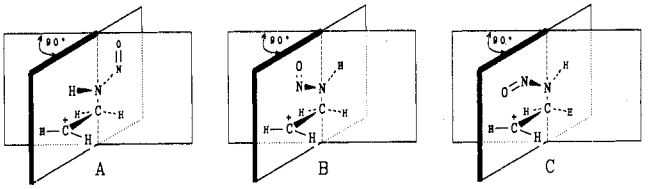
structure of the isomeric 1-alkyl-1,4-dihydro-3,4-diphenyl-1,2-diazete 2-oxide **2**, which was confirmed by X-ray analysis of the benzyl analogue[3] (Figure 2).

We believe the two dihydrodiazete *N*-oxides to be the first examples of these types of compounds. They are hydrazone *N*-oxides which are likewise unknown. The dihydrodiazete *N*-oxides easily isomerize to the corresponding azoxyalkenes upon heating by a conrotatory electrocyclic ring opening, and the latter compounds are coproducts of the nitrosation if care is not taken to control the temperature. Control experiments showed that the nitrosenamine cannot be a major product or intermediate in the aziridine nitrosation.

The dihydrodiazete *N*-oxide is perceived to arise from an isomerization of the *N*-nitrosoaziridinium ion by one of the pathways shown in Scheme I. At least two chemically novel features attend this process. Nitrosamines exhibit little chemistry emanating from reactions of the nitroso N unshared pair. Secondly, isomerization to a four-membered ring is surprising since, a priori, a pathway to the five-membered 3-alkyl-1,2,3-oxadiazolinium ion is open! We have demonstrated that protonation of the α-nitrosamino aldehyde carbonyl results in cyclization to the oxadiazolinium cation,[11] and Michejda and co-workers have shown that solvolysis of *N*-methyl-2-(tosyloxy)ethylnitrosamine occurs with neighboring-group participation to generate this heterocyclic cation.[12]

Ring opening of the *N*-nitrosoaziridinium ion **4** to the benzylic carbocation **9** followed by attack of the N lone pair produces **5**, which loses H^+ to give the dihydrodiazete *N*-oxide **2**. Alternatively, **5** can either result from the direct isomerization of **4** or involve a chelotropic ring opening (**4** → **7** + **8**) followed by a $2\pi_s + 2\pi_a$ cycloaddition. The latter pathways are reminiscent of proposals made by Greene to explain phenyltriazolinedione–alkene chemistry, which is proposed to proceed through an aziridinium imide.[13] The various mechanistic pathways shown in Scheme I have been probed by both experiment and theory. Treatment of the *threo*-β-chloro nitrosamine **10** with $AgBF_4$/HOAc gives the same product profile (HPLC and GCMS) as does the aziridine nitrosation although the yield of **3** exceeds that of **2** and more of the presumed carbocation intermediate **9** is captured by solvent.[8] Ab initio calculations[14] of the carbocation rotamers A–C (models for **9**) and the related cations **4**–**6**, where all carbon substituents have been replaced by H, show the carbocations A–C to be "unstable"[15] and to spontaneously close to **4**, **5**, or **6** depending upon the stereochemical arrangement of the RNNO group. Carbocation A undergoes a 90° C–N bond rotation and regenerates **4**, while B closes to **5**. The same carbocation with the opposite R, N=O arrangement C collapses to **6**. While N–N bond rotation in the carbocations A–C (**9**) is likely to be significantly restricted, this should not be the case in the *N*-nitrosoaziridinium ion **4**. The 180° N–N rotamer (anti) of that shown for **4** (syn) in Scheme I is only 0.6 kcal/mol more stable than the syn form. Replacement of the H atoms of the theoretical model with phenyl substituents (at the carbons) is likely to result in a distinct energetic preference for the syn conformer which is predisposed to give **5**.

