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Facile Redox Interconversion of 6,11-Diphenyldibenzo[*b*,*f*][1,4]diazocine and 2-(2-Aminophenyl)-1,3-diphenylisoindole: Reversible SET Ring Contraction and Expansion Processes[‡]

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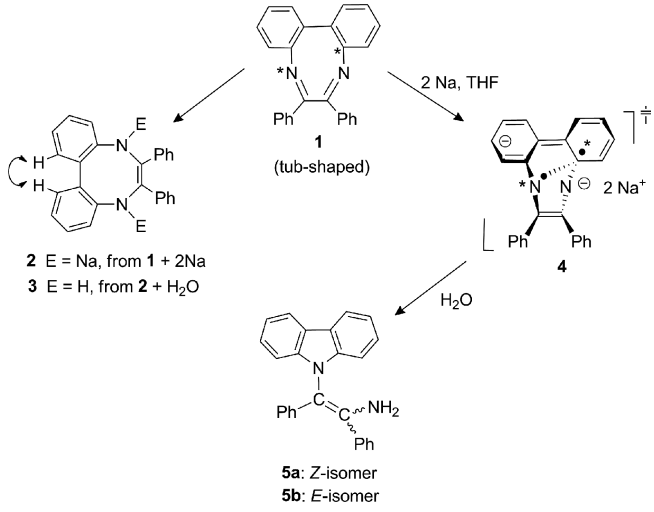
In our continuing attempts to convert tub-shaped dibenzo-[1,4]diazocines or dibenzo[1,5]diazocines into necessarily planar Hückel aromatic ten-π-electron dianions or dihydro derivatives of the central diazocine ring, we have added requisite electrons by Na or Li metal in THF. Subsequent hydrolysis yielded no evidence for the formation of such Hückel aromatic products but in each case a profound rearrangement of the tricyclic diazocine had instead occurred. In the present study we have attempted to form the unknown aromatic 6,11-diphenyldibenzo[*b*,*f*][5,12]-dihydro[1,4]diazocine at 25 °C by such a straightforward addition of two electrons to 6,11-diphenyldibenzo[*b*,*f*][1,4]diazocine. We were encouraged by the prior reduction of the unsubstituted [1,4]diazocine to 1,4-dihydro-[1,4]diazocine, which by X-ray and ^{1}H NMR evidence displays aromatic-like properties. However, this diphenyldibenzo[1,4]-diazocine upon reduction underwent instead an unusual, serendipitous rearrangement to yield quantitatively 2-(2-aminophenyl)-1,3-diphenylisoindole. Then in a purposive search for other reductants capable of reductively rearranging this [1,4]diazocine to its corresponding isoindole, we discovered three other reductants, namely *o*-diaminobenzene, titanium(II) salts, and concentrated aqueous hydriodic acid with visible light. Conversely, again in a serendipitous observation, it was found that O_2 in $CHCl_3$ with visible light could readily convert the isoindole in an oxidative rearrangement back into the [1,4]diazocine. A purposive method for achieving this oxidative rearrangement was then found to be treatment with DDQ. General mechanistic pathways are proposed via SET intermediates for both redox interconversions.

Introduction

Background: Single-Electron Transfer Processes with Dibenzodiazocines

Our interest in nitrogen analogs of cyclooctatetraene arose from our attempts to generate the Hückel-aromatic ten-π-electron, necessarily planar dianion **2** from the known tub-shaped 6,7-diphenyldibenzo[*e*,*g*][1,4]diazocine (**1**) by the addition of two equivalents of sodium or lithium metal in THF suspension and its subsequent hydrolysis (Scheme 1). Although the isolated product was found to have the proper molecular mass and some of the expected IR and ^{1}H NMR spectral features of **3**, the overall product, upon recrystallization from 95% ethanol, yielded only the mechanically separable crystals of the *Z*-isomer (**5a**) and *E*-isomer (**5b**) of *N*-(2-amino-1,2-diphenylethenyl)carbazole, as was demonstrated by individual X-ray diffraction analysis.[2,3]



Scheme 1.

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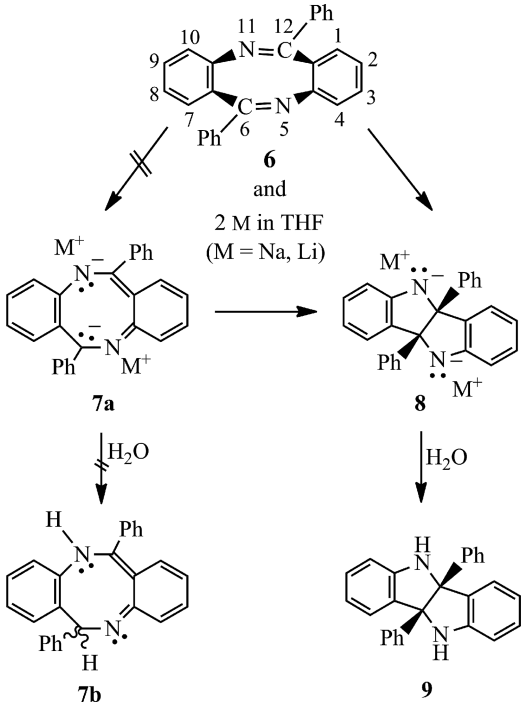
Clearly, the profound rearrangement of diazocine **1** upon reduction with sodium or lithium must have involved transannular bonding in the transition state between the asterisked N and C sites in **1** (**4** in Scheme 1). Each N center in structures **1**–**5** has an electron pair, which has been omitted for clarity.[4a] Because of the tub shape of **1**, attaining the necessary coplanarity of **1** would require more activation energy[4b] than the partial σ-bond stabilization anticipated between N* and C* in transition state **4**.

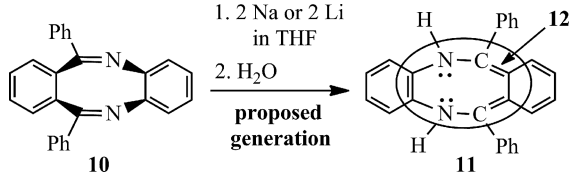
In order to avoid the destabilizing *ortho*-H repulsions in **2** (bracketed by arrows), we then examined the electron-transfer reduction of an isomer of **1**, namely, 6,12-diphenyldibenzo[]*b*,*f*[1,5]diazocine (**6**) (Scheme 2).[4b] Although the validity of structure **6** was assured both by its logical synthesis via the bimolecular dehydration of 2-aminobenzophenone and by its limited spectroscopic data,[5] its 3D stereochemistry was not. The subsequently obtained X-ray diffraction and ^{13}C NMR spectroscopic data unequivocably established the 3D-structure of **6** as that rendered in Scheme 2, with coplanarity of the transannular C=N and N=C groups and with the cross-ring N^5 and N^{11} atom separations of 3.294(3) Å and the C^6 and C^{12} atom separation of 3.000(2) Å. The cross-ring proximity of these atoms raises the probability of transannular bonding in radical-anionic or dianionic intermediates (i.e., **7a** to **8**) in SET processes (Scheme 2). In fact, treatment of **6** with sodium or lithium metal in THF must have led only to dianionic salt **8** and ultimately none of the putative Hückel ten-π-electron dianion **7a**, because subsequent hydrolysis produced only **9**.



