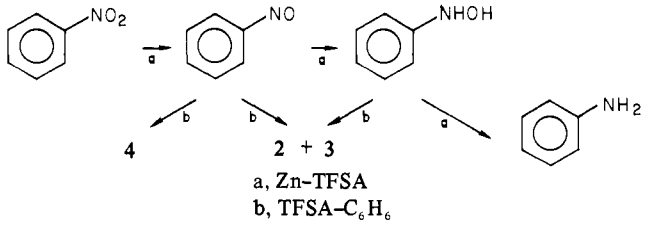
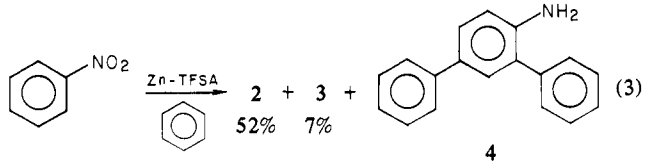
Scheme I



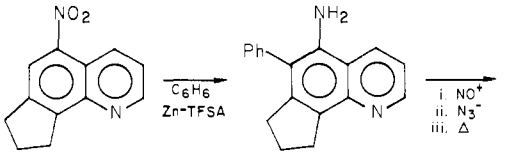
as general methods for synthesizing diphenylamine and aminobiphenyl. However, the availability of *N*-arylhydroxylamine is limited. In this work, we extended the phenylation reactions to the reductive phenylation of nitroarenes, which are far better synthetic precursors than *N*-arylhydroxylamines. Metal-acid reduction of a nitroarene to an amine is known to involve nitroso and hydroxylamine intermediates. Therefore, we expected that phenylation of nitroarenes would occur when they are reduced with metal-TFA or metal-TFSA in benzene. Since this was proved to be so, we were able to develop a practical method for the synthesis of diphenylamines and aminobiphenyls.

Zinc dust (30 mmol) was added with stirring in three portions over a period of 3 h to an ice-cold mixture of nitrobenzene (5 mmol) in benzene (150 mmol) and TFSA (75 mmol) (eq 3). The



products isolated were 4-aminobiphenyl (**2**, 52%), 2-aminobiphenyl (**3**, 7%), 4′-amino-*m*-terphenyl (**4**, 2%), and aniline (30%). A possible phenylation process is shown in Scheme I. Nitrobenzene is reduced to nitrosobenzene and *N*-phenylhydroxylamine. Then, consecutively, nitrosobenzene reacts with benzene in the presence of TFSA, giving **2**, **3**, and **4**,[5] and *N*-phenylhydroxylamine reacts with benzene, giving **2** and **3**.[2]

Nitrobiphenyls and nitronaphthalenes were similarly phenylated with benzene. For example, 2-nitronaphthalene was reductively phenylated by benzene-Zn-TFSA to yield 1-phenyl-2-aminonaphthalene in 51% yield. The intermolecular reductive phenylation has been successfully applied to the synthesis of 5-amino-6-phenylquinoline (**6**) from 5-nitro-7,8-cyclopentenoquinoline (**5**)



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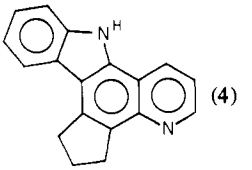
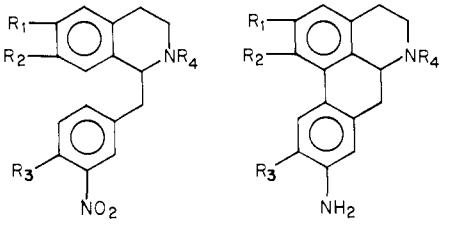


7

at the key step in the synthesis of a potent mutagen, 3,4-cyclopentenopyrido[3,2-*a*]carbazole (**7**), isolated from L-lysine pyrolysate (eq 4).[6]

This process was very effective in intramolecular phenyl-phenyl bond formation. We applied this method to the synthesis of aminoaporphines. Zinc dust (10 mmol) was added to a solution of 1-(3′-nitro-4′-methoxybenzyl)tetrahydroisoquinoline (**8a**, 2 mmol) in TFA (60 mmol) and TFSA (60 mmol) with stirring at 0 °C in three portions over a period of 3 h. After a simple workup, 9-amino-1,2,10-trimethoxy-6-methylaporphine (**9a**) was isolated in 68% yield. The structure of **9a** was confirmed by its