The relative energies (MP2/6-31G*//RHF/3-21G) calculated for **4**, **5**, and **6** are 23.7, 14.0, and 0 kcal/mol, respectively, while the relative energy of the isolated **7** and **8** combined is 46.8 kcal/mol. Interaction between **7** and **8** is likely to lower the energy of the ensemble, but theory predicts the production of **5** by this route to be disfavored compared to the **4** → **5** isomerization for kinetic reasons. The chemical properties of **6** in our system are



unknown, and we cannot rule out its formation at this time. If it is formed it must be a minor product since the combined yield of **2** and **3** is 62%. This suggests that **4** represents the preferred conformation of this *N*-nitrosoaziridinium ion, and the course of the rearrangement to the less stable four-membered ring is determined by this stereochemical arrangement through either the carbocation B (**9**) or a transition state like it.

In addition to the novel chemical features of this work and the promise of new synthetic routes to unusual compounds, this research has relevance in the area of nitrosamine carcinogenesis.[11,12] Amine nitrosation usually produces nitrosamines, 90% of which are animal carcinogens. This pathway gives other compounds as the major products and suggests means of subverting nitrosamine formation. Carbocations such as **9** have been suggested as intermediates in the carcinogenic activation of β-hydroxy nitrosamines.[12] The chemistry shown here introduces alternative pathways and merits further investigation from numerous perspectives.

Acknowledgment. The support of this research by Grant No. R37 CA 26914 from the National Cancer Institute, NIH, DHHS, is gratefully acknowledged.

Supplementary Material Available: Experimental summaries, including spectroscopic data for the synthesis of the nitrosenamine, the aziridine nitrosation, and the $AgBF_4$ reaction, details of the calculations, and tables of positional parameters, thermal parameters, interatomic distances, and interatomic angles for **2** and **3** (12 pages); listings of observed and calculated structure factors for **2** and **3** (13 pages). Ordering information is given on any current masthead page.

Facile Li/HMPA-Promoted Polymerization Method for the Synthesis of Soluble Poly(phenylenes)

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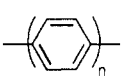
Poly(*p*-phenylene) (PPP) (**1**) has attracted much interest since it can act as an excellent organic conductor upon doping.[2] The conductivity of doped PPP has reached beyond the semiconducting



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and into the conducting region with values of 500 Ω^{-1} cm^{-1} being reported for the pressed pellets (films could not be formed due to the insolubility). There have been numerous syntheses of PPP; however, in nearly all cases, the materials are insoluble and intractable in organic solvents.[3-10] The most widely used methods

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(15) While the calculations do not reveal an independent existence for A–C, the phenyl substituents of **9** could produce sufficient stabilization to allow its existence on the reaction coordinate.

(1) Recipient of an Office of Naval Research Young Investigator Award (1989-1992).
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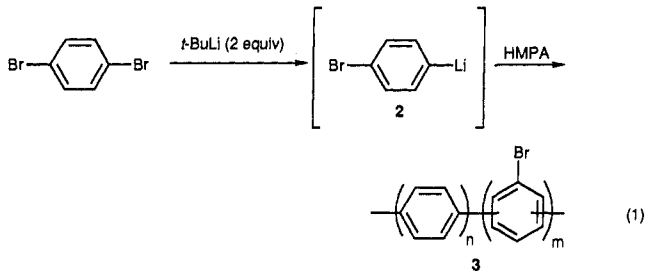
for PPP formation involve the Kovacic and Yamamoto approaches that afford materials with degrees of polymerization of 10–15.[2] Thus these are oligomeric materials.