Scheme 2.

Thus, despite the absence of the *ortho*-H group repulsions, present in the transition from **1** to **2** but absent in the path from **6** to **7b**, the Hückel dianion **7a** is not formed because of the remaining ring strain in forming a planar diazocine ring (about 23 kcal/mol.[4b]) (Again each N center in structures in 6–9 of Scheme 2 has an electron pair except **7b** that has been omitted for clarity.)

In our continuing search for an isomer of **1** or **6** that would form a stable and planar Hückel 10-π-electron dianion and dihydro derivative (**11**), we have now selected the known 6,11-diphenyldibenzo[*b*,*f*][1,4]diazocine (**10**). By examining the known properties of the unsubstituted dihydrodiazocines, we note that the X-ray structure of 1,4-dihydro-[1,4]diazocine (**12**, the enclosed substructure in **11**) reveals a planar and aromatic connectivity of its C–C and C–N bonds of almost the same length. Also, the ^1H NMR spectrum exhibits diamagnetic ring current effects similar to those of heteroaromatic rings like furan or thiophene (Scheme 3).[6]



Scheme 3.

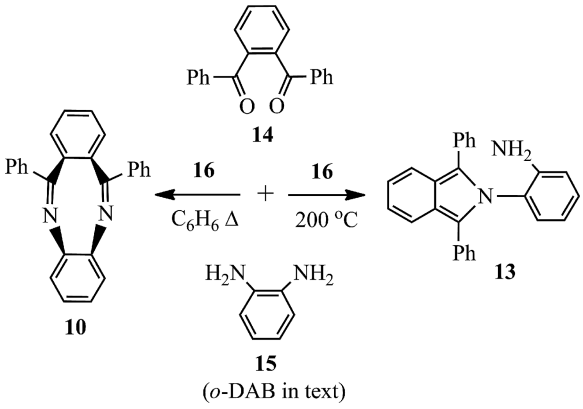
Accordingly, we have now attempted to generate the presently unknown 6,11-dibenzodiphenyl[*b*,f][5,12]-dihydro-[1,4]diazocine (**11**) by the straightforward addition of two electrons from Na or Li metal in THF to the known 6,11-diphenyldibenzo[*b*,*f*][1,4]diazocine (**10**) and hydrolysis of the resulting dianion in the hope of preparing **11**.

Results

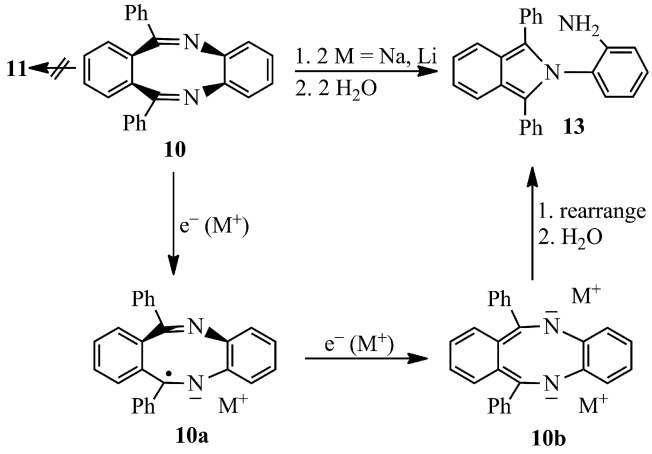
The Attempted Generation of 6,11-Diphenyldibenzo[*b*,*f*]-5,12-dihydro-[1,4]diazocine (11) by the Sodium or Lithium Metal Reduction of 10 and Subsequent Hydrolysis

The key probative experiment in the present investigation as summarized in Scheme 3 was put to the test in the following manner. The requisite starting material (**10**) was prepared according to our modification of the original procedure of Olliéro and Solladié,[7] which now uses the acid-catalyzed condensation of **14** and **15** in toluene, instead of benzene with *p*-toluenesulfonic acid (**16**) to generate cyclic dianil **10** (m.p. 197–198 °C; ref.[8] 184–189 °C)[7,8] (Scheme 4).

When **10** (one equiv.) was allowed to react with finely divided pieces of freshly cut Na or Li metal (ten equiv.) in THF at room temp. for 10 h for Na or for 24 h with Li, followed by mechanical removal of metal and then hydrolysis, workup in either case provided a quantitative yield of **13** with no remaining **10** or any other product such as the expected Hückel 10-π-electron system **11** (Scheme 5). The most likely initial intermediates formed from such alkali-metal additions to **10** would be radical-anion **10a** and dianion **10b**[9] and either of these would undergo transannular rearrangement to the isoindole skeleton in **13** (see below).



Scheme 4. Method of Olliéro and Solladié.[7]



Scheme 5.

The sample of **13**, obtained from **10** and Na in THF (Scheme 5), was recrystallized from absolute ethanol as pale yellow crystals, m.p. 212–213 °C (ref.[7] 201–202 °C). Even when mixtures of **10** and Na metal were allowed to react in different ratios or for shorter reaction times, **13** was found as the only product.

Confirmation of the Structures of Diazocine 10 and Isoindole 13 as Originally Proposed by Olliéro and Solladié[7]

The requisite diazocine **10** required for the attempted synthesis of the planar Hückel aromatic system **11** and the unexpected, serendipitous product **13** obtained by treating **10** with Na or Li in THF have both been reported in a brief paper by Olliéro and Solladié.[7] Both had previously been prepared (Scheme 4)[8] and partially characterized by elemental analyses, molecular mass estimate and IR and ^{1}H NMR spectroscopic analysis for which no actual measured values are given. Moreover, the melting points of their **10** and **13** are 10 °C lower than we have observed in our work. However, the 3D X-ray structure and the ^{13}C NMR spectroscopic data were lacking.

In this work, the sample of **10** isolated from **14** and **15** at 110 °C in toluene, was recrystallized from absolute ethanol as yellow crystals, m.p. 197–198 °C (ref.[7] 184–189 °C). Its IR spectrum ($CDCl_3$) displays one C=N stretch at 1625 cm^{-1}; the ^{1}H NMR spectrum displayed 18 aromatic protons; and the ^{13}C NMR spectrum 11 ^{13}C singlets, including a C=N peak at δ = 169.7 ppm. The 3D X-ray diffraction data for **10** is given in Figure 1 as a thermal ellipsoid diagram. Especially noteworthy are the nonplanar tub-like structure, the coplanarity of the two transannular C=N groups and the cross-ring N^1 and N^2 and the C^7 and C^{14} atom separations of 2.901(2) and 2.876(2) Å, respectively. As with the nonplanar structure of **6**, the cross-ring proximity of these atoms enhances the likely significance of transannular electronic delocalization/bonding in radical anionic intermediate **10a** (or depicted in Scheme 13, as resonance structures **28** and **29**, where E_n = Na).