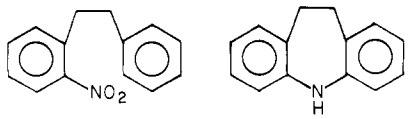


8 9

a, $R_1 = OCH_3$, $R_2 = OCH_3$, $R_3 = OCH_3$, $R_4 = CH_3$ (yield 68%)
b, $R_1 = OCH_3$, $R_2 = OCH_3$, $R_3 = OCH_3$, $R_4 = H$ (yield 61%)
c, $R_1 = OCH_3$, $R_2 = OCH_3$, $R_3 = OCH_3$, $R_4 = COCH_3$ (yield 82%)
d, $R_1 = OCH_3$, $R_2 = OCH_3$, $R_3 = H$, $R_4 = CH_3$ (yield 52%)

conversion to (±)-*N*-methyllaurotetanine[7] by hydroxydediazotization. As a reducing agent, catalytic hydrogenation over Pd-C also worked well. Several aporphines (**9b-d**) were prepared.

The TFA-catalyzed reductive phenylation should give a diphenylamine. Zinc dust (60 mmol) was added to an ice-cold mixture of nitrobenzene (10 mmol) in benzene (100 mmol) and TFA (100 mmol) with stirring for 2 h, and diphenylamine was isolated in 31% yield. This process was applied to an intramolecular cyclization. Thus, 2-nitrodibenzyl (**10**), on the reductive *N*-phenylation in TFA, gave dihydrodibenz[*b*,*f*]azepine (**11**) in 38-45% yield.



10 11

The new method presented here has several merits: The starting nitro compound is readily prepared; the reaction conditions are mild enough to keep a functional group such as amine, phenol, amide, ether, and methylenedioxy groups intact; activation of a benzene ring or the presence of a special group except a nitro group is not required; intramolecular as well as intermolecular reactions work well; workup procedure is simple. The limitations are the following: The acid-sensitive group must be masked; phenylation at the meta position to the amino group is impossible. Although we only examined a few syntheses of biphenyl derivatives, we believe this is a useful general method for the synthesis of biaryl derivatives.

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Intramolecular [2 + 2] Cycloaddition Reactions of Indene Derivatives as a Route to Polycyclic Strained Ring Systems[1]

Sir:

Strained bicyclic and polycyclic compounds continue to play an important role in the understanding of many aspects of organic chemistry.[2-6] For this reason, synthetic efforts in this area have

(1) Photochemical Transformations of Small Ring Coupounds. 115. For part 114, see A. Padwa, T. J. Blacklock, D. M. Cordova, and R. Loza, *J. Am. Chem. Soc.*, **102**, 5648 (1980).