Here we report the nearly instantaneous polymerization of 1-bromo-4-lithiobenzene (**2**) by treatment with hexamethylphosphoramide (HMPA)[11] to afford poly(phenylene) which is predominantly para linked. Some amount of meta linkages (possibly 20–30%) causes the crystallinity to be destroyed, rendering polymers that are soluble even with degrees of polymerization ~40. The ability to form soluble and tractable poly(phenylenes) which are predominantly para linked could possibly allow new applications of this material for lightweight rechargeable battery and electrochemical cell fabrications.[2,12]

Our initial approach involved the formation of **2** by the treatment of 1,4-dibromobenzene in ether at −78 °C with 2 equiv of *tert*-butyllithium in pentane (slow addition). The first equivalent was for lithium–halogen exchange to form **2** and *tert*-butyl bromide. The second equivalent of the *tert*-butyllithium was necessary for the elimination of the *tert*-butyl bromide to afford lithium bromide, isobutylene, and isobutane. This conveniently made all the byproducts innocuous. (The intermediacy of **2** was confirmed in a separate experiment by the addition of chlorotrimethylsilane to form 1-bromo-4-(trimethylsilyl)benzene in nearly quantitative yield.) Compound **2** was then treated at the same temperature with HMPA (1 equiv relative to the starting dibromide), which promoted the nearly instantaneous polymerization to poly(phenylene) with a high bromide content (**3**) (eq 1). Note that we have even quenched the reaction at −78 °C



(1)

3

by rapidly pouring the mixture into water to confirm that the polymerization was indeed taking place at that temperature. This represents a new method of extremely facile, non-transition-metal-catalyzed aryl–aryl polymerization.

Our optimal procedure[13] for forming poly(phenylene) with high concentrations of para-linked moieties was similar; however, the solvent used was dioxane, *tert*-butyllithium was added at 0 °C, and infusion of HMPA was done at 70–80 °C.[14] This afforded polymer **3** with one bromide group for approximately every three aryl rings in 25–30% yield after one fractional precipitation from ether.[15] It is clear from the FTIR analysis that predominantly para-linked material is formed by the strong band at 808 cm^{-1}. Weak bands at 882 and 790 cm^{-1} are attributed to the meta linkages.[16] A band at 1900 cm^{-1} was also attributed to the para-substituted units while the C–Br stretch was evident at 1074 cm^{-1}.[5] The polymer was soluble in THF, dichloromethane, and chloroform. The presence of phenylated polyphenylene cannot be ruled out at this point.[9] Though powder X-ray diffraction (XRD) signals have been reported for Kovacic[2b] and Yamamoto PPP,[5] no diffraction pattern was observed for **3**, consistent with the solubility of the material. Likewise, scanning electron microscopic (SEM) analysis showed a globular morphology pattern. Size exclusion chromatography (SEC) showed that **3** had M_w = 2404 and M_w/M_n = 2.33 relative to polystyrene and oligo(*p*-phenylenes).[17] There was little, if any, aliphatic material present in the polymer by ^1H NMR.

3 was dissolved in THF and cooled to −78 °C in order to accomplish debromination. *tert*-Butyllithium was added, and the solution was stirred for 1 h at the same temperature before being quenched with water to afford the debrominated polymer **4**. There was 0% bromide content by elemental analysis. Again, no aliphatic material was present in the sample. Remarkably, the M_w of our polymer increased from 2404 to 3178 (M_w/M_n = 2.80) upon debromination while the material remained soluble with degrees of polymerization >40. Some possible explanations could be that (1) the bromide content in **3** caused the polymer to be retained more tightly by the SEC columns (cross-linked polystyrene) and thus respond as a lower molecular weight material or (2) relithiation caused a further coupling of the chains. The solubility of the material suggests that there was little or no cross-linking of the chains. Again, no powder XRD signals were observable and SEM showed a globular morphology.

The reported CP/MAS/^{13}C NMR for PPP varies according to the method of preparation. Kovacic PPP shows resonances at δ 139 and 128 while commercial PPP has shifts at δ 143, 133, 130, and 124.[18] For compound **4**, the ^{13}C NMR (125 MHz, $CDCl_3$) chemical shifts obtained were at δ 140.66 (br), 128.80, and 127.26. Further, the proton spin lattice relaxation times (T_1) of oligo(phenylenes) are known to decrease with increased chain lengths, and ranges of 910 s for biphenyl to 0.48 s for PPP have been reported.[19] We found that compound **4** exhibited a T_1 range of 0.9–1.4 s, consistent with high molecular weight material.