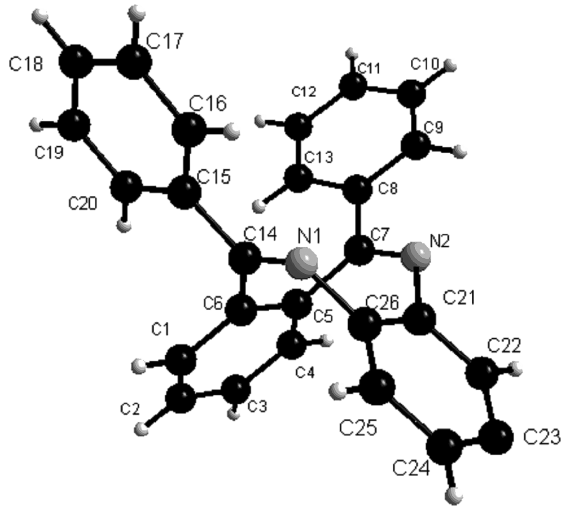


Figure 1. Thermal ellipsoid (30%) diagrams for 6,11-diphenyldibenzo[*b*,*f*][1,4]diazocine (**10**). Selected bond lengths (atom separations) [Å] and bond angles of 6,11-diphenyldibenzo[*b*,*f*][1,4]diazocine (**10**) are shown in the following: N(1)–C(14) 1.281(2), N(1)–C(26) 1.419(2), N(2)–C(7) 1.279(2), N(2)–C(21) 1.419(2), C(5)–C(6) 1.391(2), C(5)–C(7) 1.499(2), C(6)–C(14) 1.498(2), C(14)–C(15) 1.491(2), C(16)–C(17) 1.377(2), C(21)–C(26) 1.399(2), N(1)–N(2) 2.901(2), C(7)-C(14) 2.876(2), C(7)–N(1) 3.122(2), C(14)–N(2) 3.196(2), C(14)–N(1)–C(26) 121.40(11), C(7)–N(2)–C(21) 120.09(11), C(5)–C(6)–C(14) 118.77(11), N(2)–C(7)–C(8) 119.30(11), N(2)–C(7)–C(5) 123.50(12), N(1)–C(14)–C(15) 118.15(12), C(16)–C(15)–C(14) 119.99(12).

The isoindole **13** first reported by Olliéro and Solladié as the product obtained from a mixture of **14** and **15** at 200 °C[7] again was characterized in a manner similar to diazocine **10** but without X-ray data. Since the striking reductive rearrangement of **10** into **13** by Na or Li has been observed for the first time in this study, it was essential to obtain X-ray crystallographic and other spectral confirmation of its structure. Its IR spectrum ($CDCl_3$) exhibits the N–H stretches at 3478 and 3383 cm^{-1}; the ^{1}H NMR spectrum displayed 18 aromatic protons, as well as a broad two-

proton doublet for the NH_2 group at δ = 3.47 ppm and with IR bands at 3478 and 3383 cm^{-1}. Finally, the thermal ellipsoid diagram for the X-ray diffraction data for **13** is exhibited in Figure 2.

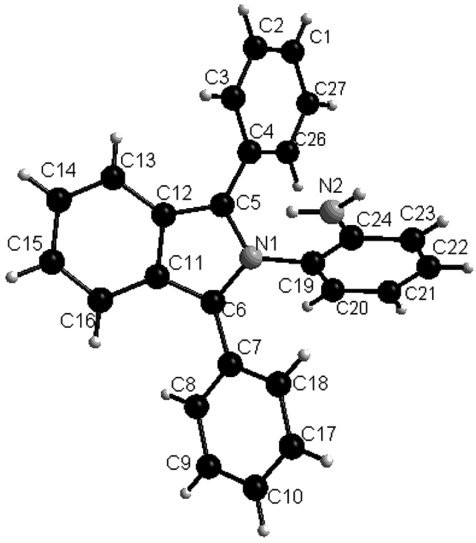
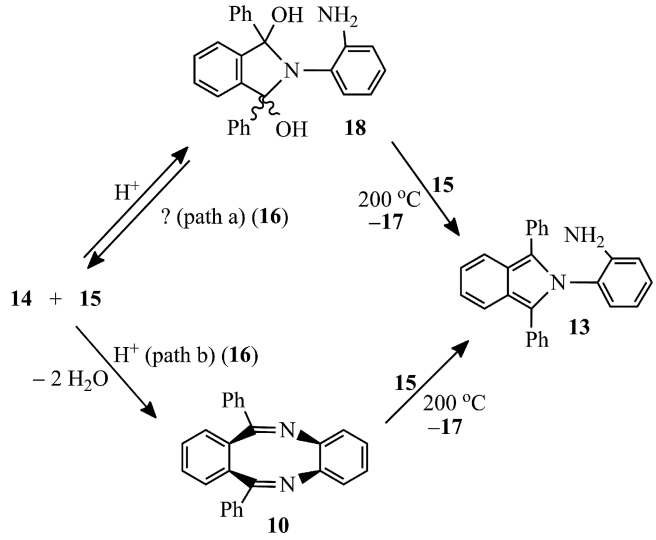


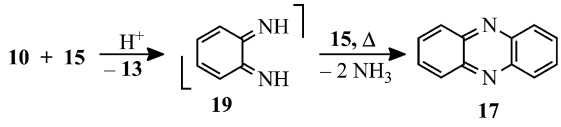
Figure 2. Thermal ellipsoid (30%) diagrams for 2-(2-aminophenyl)-1,3-diphenylisoindole (**13**). Selected bond lengths (atom separations) [Å] and bond angles of 2-(2-aminophenyl)-1,3-diphenylisoindole (**13**) are shown in the following: N(1)–C(5) 1.387(2), N(1)–C(19) 1.440(2), N(2)–C(24) 1.354(2), C(2)–C(3) 1.383(2), C(4)–C(5) 1.471(2), C(11)–C(12) 1.437(2), C(13)–C(14) 1.364(2), C(14)–C(15) 1.426(2), C(19)–C(24) 1.400(2), N(1)–N(2) 2.806(2), N(2)–C(5) 3.182(2), N(2)–C(6) 3.657(2), C(6)–N(1)–C(5) 111.02(12), C(6)–N(1)–C(19) 125.53(12), C(3)–C(4)–C(5) 118.74(13), N(1)–C(5)–C(12) 106.93(13), C(13)–C(12)–C(11) 119.38(13), C(14)–C(13)–C(12) 118.95(15), C(24)–C(19)–N(1) 118.39(13).



Scheme 6.

presence of **13** and the absence of **10**. Column chromatographic separation provided 80% of **13**, 10% of **14** and **15** combined and about 10% of phenazine (**17**) (excluding other unknown amines) (Scheme 6).

These findings support the viability of path b and the role of **15** as the reductant of **10** to **13** (Scheme 7). The condensation of putative diimino *ortho*-quinone **19** with **15** would lead to the phenazine (**17**) identified among the products (Scheme 7).[11]



Scheme 7.