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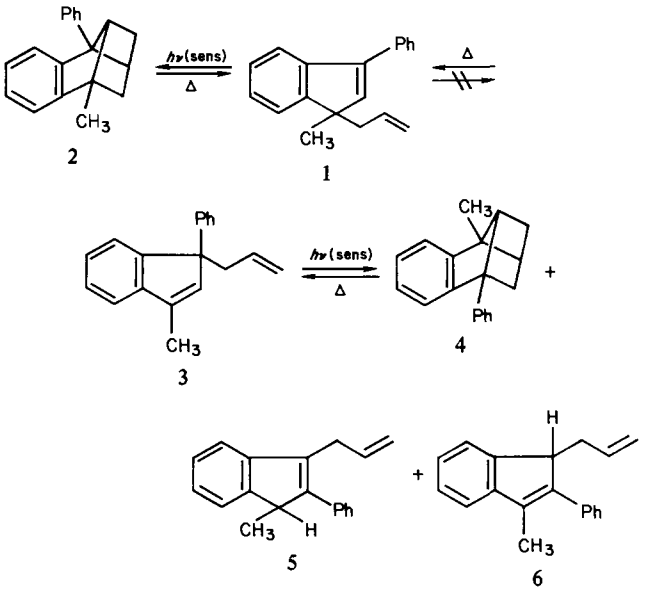
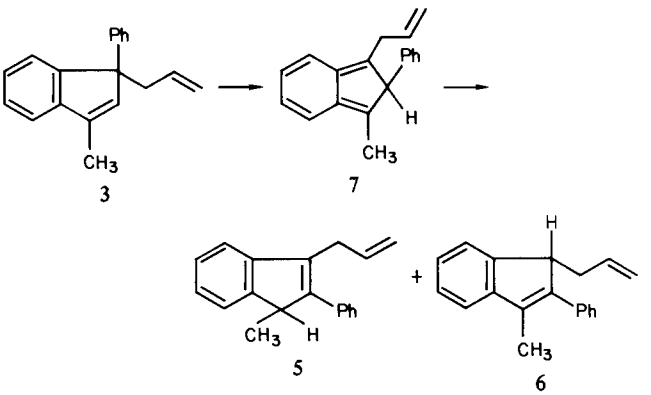
been extensive. One of the more common methods used to prepare such systems involves a photochemical [2 + 2] cycloaddition.[7,8] Recently, we have described an approach to a number of tricyclic ring systems based on an intramolecular variant of this reaction.[9,10] In continuation of our research on the potential of intramolecular [2 + 2] cycloadditions for the synthesis of fused carbocycles, we have explored the photochemistry of several bichromophoric systems. In this communication, we describe the photosensitized behavior of a number of allyl-substituted indenes which leads to the elaboration of the benzotricyclo[3.3.0.$0^{2,7}$]octane and benzotricyclo[3.2.1.$0^{3,8}$]octane ring systems.

While intramolecular [2 + 2] photocycloadditions of olefins to carbon–carbon double bonds are well-documented reactions[11-13] often employed in synthetic schemes,[14] similar photoreactions of indene derivatives are unknown. Previous studies of the photochemistry of indene and alkyl-substituted indenes have only dealt with the sensitized bimolecular cycloadditions of these systems.[15] We began our search for an intramolecular [2 + 2] cycloaddition by studying the photosensitized behavior of 1-allyl-1-methyl-3-phenylindene (**1**).[16] The thioxanthone-sensitized photolysis of



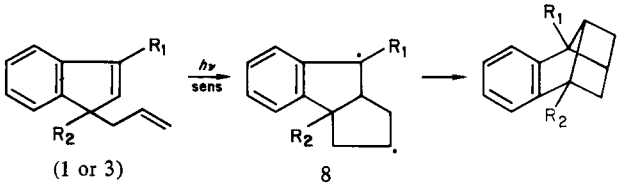
1 gave a quantitative yield of 2,2a,7,7a-tetrahydro-7-methyl-2a-phenyl-2,7-methano-1*H*-cyclobut[*a*]indene (**2**): NMR ($CDCl_3$, 270 MHz) δ 1.17 (br d, 1 H, J = 10.3 Hz), 1.24 (d, 1 H, J = 7.3 Hz), 1.60 (s, 3 H), 1.74 (d, 1 H, J = 10.3 Hz), 1.97 (dd, 1 H, J = 7.3, 2.2 Hz), 2.85–2.94 (m, 2 H), and 6.59–7.53 (m, 9 H); ^{13}C NMR ($CDCl_3$, ppm) 16.8 (q), 3.26 (t), 43.4 (d), 44.2 (t), 49.8 (s), 66.9 (d), 67.4 (s). The identity of structure **2** was based on its spectroscopic and analytical properties and was further supported by its chemical behavior. Photoproduct **2** undergoes a thermal [2 + 2] retrogression reaction to indene **1** in toluene at 130 °C with a half-life of 10 h.