The UV data for oligo(phenylenes) have been reported. The value of λ_{max} for *p*-sexiphenyl and *m*-sexiphenyl are 318 and 248 nm, respectively.[20] Polymers **3** and **4** showed λ_{max} at 274 and 278 nm, respectively. Again, these values are indicative of mixtures of para- and meta-linked units.

We demonstrated that the polymers prepared by this Li/HMPA-promoted coupling are electroactive. A Pt electrode was

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(11) **CAUTION**: HMPA is a highly toxic cancer suspect agent. All manipulations with this material should be carried out in a well-ventilated hood, and rubber gloves should be worn.

(12) (a) Wegner, G. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 361. (b) Ellis, J. R.; Schotland, R. S. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1982**, *23*, 134. (c) Shacklette, L. W.; Elsenbaumer, R. L.; Chance, R. R.; Sowa, J. M.; Ivory, D. M.; Miller, G. G.; Baughman, R. H. *J. Chem. Soc., Chem. Commun.* **1982**, 361. (d) Shacklette, L. W.; Elsenbaumer, R. L.; Baughman, R. H. *J. Phys. Colloq.* **1983**, 559. (e) Pruss, A.; Beck, F. *J. Elec,roanal. Chem. Interfacial Electrochem.* **1984**, *172*, 281.

(13) The optimal procedure described provided the highest molecular weight material by SEC analysis with the greatest para/meta-containing ratio as determined by FTIR analysis. Using ether as the solvent, the M_w values for −78 °C and 35 °C HMPA additions were 1064 and 1739, respectively. When THF was used as the solvent, the M_w values for −78 °C and 60 °C HMPA additions were 668 and 1663, respectively. When dioxane was used as the solvent with HMPA addition at 22 °C, the M_w value was 1950.

(14) A reflux condenser is needed since a strong exothermic reaction ensues during the HMPA addition. The polymerization is complete immediately after the HMPA addition.

(15) Calculated elemental data for one Br per three aryl units, $C_{18}H_{11}Br$: C, 70.36; H, 3.58; Br, 26.06. Found: C, 68.94; H, 4.11; Br, 25.22.

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(17) The oligo(*p*-phenylene) standards used were biphenyl, *p*-triphenyl, *p*-quaterphenyl, and *p*-sexiphenyl with a correlation between the four standards of ≥0.997. The M_w values for our materials using oligo(*p*-phenylene) standards were very close to the values obtained with polystyrene standards.

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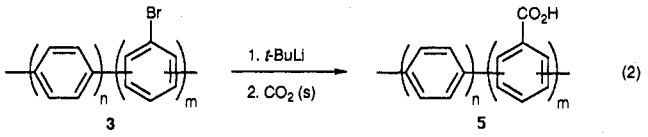
coated with films of both compounds **3** and **4**. Anodic peak potentials (E_{pa}) for the oxidation were at 1.44 and 1.45 V, respectively.[21]

Additionally, we used the lithiated polymer to prepare functionalized derivatives. For example, **3** was lithiated as described above and quenched with dry ice to afford the carboxylated polymer **5** with one carboxylic acid moiety per three aryl units (eq 2).[22] The FTIR (KBr) spectrum was free of the C–Br stretch



(2)

at 1074 cm^{-1} with the major stretch at 1686 cm^{-1} for the carbonyl moiety. The O–H stretch was weak presumably due to restricted hydrogen bonding in the solid. This procedure could have applications for the synthesis of functionalized polymers for self-doped conducting systems with fast electrochromic switching times and the fabrication of polymer-based batteries with high charge storage capacities.[23]