Possible Reaction Pathways Leading from *o*-Dibenzoylbenzene (14) and *o*-Diaminobenzene (15) to Diazocine 10 or to Isoindole 13

Although Olliéro and Solladié prepared both **10** and **13**, as depicted in Scheme 5, and correctly identified their atom connectivity, they offered no proof of the pathway(s) by which these structures would form. In fact, they left the origin of **13** from **14** and **15** or from **10** and **15** as an open question to be answered by further investigation.[10]

Now the products **10** and **13** could arise from **14** and **15** by way of at least two distinct paths (Scheme 6): 1) path a, through adduct **18** (possibly reversibly formed) with further reductive dehydroxylation with reagent **15** to yield **13**, accompanied with loss of phenazine (**17**); or 2) path b, formation of diazocine **10** with further reductive rearrangement by **15** to **13** with loss of **17**.

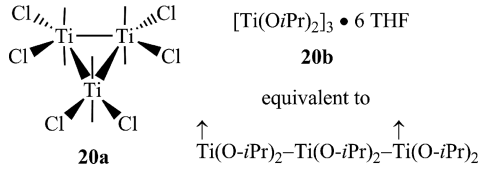
To test the viability of path b, a dry mixture of **10** and **15** in a 1:3 molar equiv. ratio was heated at 200 °C with **16**. Hydrolytic workup, followed by both TLC and ^1H NMR spectral analyses of the crude reaction mixture showed the

Additional Reductants of Diazocine 10 Causing Rearrangement to Isoindole 13

The direct conversion of **10** into **13** by treatment of Na or Li in THF can be counted as the first authentic and serendipitous[12] example of this reductive rearrangement (Scheme 4). The conversion of **10** into **13** with *o*-diaminobenzene and catalysis by **16** at 200 °C was carried out by us *after* the method shown in Scheme 4 and thus is a second but purposive method for achieving this novel conversion.

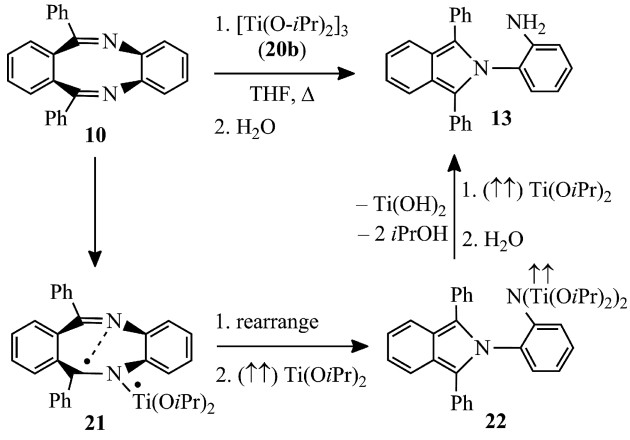
In order to gain further mechanistic insight into the pathway leading from diazocine **10** in its unusual rearrangement to the 2-(2-aminophenyl)isoindole (**13**), we searched for other reductants that would induce the same reductive rearrangement. The third reductant employed were titanium(II) salts, such as oligomers of $TiCl_2$ (**20a**) and $Ti(O\text{-}iPr)_2$ (**20b**) units, readily prepared at 25 °C in THF by the alkylative reduction of the corresponding TiE_4 salts (E = Cl or O-*i*Pr) with *n*-butyllithium.[13–18] Although the

degree of association of TiE_2 units could not be measured directly by their colligative properties, ESR measurements of Ti(O-*i*Pr)$_2$ in THF showed that **20b** is paramagnetic and exhibits a triplet signal indicative of two unpaired electrons. The magnitude of the coupling constants of the electrons was in best accord with titanium centers located 1,3 to each other in an open chain[18] (**20b**, Scheme 8).



Scheme 8.

Since in parallel ESR studies, $TiCl_2$ in THF proved to be diamagnetic,[18] we have made the likely assumption that $TiCl_2$ is also a trimer but having a cyclic structure (**20a**). In reaction with unsaturated substrates like carbonyl or imino derivatives, **20a** and **20b** act as if they deliver carbenoid-like TiE_2 units to the organic substrate in a singlet or triplet form. In fact, the reaction of three equivalents of **10** with two equivalents of trimeric **20b** in refluxing THF leads upon hydrolysis to a quantitative yield of **13** (Scheme 9). A reasonable proposed pathway would be the addition of the Ti(O-*i*Pr)$_2$ biradical to **10** to yield **21** followed by its subsequent rearrangement to **22**. The superiority of **20b** to provide the triplet monomer, Ti(O-*i*Pr)$_2$ (↑ ↑), to generate key intermediate **21** is clearly evident by employing the diamagnetic reductant **20a** in its place. At 25 °C for 48 h a 3:2 ratio of **10** and **20a** in THF gave after hydrolysis 62% of **13**. A similar mixture held at reflux for 48 h before hydrolysis yielded only 6% of **13**. This indicates that the corresponding $TiCl_2$ adduct **21** is thermally unstable and tends to dissociate to **10**.[17]



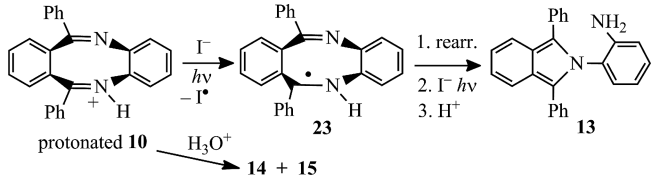
Scheme 9.

A fourth alternative reductant system capable of converting **10** to **13** proved to be aqueous hydriodic acid. Thus trial reactions of a standard sample of **10** dissolved in 55% aqueous HI at various selected temperatures under laboratory fluorescent light led to the following yields of **13** (Table 1, Scheme 10).

Table 1. Reactions of diazocine 10 to isoindole 13 in 55% aqueous HI in Lab Light.[a]

Products[b] (percentages)	Run 1 60 °C (light)	Run 2 60 °C (dark)	Run 3 25 °C	Run 4 0 °C
Diazocine **10**	15	38	17	88
Isoindole **13**	59	43	70	12
o-Dibenzoylbenzene **14**	26	18	13	–

[a] See the Experimental Section for the details of standard run size, hydrolytic workup, discharge of the I_2 generated and the ^{1}H NMR analysis for the proportion of components **10**, **13** and **14**. [b] The duration of reaction runs 1 and 2 was 2 h; that of reaction runs 3 and 4, 6 h.



Scheme 10.

