the Diisocyanoarenes Ia-d

| compd   | <sup>1</sup> H NMR, <sup>a</sup> $\tau$ |               | <sup>13</sup> C NMR, <sup>b</sup> $\delta$ (relative to $\text{Me}_4\text{Si}$ ) |                                    |       |                    |       |      |
|---|---|---------------|--|------------------------------------|-------|--------------------|-------|------|
|   | aromatic                                | other         | C(0)<br>( $J^\circ$ , Hz) <sup>c</sup>   | C(1)<br>( $J^1$ , Hz) <sup>d</sup> | C(2)  | C(3)               | C(4)  | C(5) |
| Ia   | 2.70 (m)                                |               | 168.4 (3.0)  | 128.1 (12.5)                       | 125.4 | 128.6 <sup>e</sup> | 132.2 |      |
| Ib   | 2.87 (m)                                |               | 168.8 (3.0)  | 127.8 (13.5)                       | 128.9 |                    |       |      |
| Ic   | 2.60 (m)                                |               | 167.3 (3.5)  | 127.1 (12.0)                       | 129.2 | 127.9              | 141.2 |      |
| Id  | 2.85 (8 H, m)                           | 6.00 (2 H, s) | 165.9 (3.5)  | 125.6 (13.5)                       | 127.4 | 130.9              | 143.4 | 41.3 |

<sup>a</sup> Spectra, taken on samples dissolved in  $\text{CDCl}_3$ , were recorded on a Varian A-60 spectrometer. <sup>b</sup> Spectra, taken on samples dissolved in acetone- $d_6$ , were recorded on a HFX-10 Bruker 90-MHz NMR spectrometer. The estimated accuracy of  $\delta$  is  $\pm 0.1$  ppm. <sup>c</sup>  $J^\circ$  stands for  $^{14}\text{N}$ - $^{13}\text{C}(0)$  couplings; its estimated accuracy is  $\pm 0.5$  Hz. <sup>d</sup>  $J^1$  stands for  $^{13}\text{C}(1)$ - $^{14}\text{N}$  couplings; its estimated accuracy is  $\pm 0.5$  Hz. <sup>e</sup> In the spectrum of Ib, the relative intensity of the C(3) signal is approximately twice that of either C(2) or C(4) signal.

the facile diphosgene route to Ib-d presents clear advantages over the phosgene method. Reactions with diphosgene are simple to perform and do not require the elaborate backup system needed in order to handle the toxic phosgene. On the basis of our extensive experience with both methods, it may be concluded that the diphosgene approach to Ib-d provides a viable and facile synthetic route with yields of products being more consistent than those obtained with phosgene.

Purification of the diisocyanides prepared during the course of the current study was achieved by chromatography on neutral alumina columns. The quality of the samples purified by this technique is indicated by the elemental composition data (Table I). The infrared stretching frequencies of the isocyanides in Ia-d are consistent with earlier reported data,<sup>5</sup> except in the case of Ia where an additional shoulder has been detected at  $2128 \text{ cm}^{-1}$ .

The <sup>1</sup>H and <sup>13</sup>C NMR spectra of Ia-d are summarized in Table II. Noteworthy are the latter spectra, since relatively little information is currently available on the <sup>13</sup>C NMR spectra of monoisocyanides, while those of diisocyanides have not yet been reported. Two well-resolved triplets (approximate intensity ratio 1:1:1) found in all four spectra permit unequivocal assignments of the C(0) [ $J^\circ(^{14}\text{N}-^{13}\text{C}(0)) = 3.0$ - $3.5$  Hz] and C(1) [ $J^1(^{14}\text{N}-^{13}\text{C}(1)) = 12.0$ - $13.5$  Hz] resonances. Other unequivocal assignments in these spectra pertain to resonances associated with C(3) [Ia], C(2) [Ib], C(4) [Ic and Id], and C(5) [Id]. The assignments of the resonances associated with C(2) and C(4) in the spectrum of Ia were made by implicating additivity relationships.<sup>6</sup> The tentative assignments of the reso-

nances associated with C(2) and C(3) in the spectra of Ic and Id were made by comparison with the appropriate spectra of related known systems.