We do not have a clear understanding of the mechanism of the aryl couplings. The surprising aspect is that **3** unquestionably exhibits a predominance of para linkages while much of the bromide content is retained. Migrations of lithium and bromide in bromo lithio heteroaromatics are known under the base catalyzed halogen dance (BCHD) conditions.[24] The Taylor approach to PPP involving 1,4-dichloro-2-butene as a promoter for the polymerization of (4-bromophenyl)magnesium bromide may involve similar electron-transfer phenomena.[6] Additionally, the copolymerization of 2,5-dilithiothiophene with 2,5-dibromothiophene to afford poly(thiophene) has been reported.[25] However, as we described here, the addition of HMPA dramatically facilitates the aryl–aryl coupling process. A study of the scope and mechanism[26] of the polymerization as well as the detailed electrical and thermal analyses of the materials is in progress.

Acknowledgment. We thank the Department of the Navy, Office of the Chief of Naval Research, Young Investigator Program (N00014-89-J-3062), and the National Science Foundation (RII-8922165) for their generous support of this work. We also thank Professor R. Philp (University of South Carolina), Dr. R. Beckerbauer (Du Pont), and Dr. A. Diaz (IBM) for helpful suggestions. The scanning electron microscope was purchased with a grant from the National Science Foundation (BIR-8805143).

(21) Recorded relative to $Ag/AgNO_3$ (0.01 M) in CH_3CN at 50 mV/s scan rate with 0.1 M tetraethylammonium perchlorate (TEAP) as the electrolyte and a Pt working electrode. For related studies on oligo(phenylenes), see: (a) Diaz, A.; Crowley, J.; Bargon, J.; Gardini, G. P.; Torrance, J. B. *J. Electroanal. Chem.* **1981**, *121*, 355. (b) Meerholz, K.; Heinze, J. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 692.

(22) Calculated elemental data for one CO_2H unit per three aryl units, $C_{19}H_{12}O_2$: C, 83.82; H, 4.41. Found: C, 76.10; H, 4.99.

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Studies on DNA-Cleaving Agents: Synthesis of a Functional Dynemicin Analogue[1]

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Neocarzinostatin, esperamicin, and calicheamicin are structurally unprecedented DNA-cleaving agents that operate putatively through the triggerable generation of diyl intermediates.[2] Recently, the groups of Konishi and Clardy[3a] reported the structure of dynemicin (**1**) (Scheme I), the newest member of this emerging class of chemotherapeutic leads. Dynemicin exhibits potent inhibitory activity against various tumor cell lines and in vivo activity in P388 leukemia and B16 melanoma inoculated mice.[3b] Dynemicin is proposed[1a,3,4] to be activated for DNA lesion through reductive cleavage of its epoxide ring. Addition to the resultant anthraquinone methide would then provide the activated enediyne **2**. In this overall process, carbons 2, 3, 8, and 7 initially fixed in an anti-like conformation by the epoxide ring in **1** are released to assume a gauche-like conformation in **2**, thereby allowing for facile cycloaromatization[5] to a diyl (**3**) capable of effecting lesions at proximate nucleotide sites.[6] We describe herein the first synthesis of an analogue of dynemicin that fully emulates the acid-inducible activation and cycloaromatization behavior exhibited by dynemicin itself.[3c]

Our approach to analogue design was based on the view that the diyl-generating capability of dynemicin could be mimicked by various dihydroquinoline epoxides spanned by an enediyne bridge (bold face in **1**). Activation of such systems was expected to arise through modification or cleavage of various aryl substituents or nitrogen protecting groups, which by increasing electron density in the surrogate C ring would result in epoxide cleavage. Importantly, this approach would allow for activation under a variety of chemical or physiological conditions.[7]

Synthesis of CDF-ring analogues of **1** started with reduction of commercially available aldehyde **4**[8] (Scheme II). Treatment of the resultant alcohol with the magnesium salt of (trimethylsilyl)acetylene and $ClCO_2Me$ gave the 1,2-addition product **5** along with minor amounts of the 1,4-addition product.[9] Attempts to

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