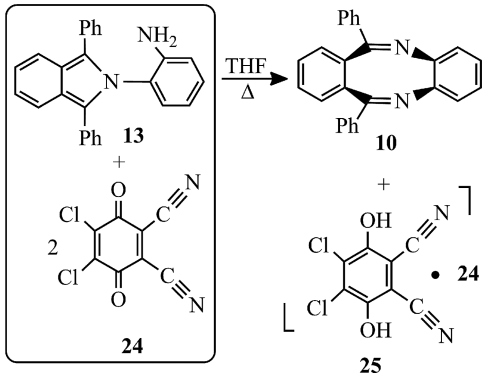
It is seen that the acidic hydrolysis of **10** into **14** is in more serious competition with the redox reaction at 60 °C than at 25 °C and that the redox reaction is photo-promoted. The redox reaction can be readily ascribed to the SET reaction of the iodide with protonated **10** to form radical **23**, similar to **21** in Scheme 9, which can isomerize to **13** (Scheme 10). As is evident, by lowering the reaction temperature the SET reaction can be fostered over hydrolysis and could be used as a preparative method for **13** if a chromatographic separation of the products is performed.[19]

Accidental Discovery of the Oxidative Rearrangement of Isoindole 13 to Diazocine 10

An equally impressive oxidative rearrangement is the reverse reaction of **13** into **10**, occurring spontaneously and completely at 25 °C in the presence of atmospheric oxygen and visible light. This serendipitous reaction was revealed by allowing a pure sample of **13**, dissolved in $CDCl_3$ in a loosely stoppered NMR tube to stand in the lab for about a week after recording its ^{1}H NMR spectrum. Upon recording the ^{1}H NMR spectrum again after such storage, the solution, now darker yellow, exhibited the proton spectrum of essentially pure **10**.

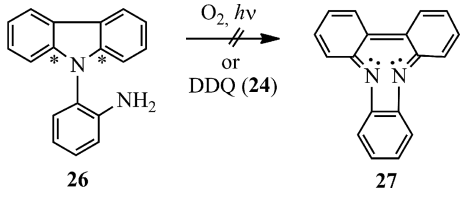
A similar outcome was obtained with larger samples of **13** heated in $CHCl_3$ under reflux in a silica gel suspension and with exposure to lab light. The recovered solid from this reaction consisted of 96% of **10** and 4% of **13**.

Encouraged by this accidental finding, we then undertook the purposive experiment of achieving such an oxidative rearrangement of **13** to **10** by DDQ (**24**). Heating 1.0 molar equivalent of **13** with 2.2 molar equivalent of DDQ at reflux in THF, followed by usual workup and column chromatography led to 83% of pure **10** (Scheme 11). The quinhydrone complex (**25**) of DDQ with its hydroquinone was the principal by-product of this reaction.



Scheme 11.

Finally in an attempt to apply this unusual reaction to the synthesis of unknown diazocine derivative **27**, the known carbazole **26** was treated, first with O_2 in lab light and then with DDQ without success (Scheme 12). The possible structural reasons for the failure of **26** to undergo oxidative rearrangement to **27** will be considered in the next section.

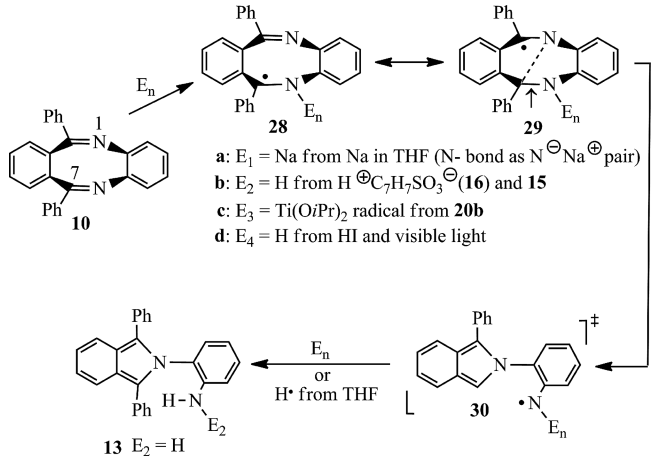


Scheme 12.

Discussion

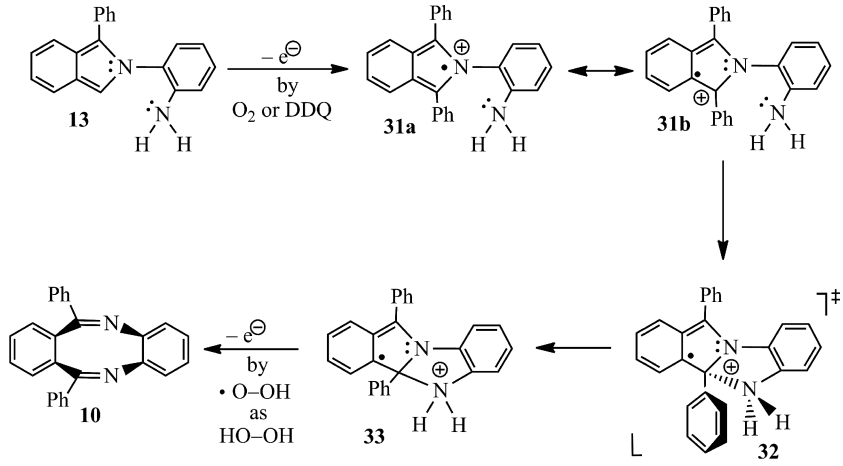
Our failed attempt to convert diazocine **10** has led to the serendipitous discovery of the first authentic synthesis of **13** from **10**.[10] This achievement then motivated our search for and discovery of other reductants causing this transformation: *o*-DAB; TiE_2; and HI. Thus the primary goal of this report has been the preparation of **13** from **10** efficiently.

That four such chemically diverse reductants can accomplish this conversion with facility raises the possibility of similar crucial intermediates in each reduction. Although the kinetic equation for the rate of reductive rearrangement varies greatly for each reagent (E_n in Scheme 13), it appears reasonable to propose that such intermediates would resemble **28**, where E_1 is respectively Na, E_2 = H, E_3 = Ti(O*i*Pr)$_2$ and E_4 = H, with a free electron on C[7]. Since the *trans*-situated imino (C=N) groups in **10** are proximate to each other, the free-radical C˙ in **28** could be delocalized transannularly, as shown in resonance structure **29**. Fragmentation of radical **28** at the C–N bond (at arrow) is fostered in the transition state by the generation of the aromatic delocalization of the incipient isoindolic system **30**. In the final step intermediate **30** could acquire another E_n radical {Na, H˙ or [↑ ↑ Ti(O*i*Pr)$_2$]} to form **13** or its *N*,*N*-dimetallic derivative [Na_2 or Ti(O*i*Pr)$_2$]. We offer such an intermediate **28** as a working hypothesis for future mechanistic studies aimed at the experimentally supported pathway followed by each reductant.[20]



Scheme 13.

