The Carbazole Connection: Unusual Products from the Diazotization of Anthranilic Acids

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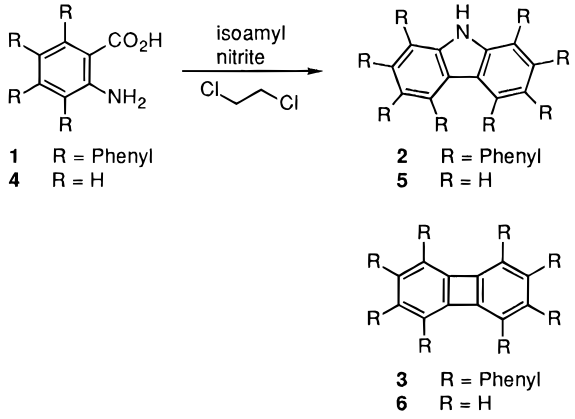
Received May 22, 1996

We have described the efficient synthesis of octaphenylnaphthalene by the diazotization of 3,4,5,6-tetraphenylanthranilic acid (**1**) in the presence of tetraphenylcyclopentadienone.[1] Since then, in an attempt to prepare even more sterically encumbered naphthalenes, we diazotized **1** in the presence of 2,5-bis(1-naphthyl)-3,4-diphenylcyclopentadienone,[2] but very little of the desired dinaphthylhexaphenylnaphthalene was detected, and this compound has not been isolated in pure form. Instead, recrystallization of a nonpolar chromatographic fraction from this reaction gave a small quantity of a quite unusual product: 1,2,3,4,5,6,7,8-octaphenylcarbazole (**2**). This unexpected observation led us to examine the diazotization of compound **1** in the absence of a diene. When **1** was added slowly to a solution of isoamyl nitrite (2 equiv) in 1,2-dichloroethane at reflux, numerous products were formed, but from this mixture compound **2** was obtained as a crystalline solid in 5% yield. We also searched for octaphenylbiphenylene (**3**), since benzyne can dimerize to biphenylene in the absence of suitable dienes;[3−5] however, no trace of **3** was ever observed, even though many fractions from this and other reactions of **1** were screened by mass spectrometry.



X-ray crystallographic analysis conclusively established the structure of **2**,[6] which is illustrated in Figure 1. Compound **2** is a crowded molecule, and intramolecular steric repulsions distort it from planarity; for example,

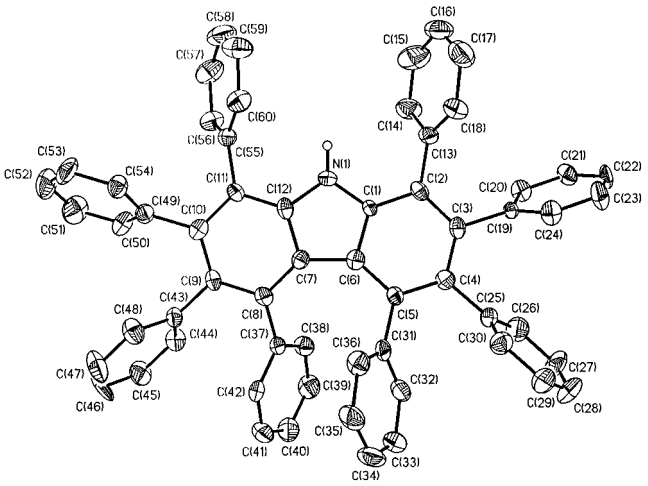


Figure 1. Molecular structure of octaphenylcarbazole (**2**). Thermal ellipsoids have been drawn at the 50% probability level, and all hydrogen atoms but that of the amine have been omitted for clarity.

in the carbazole nucleus the C(5)−C(6)−C(7)−C(8) torsion angle is 23.3° (the crystallographic numbering scheme is used). This distortion is due chiefly to repulsion between the C(5) and C(8) phenyls, which are tightly stacked (the distance between the ipso carbon atoms of these phenyls is 3.16 Å), so much so that the carbazole−phenyl bonds are bent out of the mean planes of the phenyl rings by approximately 7.3° and 11.2°, respectively. Compound **2** possesses approximate C_2 symmetry, but its ^{13}C NMR spectrum contains only 22 lines, consistent with time-averaged C_{2v} symmetry, which suggests that **2** is conformationally flexible.