The chemical shifts of the isocyanide carbon atoms in Ia-d, as well as in other aromatic isocyanides (e.g., *p*- $\text{XC}_6\text{H}_4\text{NC}$ , X = H,  $\text{CH}_3$ , Cl,  $\text{OCH}_3$ ; 2,2-dimethylisocyanobenzene),<sup>7</sup> appear in a relatively narrow range ( $\delta$  164-170) and are somewhat deshielded compared with those of aliphatic isocyanides. The  $J^\circ$  couplings in Ia-d are only slightly smaller compared with those found in aromatic monoisocyanides (4.0-5.4 Hz), whereas the  $J^1$  couplings are about the same in both systems. Shielding effects imposed by the isocyanide group on the aromatic carbon atoms in both mono- and diisocyanoarenes appear to be exceedingly small. The chemical shifts of the aromatic carbon atoms in Ia-d and *p*- $\text{XC}_6\text{H}_4\text{NC}$  have been observed to differ relatively little from those of the corresponding parent systems, benzene, biphenyl, diphenylmethane, and  $\text{C}_6\text{H}_5\text{X}$ . In terms of inductive and/or resonance effects, the foregoing imply essentially isolated isocyanide substituents in aromatic systems. This conclusion is rather surprising especially in view of the dipolar nature of such substituents. By comparison with aromatic isocyanides (e.g.,  $\text{C}_6\text{H}_5\text{NC}$ ), analogous cyanides have been found to exert a considerable shielding effect at the C-1 position [e.g.,  $-19.0$  ppm (relative to benzene) in  $\text{C}_6\text{H}_5\text{CN}$ ].<sup>8</sup>

(6) J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, 1972, pp 90-97, and pertinent references therein.

(7) R. W. Stephany, M. J. A. de Bie, and W. Drenth, *Org. Magn. Reson.*, 6, 45 (1974).

(8) F. W. Wehrli, J. W. de Haan, A. I. M. Keulemans, O. Exner, and W. Simon, *Helv. Chim. Acta*, 52, 103 (1969).

## Experimental Section

**Laboratory-Scale Preparation of Diphosgene.** Freshly distilled methyl chloroformate (1 L, 1223 g, 12.94 mol) was placed in a three-necked round-bottomed 3-L flask fitted with a gas inlet tube, an efficient reflux condenser,<sup>9a</sup> and a thermometer. The magnetically stirred solution was irradiated with an external UV flood lamp (Hanovia, 125 W) while dry chlorine<sup>9b</sup> was slowly introduced into the reaction mixture. After a brief induction period of up to 30 min, the decoloration of the yellow chlorine solution and the rising of the temperature both signify the starting of the exothermic chlorination reaction. The rate of addition of chlorine was gradually increased in order to maintain the reaction temperature in the range of 75–85 °C for approximately 35 h. Upon completion of the reaction,<sup>9c</sup> evident by the sharp drop in temperature, the mixture was carefully purged with dry nitrogen in order to remove unreacted chlorine, and then the product was distilled under reduced pressure [58 °C (69 mm)]. This procedure gave an 84% yield of diphosgene (1300 cm<sup>3</sup>) containing trace amounts (<1%) of ClCOOCHCl<sub>2</sub>. Further purification of the diphosgene can be achieved, if needed, by a repeated distillation using an efficient fractionating column.

**Syntheses of Diisocyanoarenes. Preparation of 1,4-Diisocyanobenzene (Ib).** Diphosgene (11.5 mL, 19 g 96 mmol) dissolved in dry dichloromethane (70 mL) was added dropwise, over a 2-h duration, into a boiling suspension consisting of *N,N'*-diformyl-1,4-diaminobenzene (15 g, 91.5 mmol), triethylamine (70 mL) and dichloromethane (250 mL). After an additional 30 min of reflux, the reaction mixture was allowed to cool to ambient temperature before being washed with an aqueous 10% Na<sub>2</sub>CO<sub>3</sub> solution (3 × 100 mL). The organic layer was dried over anhydrous MgSO<sub>4</sub> and then vacuum dried to afford a crude brown product. The crude material was purified on a neutral alumina oxide column, using dichloromethane–hexane (1:1, v/v) solvent mixture as an eluant. Recrystallization from the same solvent system gave 1,4-diisocyanobenzene (8.9 g) in 76% yield.

Essentially the same experimental procedure was also utilized for the preparation of 1,3-diisocyanobenzene (Ia), 4,4'-diisocyanobiphenyl (Ic), and 4,4'-diisocyanodiphenylmethane (Id). Data pertaining to the characterization of these compounds are furnished in Table I.

**Acknowledgment.** We are indebted to the KFA, NCRD, and the Minerva Foundation for partial financial support and to Dr. Hugo E. Gottlieb for assisting in the running of the <sup>13</sup>C NMR spectra.

**Registry No.** Ia, 626-17-5; Ib, 623-26-7; Ic, 1591-30-6; Id, 10466-37-2; IIa, 25227-79-6; IIb, 6262-22-2; IIc, 49645-23-0; IId, 52721-83-2; diphosgene, 503-38-8; methyl chloroformate, 79-22-1; chlorine, 7782-50-5.