The aforementioned Scheme 13 for reductive rearrangement of **10** to **13** can be simply modified to account for the general oxidative rearrangement of **13** to **10** by O_2 or DDQ, as is shown in Scheme 14.[21] Scheme 14 combines two or more steps involved in forming crucial intermediates in the rearrangement. Formation of the intermediate **31a** or **31b**, resonance representations of this cationic radical, is proposed to result from the stepwise removal of two electrons from **13** by the O_2 biradicals with an intervening cyclization of **31** to **33**. Alternative pathways for this outcome could also be involved. The conformation of resonance structure **32** having the phenyl group *alpha* to the indolic N rotated out of the plane is thought to be necessary for the close approach of the C-centered and the N-centered groups leading to transition state **32**. The necessity for close approach of these reactive centers is deduced from our failure to cyclize the corresponding indole derivative **26** to the expected cyclic dianil **27** (Scheme 12). The unrotatable benzo groups fused *alpha*, *beta* to the carbazolic nitrogen poses a great steric barrier to the approach of the *ortho* amino group to either *alpha* cation derived from **26** (* asterisks).[22]



Scheme 14.

Conclusions

(1) The attempt to generate the potential, planar Hückel ten π-electron 6,11-diphenyldibenzo[*b*,*f*]-5,12-dihydro[1,4]-diazocine (**11**) by the addition of two equiv. of Na or Li metal in THF to 6,11-diphenyldibenzo[*b*,*f*][1,4]diazocine (**10**), followed by hydrolysis, proved to be unsuccessful. Instead, this procedure led quantitatively to the first direct conversion of **10** into 2-(2-aminopheny)-1,3-diphenylisoindole (**13**).

(2) This novel conversion of **10** into **13** by such reductive rearrangement has then been found to occur with three additional reductants: a) heating **10** and excess *o*-diaminobenezene (**15**) at 200 °C in the presence of *p*-toluenesulfonic acid (**16**) as catalyst; b) heating **10** with two equiv. of titanium(II) isopropoxide in THF; and c) stirring **10** in a solution of 55% aqueous hydriodic acid.

(3) All four reduction procedures convert **10** into **13** in yields ranging from 70 to 100%. However, pure **13** can be more readily isolated from the first and third procedures using Na or Li metal or titanium(II) isopropoxide, respectively.

(4) The oxidative rearrangement of **13** to **10** was another accidental discovery made in the course of this study. When $CDCl_3$ was allowed to stand in laboratory light in a loosely capped NMR tube, it reverted to **10**. Such adventitious air oxidation of **13** could be purposively achieved by heating **13** with two equiv. of DDQ.

(5) Careful comparison of the reaction conditions prevailing for the facile reductive rearrangement of **10** into **13** and the equally smooth oxidative rearrangement **13** into **10** has led us to propose a similar crucial intermediate **28** and chains of SET processes between the two redox products, whose actual individual steps remain to be corroborated by future kinetic and physiochemical studies.

Experimental Section

General Reaction and Hydrolytic Workup Procedures: All reactions were carried out under a positive pressure of anhydrous, oxygen-free argon. All solvents employed with organometallic compounds were dried and distilled from a sodium metal/benzophenone ketyl mixture prior to use.[23]

Routinely, the organometallic reaction mixtures were hydrolyzed with deoxygenated water. Ether was added to the hydrolysate, the organic layer was separated and the organic layer then dried with anhydrous Na_2SO_4. The volatile solvent was removed and ^1H and ^{13}C NMR spectra and TLC were recorded on the crude organic products. Where preparative yields were to be corroborated, column chromatographic separation of products on silica gel with a hexane/ethyl acetate eluent was carried out.

Analytical Methods: The IR spectra were recorded with a Perkin–Elmer instrument, model 457, and samples were measured either as mineral oil mulls or as KBr films. The NMR spectra (^1H and ^{13}C) were recorded with a Bruker spectrometer, model Avance III 600, and tetramethylsilane Me_4Si was used as the internal standard. The chemical shifts reported are expressed on the scale in parts per million (ppm) from the Me_4Si reference signal. Melting points were determined on a Thomas–Hoover Unimelt capillary melting point apparatus and are uncorrected.

Authentic ^1H and ^{13}C NMR spectra for comparison with those of all known compounds listed in Supplemental Information are accessible from AIST: Integrated Spectral Database System of Organic Compounds.[24]

Preparation of Starting Materials and Products

6,12-Diphenyldibenzo[*b*,f][1,4]-diazocine (10): The requisite *o*-dibenzoylbenzene (**14**) was prepared in strict adherence to a published procedure[25] from phthaloyl chloride and phenylmagnesium bromide in ethyl ether, in 27% yield and recrystallized from 95% ethanol, m.p. 146–147 °C.

The procedure for preparing **10** has been modified from that employed by Olliéro and Solladié,[7] namely by condensing **14** and *o*-diaminobenzene (**15**) in a 1:3 molar ratio in benzene and heating at reflux for 10 days with *p*-toluenesulfonic acid monohydrate (**16**) in a ratio of **14**:**16** = 1:0.25. Instead, we have conducted the reaction in refluxing toluene with the condenser attached to a Dean–Stark trap. With this procedure the expected amount of water was collected after 12 h. The resulting solution was subjected to rotary evaporation. The dark residue was purified by column chromatography on silica gel employing a 3:1 by volume hexane/ethyl acetate eluent. From 5.73 g of **14** and 6.50 g of **15**, 6.32 g of **10** (100%) was

obtained, yellow crystals, m.p. 197–198 °C (ref.[7] 184–189 °C). ^{1}H NMR ($CDCl_3$): δ = 7.82 (d, 4 H), 7.43 (t, 2 H), 7.40 (q, 2 H), 7.37 (t, 4 H), 7.16 (q, 2 H), 7.00 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 169.73, 141.91, 137.8, 136.43, 130.99, 128.97, 128.74, 128.25, 127.11, 124.05, 121.18 ppm.

2-(2-Aminophenyl)-1,3-diphenylisoindole (13): According to a published procedure,[7] an intimate mixture of 5.73 g (20 mmol) of **14**, 2.16 g (20 mmol) of **15** and 1.0 g (5.3 mmol) of *p*-toluenesulfonic acid monohydrate (**16**) was heated in an oil bath at 200 °C ± 5 °C for 2 h, whereupon it became a viscous melt. Although the authors claim they obtained a quantitative yield, the operative steps and criteria are not given. In our procedure the reaction mixture was stirred with a water/ethyl ether slurry and the organic layer was separated and dried with anhydrous Na_2SO_4. Filtration of the dried solution and evaporation of the solvent left a dark residue of crude **13** and other amino components. Column chromatography on silica gel with a 3:1 v/v hexane/ethyl acetate eluent yielded 4.18 g (85%) of **13**, 10% of phenazine (**17**) (by ^{1}H NMR and TLC) and ca. 5% of other amines: **13** from 95% ethanol, yellow crystals, m.p. 212–213 °C (ref.[7] 201–202 °C). ^{1}H NMR ($CDCl_3$): δ = 773 (q, 2 H), 7.30 (d, 3 H), 7.25 (m, 4 H), 7.17 (t, 2 H), 7.08 (t, 1 H), 7.04 (m, 2 H), 6.96 (d, 1 H), 6.62 (t, 1 H), 6.58 (d, 1 H), 3.47 (b, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 143.17, 131.78, 130.16, 129.59, 129.54, 128.13, 126.45, 124.47, 124.41, 123.12, 122.5, 119.88, 118.29, 115.97 ppm.