Does the diazotization of ordinary anthranilic acid (**4**) yield carbazole? When compound **4** was added to a solution of isoamyl nitrite (2 equiv) in hot dichloroethane, GC and GC−MS analysis of an organic extract of the reaction mixture revealed the presence of 13% biphenylene (**6**) and 2% carbazole (**5**) as well as many other products.[7] We know of no report of the formation of carbazole under these conditions; however, there are two reports of carbazole derivatives from similar reactions, but not of carbazole itself. Ghosh et al.[8] observed the formation of *N*-[(2-halophenyl)amino]carbazoles **7** from the decomposition of benzenediazonium 2-carboxylate hydrohalides in the presence of propylene oxide, and Miwa et al.[9] proposed structure **8** for a compound isolated after decomposition of benzenediazonium 2-carboxylate in acetone. No compounds with parent ions corresponding to **7** or **8** were observed in the GC−MS analyses of our reaction mixtures, but Ghosh et al. had noted that compound **7** "decomposed readily in the gas chromatograph" to give carbazole.[8] For this reason, our organic extract was fractionated by preparative TLC. Both biphenylene and carbazole were isolated, and their

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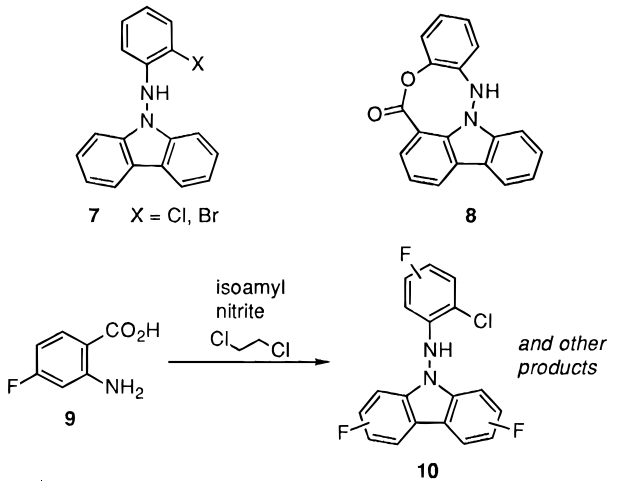
(2) Ogliaruso, M. A.; Romanelli, M. G.; Becker, E. I. *Chem. Rev.* **1965**, *65*, 261−367.
(3) Wittig, G. *Angew. Chem.* **1957**, *69*, 245−251.
(4) Berry, R. S.; Spokes, G. N.; Stiles, M. *J. Am. Chem. Soc.* **1962**, *84*, 3570−3577.
(5) Logullo, F. M.; Seitz, A. H.; Friedman, L.; Abrams, G. D.; Ertl, H.; Yates, P. *Organic Syntheses*; Wiley: New York, 1973; Collect Vol. V, pp 54−59.
(6) The authors have deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.
(7) Other compounds observed included phenyl benzoate (3%), 2-nitrodiphenylamine (4%), acridone (20%), and *N*,*O*-diphenylanthranilate (23%). The identities of all but the last of these are based upon chromatographic and mass spectral comparisons of the reaction products with authentic standards; the structure of *N*,*O*-diphenylanthranilate is proposed on the basis of its mass spectral fragmentation pattern.
(8) Ghosh, R.; Sheinin, E. B.; Bell, C. L.; Bauer, L. *J. Heterocycl. Chem.* **1975**, *12*, 203−206.
(9) Miwa, T.; Kato, M.; Tamano, T. *Tetrahedron Lett.* **1968**, 2743−2745.

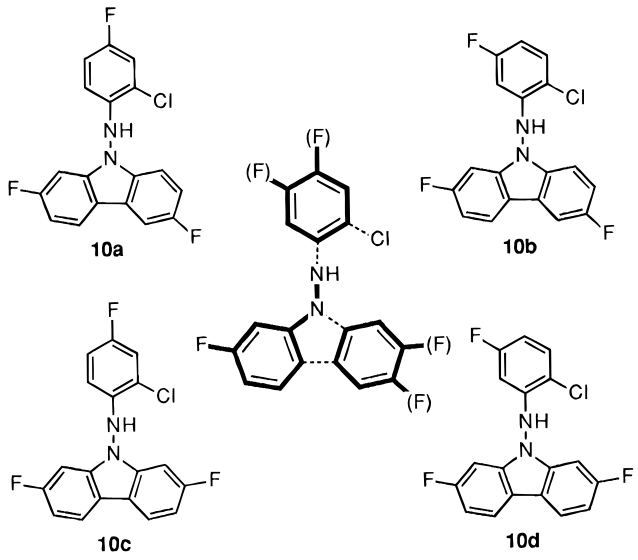
S0022-3263(96)00949-8 CCC: $12.00

identities were confirmed by comparison with authentic standards, but no trace of compound **7** was observed.