The photosensitized behavior of the closely related 1-allyl-1-phenyl-3-methylindene (**3**) was also studied and was found to give rise to a mixture of three compounds. The major product formed was assigned as 2,2a,7,7a-tetrahydro-2a-methyl-7-phenyl-2,7-methano-1*H*-cyclobut[*a*]indene (**4**) (32%) on the basis of its spectral properties and thermal behavior; NMR ($CDCl_3$, 270 MHz) δ 1.19 (d, 1 H, J = 8.1 Hz), 1.40 (br d, 1 H, J = 10.3 Hz), 1.69 (s, 3 H), 2.21–2.25 (m, 2 H), 2.39–2.43 (m, 1 H), 3.02 (dd, 1 H, J = 6.6, 2.9 Hz), 6.80–7.41 (m, 9 H). Photoproduct **4** was found to thermally isomerize to indene **1** at 160 °C. Subsequent studies showed that this reaction proceeds via conversion first to indene **3** followed by a thermal Cope rearrangement to **1**. This was confirmed by carrying out the thermolysis of **4** at 150 °C for short periods of time and isolating indene **3** in quantitative yield. Heating a pure sample of **3** at 160 °C resulted in the exclusive formation of the thermodynamically more stable indene **1**. The structures of the two minor photoproducts [**5** (30%) and **6** (24%)] were assigned on the basis of their spectral properties and were further confirmed by comparison with independently synthesized samples.[17] The formation of the rearranged indenes most likely proceeds via a 1,2-phenyl shift to give isoindene **7** followed by a



1,5-sigmatropic hydrogen migration. This process is analogous to that previously described by Miller[18] and McCullough[19] for the thermolysis of 1,1-diaryl-substituted indenes. The structurally related 3-phenyl-substituted indene **1** cannot undergo this type of di-π-methane rearrangement.

Structures **2** and **4** can be considered to be intramolecular [2 + 2] cycloadducts formed on cross-cycloaddition of the double bonds present in indenes **1** and **3**. The preference for forming cross-addition products over parallel-addition products in the photocycloaddition reaction of 1,5-hexadienes is a well-known phenomenon.[20] With the above systems, the formation of the five-membered ring intermediate **8** is preferred to the other possible ring intermediate in terms of strain, entropy factors, and radical stability.



Regiospecificity in intramolecular photocycloaddition of 1,5-hexadienes to yield bicyclo[2.1.1]hexanes (and not bicyclo-

(2) J. Meinwald and Y. C. Meinwald, *Adv. Alicyclic Chem.*, **1**, 1 (1966).
(3) J. M. Lehn and G. Wipff, *Theor. Chim. Acta*, **28**, 223 (1973).
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(7) P. E. Eaton, *Acc. Chem. Res.*, **1**, 50 (1968).
(8) P. deMayo, *Acc. Chem. Res.*, **4**, 41 (1971).
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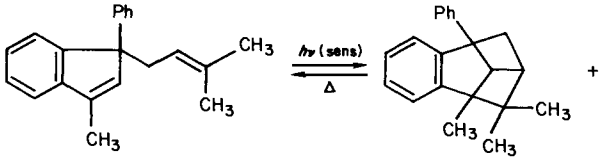
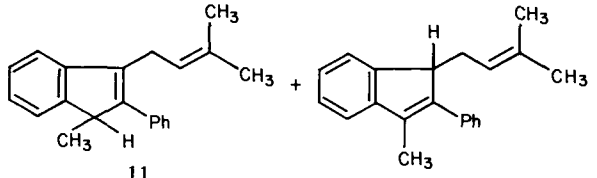
(15) McCullough and co-workers have described a few examples of the sensitized cross-addition reactions of indene with some electron-deficient olefins: J. J. McCullough and C. W. Huang, *Chem. Commun.*, 815 (1967); *Can. J. Chem.*, **47**, 757 (1969); R. M. Bowman, J. J. McCullough, and J. S. Swenton, *ibid.*, **47**, 4503 (1969).
(16) Allylindenes **1** and **3** were prepared by treating 1-phenyl-3-methylindene with *n*-butyllithium followed by quenching of the anion with allyl bromide and separating the mixture of products. Satisfactory spectral and analytical data were obtained for each new compound.
(17) Indenes **5** and **6** were prepared by treating 1-methyl-2-phenylindene with *n*-butyllithium followed by quenching with allyl bromide.
(18) L. L. Miller and R. F. Boyer, *J. Am. Chem. Soc.*, **93**, 650 (1971).
(19) J. J. McCullough and M. R. McClory, *J. Am. Chem. Soc.*, **96**, 1962 (1974).
(20) For a review and leading references, see W. L. Dilling, *Chem. Rev.*, **66**, 373 (1966).