Preparation of 2(9*H*-Carbazo-yl)aniline (27): This known compound **27** was prepared in two steps from carbazole in two straightforward procedures.

9-(2-Nitrophenyl)-9*H*-carbazole (28): 9*H*-Carbazole (0.24 g, 1.44 mmol), 2-fluoronitrobenzene (0.21 g, 1.51 mmol) and cesium carbonate (0.13 g, 2.14 mmol) were heated to reflux in 5 mL of DMSO for 4 h. Then the reaction mixture was poured into ice water to give a yellow precipitate. After workup 9-(2-nitrophenyl)-9*H*-carbazole (0.32 g, 86% yield) was obtained by recrystallization from an ethyl acetate/hexane mixture as beige needles, m.p. 171–172 °C (ref.[26] 156 °C). ^{1}H NMR ($CDCl_3$): δ = 8.18 (m, 3 H), 7.83 (m, 1 H), 7.68 (m, 2 H), 7.42 (t, 2 H), 7.33 (t, 2 H), 7.14 (d, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 147.39, 140.78, 134.22, 131.39, 131.25, 129.13, 126.31, 125.92, 123.84, 120.66, 120.56, 109.06 ppm.

2-(9*H*-Carbazol-9-yl)aniline (27): The 9-(2-nitrophenyl)-9*H*-carbazole (0.65 g, 2.25 mmol) and stannous chloride (1.61 g, 7.13 mmol) were mixed in 15 mL absolute ethanol and the mixture heated at reflux for 8 h. Then 15 mL aqueous 1 N sodium hydroxide was added and the suspension was stirred at room temperature for 1 h. The suspension was filtered and after workup 2-(9*H*-carbazol-9-yl)aniline (**27**) was obtained by recrystallization from absolute ethanol (0.44 g, 75% yield) as colorless crystals, m.p. 124–125 °C (ref.[26] 119–121 °C). ^{1}H NMR ($CDCl_3$): δ = 8.16 (d, 2 H), 7.41 (t, 2 H), 7.29 (m, 4 H), 7.18 (d, 2 H), 6.96 (d, 1 H), 6.92 (t, 2 H), 3.55 (b, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 143.86, 140.64, 129.63, 129.60, 126.01, 123.35, 122.40, 120.31, 119.87, 118.98, 116.63, 110.13 ppm.

Reactions Effecting the Reduction of 6,11-diphenyldibenzo-[*b*,*f*][1,4]-diazocine (**10**) to 2-(2-aminophenyl)-1,3-diphenylisoindole (**13**).

First Method: Treatment of 10 in THF with Sodium or Lithium Metal and Subsequent Hydrolysis: See Scheme 4. A solution of 540 mg of **10** in 15 mL of THF under argon was treated with either 400 mg (17 mmol) of sodium metal pieces (2–3 mm in size) at 25–30 °C with stirring for 10 h. Quenching with water (some as $H_2\uparrow$) and usual workup gave a quantitative yield of **13**, yellow crystals (^{1}H NMR and TLC identical with those of authentic **13**), m.p. 212–213 °C.

When a reaction of the same scale was conducted with lithium metal at 25 °C but for 24 h, again a quantitative yield was isolated.

Second Method: Heating a 1:3 Molar Mixture of 10 with o-Diaminobenzene (15) with Catalytic p-Toluenesulfonic Acid (16): See Scheme 6, **10**→**13**. Heating of an intimate mixture of 500 mg (1.4 mmol) of 10, 500 mg (4.6 mmol) of 15 and 50 mg of 16 in an oil bath at 200 °C ± 5 °C for 60 min. gave a viscous melt. After cooling the reaction mixture with a water/ethyl ether slurry and the ether lay was worked up and underwent column chromatography, as in the preparation of authentic 13 (Cf. *supra*). The yield of pure 13 was 75% and 10% of phenazine was isolated (^{1}H NMR and TLC). About 15% of unidentified amines were recovered.

Third Method: Heating 10 in THF with Titanium dichloride (20a) or with Titanium Diisopropoxide (20b): See Scheme 9. The titanium(II) reagents, **20a** or **20b**, can be readily prepared, just before use for reduction of **10**, by suspending 1.00 mmol of $TiCl_4$ or Ti(O-*i*Pr)$_4$ in 10 mL of THF under argon at –75 °C with stirring. Then 2.2 molar equivalents of *n*-butyllithium in hexane of known molarity was transferred to the brown suspension of the respective TiE_4. As the reaction mixture was allowed to come to 25 °C over 90 min, the reaction suspension turned pitch black, signaling the respective formation of $TiCl_2$ or Ti(O-*i*Pr)$_2$.[11,12,14]

Reaction of 10 with Titanium(II) Dichloride (20a): When **10** (180 mg, 0.5 mmol) in 10 mL of THF was mixed at 25 °C with the foregoing batch of 1.0 mmol of **20a** in 15 mmol of THF and stirred for 48 h, the usual hydrolytic workup yielded 62% of **13**.

Moreover, when a 2:1 mixture of **20a** and **10** in THF was allowed to reflux for 24 h, only 6% of **13** was obtained upon workup. This result indicates that titanium dichloride adduct of **10**, formed to the extent of 62% at 25 °C, to dissociate largely at 70 °C in boiling THF.

Reaction of 10 with Titanium Diisopropoxide (20b): When **10** (180 mg, 0.5 mmol) in 10 mL of THF was mixed at 25 °C with the foregoing batch of 1.0 mmol of **20b** in 15 mL of THF and stirred for 48 h, the usual hydrolytic workup yielded **13** quantitatively. When a 1:1 molar equivalent reaction was carried out at 25 °C, the usual workup yielded 41% of **13** with 59% of **10** being recovered.

Fourth Method: Reaction of 10 with 55% Aqueous Hydriodic Acid: With reference to the data in Table 1 and the reactions depicted in Scheme 10, the sample composition in each of the four test tubes was 150 mg (0.420 mm) of **10** admixed with 1.24 mL (10 molar equiv.) of 55% aqueous hydriodic acid (containing no stabilizer, from Sigma–Aldrich). All Pyrex tubes were equipped with glass stoppers and the tube for Run 2 only was completely enveloped in aluminum foil, so as to exclude all lab (fluorescent) light. The samples were placed in water baths set at 60 ± 2 °C, 25 ± 2 °C and 0 °C, respectively. After reaction each sample was quenched with 10% aqueous sodium bisulfite to remove the I_2 and HI. The organic products were extracted into ethyl ether and the ether extract dried with anhydrous Na_2SO_4. After solvent removal the product mixture was analyzed by TLC and quantitative ^{1}H NMR spectroscopy.