However, a parallel experiment provided strong evidence that **7** or its derivatives are intermediates in these reactions. In order to better define the role of arynes, if any, in the formation of carbazoles, 2-amino-4-fluorobenzoic acid (**9**) was diazotized under similar conditions, since the presence of intermediates such as fluorobenzyne would lead to the formation of more than one isomer of the expected difluorocarbazole. GC−MS analysis of the organic extract of this reaction mixture showed a trace of difluorobiphenylene and 4% difluorocarbazole, but when the reaction mixture was fractionated by preparative TLC, the only band found to give the difluorocarbazole mass spectrum (in GC−MS analysis) was much less polar than ordinary carbazole. Indeed, this compound proved to be a mixture of isomers **10**—fluorinated analogs of Ghosh et al.'s compound **7**.

Compound **10** was isolated by preparative TLC, and it appears homogeneous by TLC analysis in several solvent systems. This material does decompose upon GC−MS analysis to give difluorocarbazole, but a direct inlet mass spectrum shows only **10**, and an exact mass determination confirmed the molecular formula of $C_{18}H_{10}ClF_3N_2$. The 1,2-dichloroethane solvent must be the source of the chlorine in **10**, and this was supported by repeating the diazotization of **9** in 1,2-dibromoethane; direct inlet mass spectral analysis of the carbazole product of this reaction gave a parent ion at *m*/*z* 390 that contained one bromine atom and no chlorine, consistent with a molecular formula of $C_{18}H_{10}BrF_3N_2$. ^{1}H NMR analysis clearly indicates the presence of more than one isomer of **10**, and its ^{19}F NMR spectrum shows 10 resonances (two of them nearly superimposed) in ratios suggesting the presence of two isomers (63% and 18%) with three inequivalent fluorine atoms and two isomers (15% and 4%) with two types of fluorine atoms in a 2:1 ratio. This situation can result only if at least two *m*-fluorobenzynes (or other "symmetric" intermediates) are involved in the formation of **10**. If one assumes that the two nitrogens arise from a single diazonium group, then the four observed isomers are most likely compounds **10a**−**d**.[10]



In conclusion, carbazoles are formed in the diazotization reactions of anthranilic acids (at least when halogens are available), and arynes and *N*-[(2-halophenyl)amino]-carbazoles are likely intermediates. A detailed mechanism for this process is not obvious, nor are the factors governing whether a particular (phenylamino)carbazole will decompose to the corresponding carbazole. However, dodecaphenyl-**7**, the presumed precursor of **2**, if formed must be extremely crowded, so that homolysis of the N−N bond should be facile. Given that the carbazoles are only minor products in these complex diazotization reactions, further mechanistic studies may be difficult, and we gladly leave further consideration of this problem to the interested reader.