(9) (a) The top of the condenser should be connected to alkaline traps capable of absorbing the large volume of HCl gas which evolves during the reaction. (b) Chlorine used in this reaction was dried by passage through several gas-washing bottles containing concentrated H<sub>2</sub>SO<sub>4</sub>. (c) The progress of this reaction can conveniently be followed by <sup>1</sup>H NMR techniques. The chemical shifts (τ) of the precursors are ClCOOCH<sub>3</sub> (6.23), ClCOOCH<sub>2</sub>Cl (4.43), and ClCOOHCl<sub>2</sub> (2.55).

## Isobenzofuran: New Approaches from 1,3-Dihydro-1-methoxyisobenzofuran

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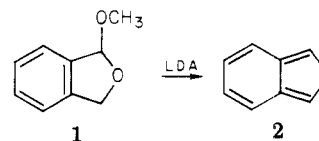
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We have found that the strong base induced 1,4-elimination of allylic ethers is a general reaction,<sup>2</sup> and it was

(1) K.N. expresses his gratitude to Sanyo Chemical Industries, Ltd., of Japan for support during the course of this work.

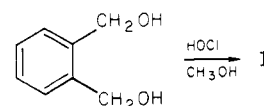
of interest to see if this method was capable of disrupting aromaticity. To this end, we chose first to examine the reactivity of 1,3-dihydro-1-methoxyisobenzofuran (1) and report here that 1 reacts readily with lithium diisopropylamide (LDA) to give reasonably stable solutions of isobenzofuran (2).



Other approaches to 2 have involved reverse Diels–Alder reactions;<sup>3–5</sup> of these only one<sup>5,6</sup> appears to be suitable for modest-scale preparations. The reaction reported here is the first ambient temperature synthesis and gives good yields (50–70%, not optimized) of 2 from a readily accessible starting material. The structure of 2 was confirmed by comparison with literature spectra and by reaction with maleic anhydride to give the previously reported Diels–Alder adducts.<sup>7</sup>

Solutions of 2 in benzene or ether are, in agreement with earlier reports, of moderate stability; 1.8% solutions had an approximate half-life of 6 days at room temperature. The reaction of 1 with LDA is quite rapid, and 2 appears to be stable toward further reaction with this base. Thus, holding the reaction mixture for 1 day at room temperature before quenching gave 80–90% of the yield of 2 found with quenching a few minutes after mixing, about the value anticipated from polymerization of 2 alone.

The starting material 1 was prepared by LiAlH<sub>4</sub> reduction of phthalide to phthalyl alcohol,<sup>8</sup> treatment of this diol in a two-phase system (pentane/methanol–sulfuric acid) with aqueous sodium hypochlorite solution (commercial laundry bleach) gave 1 in ca. 60% yield.



An alternative preparation of 1 has recently been reported by Tidwell and co-workers.<sup>9</sup>

Analysis of 1 by VPC at temperatures above 115 °C resulted in a minor shorter retention time peak that proved to be 2. Also, distillation of 1 usually resulted in viscous pot residues. Refluxing a solution of 1 in toluene for 1 day caused loss of the material with formation of polymer. These observations suggested that 1 might be a convenient source of 2 by direct<sup>10</sup> elimination of methanol, and this was subjected to experimental test.

A solution of 1 with maleic anhydride in toluene was refluxed for 2 h. After evaporation of the solvent and washing of the resultant solid with chloroform, a quanti-

(2) Unpublished work of B. Rickborn, B. H. Williams, K. Blonski, D. Svedberg, and T. Tuschka; portions of this work have been presented at the Pacific Conferences on Chemistry and Spectroscopy, San Diego, CA, Nov 1973, and Pasadena, CA, Oct 1979.

(3) R. N. Warrener, *J. Am. Chem. Soc.*, **93**, 2346 (1971).

(4) W. Wege, *Tetrahedron Lett.*, 2337 (1971).

(5) U. E. Wiersum and W. J. Mijs, *J. Chem. Soc., Chem. Commun.*, 347 (1972).

(6) A review of isobenzofuran chemistry has appeared recently: M. J. Haddadin, *Heterocycles*, **9**, 865 (1978).

(7) Wiersum and Mijs<sup>5</sup> reported that 2 and maleic anhydride gave an unseparated mixture of exo and endo adducts in quantitative yield.

(8) R. F. Nystrom and W. G. Brown, *J. Am. Chem. Soc.*, **69**, 1198 (1947).

(9) C. M. Rynard, C. Thankachan, and T. T. Tidwell, *J. Am. Chem. Soc.*, **101**, 1196 (1979).

(10) Whether these observations are associated with an uncatalyzed thermal elimination, or trace acid catalyzed reaction, has not been established.