Oxidation of 2-(2-Aminiophenyl)-1,3-diphenylisoindole (13) to 6,11-Diphenyldibenzo[*b*,*f*][1,4]diazocine (10)

Serendipitous Route: Isoindole **13** (100 mg) was mixed with silica gel (SiliaFlash®, P60 40–63 μm, pH = 7.2, Silicycle) (5.0 g) and chloroform (15 mL) (containing 0.75% ethanol as stabilizer, Fisher) and then magnetically stirred in the open air at room temperature for 48 h. After workup [1,4]diazocine **10** was obtained in

94% yield. When the reaction was carried out under the same conditions but at reflux for 8 h, then a 96% yield of [1,4]diazocine **10** was formed.

Purposive Route: 2-(2-Aminophenyl)-1,3-diphenylisoindole (**13**) (360 mg, 1 mmol) was heated at reflux for 10 h in 15 mL of THF with DDQ (**24**) (0.50 g, 2.2 mmol). After workup 6,11-diphenyldibenzo[*b*,*f*][1,4]diazocine (**10**) was separated by column chromatography (eluent: hexanes/ethyl acetate, 10:1) in 83% yield, along with other unidentified products. The melting point and NMR criteria for the separated product were used to confirm that **10** was indeed generated.

Attempted Oxidations of 2-(9*H*-Carbazo-9-yl)aniline (26): See Scheme 12. 2-(9*H*-Carbazol-9-yl)aniline (**26**) (100 mg, 0.39 mmol) was mixed with silica gel (5.0 g) and 15 mL of chloroform and then heated at reflux in the open air for 7 h. After workup only the starting material was detected.

Compound **26** (100 mg, 0.39 mmol) and DDQ (**24**) (0.27 g, 1 mmol) were heated at reflux in 15 mL of THF for 10 h. After workup the starting compound **26** was recovered unchanged.

CCDC-956942 (for **10**) and -956941 (for **13**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): Copies of the ^{1}H NMR and ^{13}C NMR and fully displayed DEPT and IR spectra.

Acknowledgments

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Finally, we, his co-authors, mourn the loss of Dr. Wei Liu, a promising young scientist in lithium battery research, who in February 2014 was appointed Research Manager for Novel Organic Battery Electrolyte Development at the Shandong Hairong Power Supply Materials Co., Ltd., Shandong Province, China. This article is largely based upon his doctoral dissertation, *Novel Aspects of Epimetalation in Organic Synthesis*, completed in October 2013, and supervised by Professor John Eisch at Binghamton University, Binghamton, New York, USA. Dr. Wei Liu collaborated extensively in the composition of this article by E-mail exchange after his return to China.

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[3] The melting point given for the *E* isomer of *N*-(2-amino-1,2-diphenylethenyl)carbazole on page 4061, column A, paragraph 2, line 14 in ref.[2] as **5b**, is incorrect; the correct m.p. is 124–125 °C.
[4] a) The necessary planarity of **1** required for Hückel aromaticity involves two energy barriers. First, previous research on the barrier to inversion of the optical active derivative of **1** bearing carboxyl groups at the 3- and 10-positions has estimated the minimum repulsion energy of such *ortho* H groups in a transition of **1** to planar **3** at 20 kcal/mol (N. L. Allinger, W. Szkrybalo, M. A. DaRooge, *J. Org. Chem.* **1963**, *28*, 3007–3009). In addition, the ring strain energy of producing an all-planar eight-membered ring is assessed at about 23 kcal/mol more (A. Streitweiser Jr., *Molecular Orbital Theory for Organic Chemists*, Wiley, New York, **1962**, p. 283). b) Up to 81 kcal/mol, the mean bond stabilization energy for the fully formed $C_{sp}{}^3$–$C_{sp}{}^3$ σ-bond between C6 and C12, in: resonance structures **6**→**7** in Scheme 2, see: J. Waser, K. N. Trueblood, C. M. Knobler, *Chem. One*, McGraw-Hill, New York, **1976**.
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[7] D. Olliéro, G. Solladié, *Synthesis* **1975**, 246–247.
[8] The original method of ref.[7] employed refluxing benzene as the reaction medium and required 10 days, whereas our use of toluene required less than half a day. Their workup utilized column chromatography and gave a yield of 72% of **13**. Our workup gave almost 100% of **13** and 10% of **17**. The detection of **17** is first evidence that **15** did function as a reductant (see Scheme 7).
[9] The structural akin phenanthridines, phenanthridine itself, 6-*p*-phenylphenanthridine and 6-*p*-biphenylylphenanthridine, have been shown by alkali-metal reduction in THF and ESR spectroscopy to produce monomeric radical-anions and dianions, similar to **10a** and **10b**; see: J. J. Eisch, R. M. Thompson, *J. Org. Chem.* **1962**, *27*, 4171–4179.
[10] In ref.[7] the authors conclude their brief discussion with the statement: "The mechanism of the formation of **4** [i.e., 2-(2-aminophenyl)-1,3-diphenylisoindole] is presently under investigation." A subsequent search of the authors' publications since 1975 reveals no further information on such promised research. Further, it is remarkable that these authors have not ever reported any attempt to interconvert **10** and **13**.
[11] The detection of phenazine in our work (Scheme 7) is the first actual evidence that **15** functions as a reductant in these reactions. In Scheme 7 a possible pathway, out of several, for the formation of **17** is offered. A comprehensive summary of such phenazine syntheses is given in: A. Albert, *Heterocyclic Chemistry*, 2nd edition, Oxford University Press, New York, **1968**, p. 180–182.
[12] The term "serendipitous" is used throughout this report in its primary meaning of the finding of valuable things not sought for. By contrast, we also employ the expressions, purposive reductive rearrangement of **10** to **13** or purposive oxidative rearrangement **13** to **10** to denote the *intentional* promotion of these transformations.
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[19] Such a column chromatography separation has been found to be straightforward. Further modifications of this procedure would be to study the use of solutions of anhydrous HI gas in CH_2Cl_2, as the reagent for converting **10** into **13**.
[20] That such a general intermediate **28** plays a pervasive role in alkali metal and carbanion reductions has been recently reviewed: J. J. Eisch, *Res. Chem. Intermed.* **1996**, *22*, 145–187.
[21] The likely electronic steps involved in Scheme 14, electron loss (**13**→**31**), cyclization (**31**→**32**→**33**) and electron loss (**33**→**10**) were suggested by an anonymous reviewer, as well as

by our reading of research articles on aminium cation radicals (see J. H. Horner, F. N. Martinez, O. M. Musa, M. Newcomb, H. E. Sheridan, *J. Am. Chem. Soc.* **1995**, *117*, 11124–11133). We are grateful for the reviewer's recommendations in formulating the SET pathways given in Scheme 14.

[22] The foregoing steric repulsion argument for the failure of ring closure of biradical **33** to form **27** is based upon kinetic control. Examinations of the structure of product **27** reveals aspects of thermodynamic control hindering its formation, such as an anti-Hückel 16-π-electron ring, two nonbenzenoid rings and two repelling unshared electron pairs on the N-centers.

[23] General detailed procedures for purification of solvents and conducting organometallic reactions under an inert atmosphere are also available: J. J. Eisch, *Organomet. Synth.* **1981**, *2*, 7–25; J. J. Eisch, *Organomet. Synth.* **1981**, *2*, 94–96.

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