Experimental Section

1,2,3,4,5,6,7,8-Octaphenylcarbazole (2). A solution of isoamyl nitrite (0.150 mL, 1.12 mmol) in 1,2-dichloroethane (10 mL) was heated to reflux under argon. A solution of 3,4,5,6-tetraphenylanthranilic acid[1] (246 mg, 0.56 mmol) in 1,2-dichloroethane (30 mL) was added dropwise to the reaction flask over 2 h, and heating was continued for 3 h. Ethanol (8 mL) and 1% NaOH (32 mL) were added to quench the reaction, and the resulting mixture was extracted with $CHCl_3$ (100 mL). The organic extract was washed with saturated $NaHCO_3$ (2 × 50 mL) and water (2 × 50 mL), dried over $MgSO_4$, and concentrated to dryness. The residue was chromatographed on a silica gel column (solvent, 3:1 hexanes−$CHCl_3$), and the fractions containing **2** were further subjected to preparative TLC (silica gel GF; solvent, 1:1 hexanes−benzene) to give pure compound **2** as a colorless solid (10 mg, 4.6%): mp 300−303 °C dec; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.46 (d, J = 7 Hz, 4H), 6.58 (m, 8H), 6.67 (m, 2H), 6.75 (m, 6H), 6.84 (m, 10H), 7.14 (m, 2H), 7.20 (m, 4H), 7.27 (m, 4H), 8.04 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 120.9, 122.7, 124.6, 124.7, 125.2, 126.0, 126.5, 126.8, 126.9, 128.2, 130.4, 130.5, 131.6, 131.9, 134.3, 136.7, 137.4, 138.3, 139.0, 140.5, 140.9, 141.0 (22 of 22 expected resonances); IR (KBr) ν_{max} 3452 (NH), 3078, 3052, 3021, 1596, 1493, 1441, 1379, 1068, 793, 751, 694 cm^{-1}; MS *m*/*z* 775 (M^+, 100), 698 (M − C_6H_5, 9), 697 (M − C_6H_6, 9); exact mass 775.3241, calcd for $C_{60}H_{41}N$ 775.3239. Crystals of **2**·3CH_2Cl_2, suitable for X-ray analysis, were obtained by recrystallization from CH_2Cl_2−CH_3OH.

Reaction of 2-Amino-4-fluorobenzoic Acid with Isoamyl Nitrite. A solution of isoamyl nitrite (0.878 mL, 6.54 mmol) in 1,2-dichloroethane (50 mL) was heated to reflux under argon. A solution of 2-amino-4-fluorobenzoic acid (507 mg, 3.27 mmol) in 1,2-dichoroethane (50 mL) was added dropwise over 1 h, and heating was continued for 10 h. Ethanol (20 mL) and 1% NaOH (60 mL) were added to quench the reaction, and the mixture was extracted with $CHCl_3$ (200 mL). The extract was washed

(10) Four isomers will result if one of the carbazole rings of **10** is derived from a diazonium-containing fragment, which must have the fluorine atom and diazonium group meta to each other, but only three isomers would be formed if the chlorofluoroaniline is derived from the diazonium-containing fragment. Of course, it may be that more than one pathway exists for the formation of **10**.

with saturated $NaHCO_3$ (3 × 50 mL) and water (2 × 50 mL), dried over $MgSO_4$, and concentrated to dryness. The resulting residue (59 mg) was fractionated by preparative TLC (silica gel GF; solvent, 1:1 hexanes−benzene). The mixture of isomers **10** was obtained from a band of R_f 0.80, and this material was further purified by preparative TLC (silica gel GF; solvent, hexanes; R_f 0.18) to give **10** as a colorless solid (0.5 mg): ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.87 (m, 0.8 H), 6.10 (m, 0.2 H), 6.58 (m, 0.8 H), 6.71 (m, 0.2 H), 7.04−7.24 (m, 5 H), 7.36 (m, 1 H), 7.71 (m, 0.8 H), 7.96 (m, 1.2 H); ^{19}F NMR (470 MHz, $CDCl_3$, $CFCl_3$ reference) δ −112.68 (m, 0.81 F; isomers **10a** and **10b**, carbazole F), −113.16 (m, 0.63 F; **10a**, carbazole F), −113.27 (m, 0.18 F; **10b**, carbazole F), −114.74 (m, 0.30 F; **10c**, carbazole F_2), −114.84 (m, 0.08 F; **10d**, carbazole F_2), −121.43 (m, 0.04 F; **10d**, phenyl F), −121.62 (m, 0.18 F; **10b**, phenyl F), −122.82 (m, 0.63 F; **10a**, phenyl F), −123.05 (m, 0.15 F; **10c**, phenyl F); MS m/z 346 (M^+, 25), 311 (M − Cl, 6), 202 ($C_{12}H_6F_2N$, 100); exact mass 346.0490, calcd for $C_{18}H_{10}F_3{}^{35}ClN_2$ 346.0485.

Acknowledgment. This work was supported by National Science Foundation Grant CHE-9408295, which is gratefully acknowledged. We thank Dr. Istvan Pelczer for recording the ^{19}F NMR spectrum of **10**.

Supporting Information Available: Copies of the ^{1}H NMR, ^{13}C NMR, and mass spectra of compound **2** and the ^{1}H NMR, ^{19}F NMR, and mass spectra of **10** (6 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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