[2.2.0]hexanes) is quite common and is generally thought to be insensitive to the nature and position of substituents on the reacting double bonds.[20] We have found, however, that the normal closure predicted[21] by the "rule of five" does not occur in the photosensitized irradiation of the corresponding phenyl system. Thus, the triplet-sensitized reaction of indene **9** gave rise to a [2 + 2]-



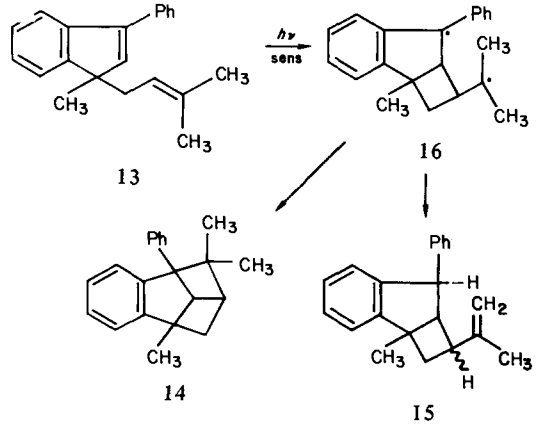
9 10



11 12

cycloadduct, **10** (13%), as well as two rearranged indenes [**11** (34%) and **12** (33%)]. The structures of the latter two compounds were established by comparison with independently synthesized samples. Careful examination of the NMR spectrum of **10** prompted us to assign it as a benzotricyclo[3.2.1.$0^{3,8}$]octane.[22] Thermolysis of cycloadduct **10** at 170 °C led to the rupture of the cyclobutane ring and regeneration of indene **9**.

Subjection of the isomeric phenyl-substituted indene **13** to similar sensitized conditions produced cycloadduct **14**[23] and a



13 16

14 15

mixture of isomeric 2,2a,7,7a-tetrahydro-1-isopropenyl-2a-methyl-7-phenyl-1*H*-cyclobut[*a*]indenes (**15**) (37%). In this case, cyclization of the triplet state of **13** proceeds to give intermediate **16**, undoubtedly a result of the added stabilization of the radical center by the two methyl groups. In simple cases, the activation energies for combination and disproportionation of radicals have been found to be equal.[24] This would explain the formation of both **14** and **15** in the above reaction. It should also be noted that the diradical (i.e., **16**) produced from the sensitized cyclization of **13** is long-lived enough to allow internal disproportionation to compete with radical coupling. This was not the case with indene **9**. The difference in behavior of the two systems parallels the well-documented increase in disproportionation to coupling ratios of free radicals as they become more stable.[24]

The facility with which the intramolecular [2 + 2] indene photocycloadditions occur makes this type of approach particularly attractive for the synthesis of some unusual polycyclic ring compounds.

Acknowledgment. We gratefully acknowledge support of this work by the National Science Foundation.

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Assignment of Proton-Decoupled Carbon-13 Spectra of Complex Molecules by Using Polarization Transfer Spectroscopy. A Superior Method to Off-Resonance Decoupling

Sir:

Off-resonance proton decoupling is one established assignment aid in ^{13}C NMR spectroscopy. It suffers from two disadvantages when used in assigning the ^{13}C spectra of a complex molecule: the resulting spectra may not be first order, and severe overlap of resonance lines may render the technique of limited value when the spectral region under investigation contains many resonance lines. We point out in this communication that pulse sequences[1] used to induce ^1H–^{13}C polarization transfer (PT) when combined with appropriate delay times (Δ) prior to data acquisition and broad-band decoupling result in (a) spectra containing only CH carbons if $\Delta = (2J)^{-1}$ ($J \equiv {}^{13}C$ and ^1H scalar coupling constant) and (b) predictable phase variations between the resonance of CH_2 carbons and those of CH and CH_3 carbons if $\Delta = 3(4J)^{-1}$. The resonances always appear as sharp singlets, resulting in dramatic time saving for acquiring useful information and enabling a one-to-one comparison to be made to the normal spectrum. We illustrate the technique by using the ^{13}C spectrum of cholesterol.

The polarization transfer pulse sequence is shown in Figure 1; τ is set equal to $(4J)^{-1}$. As pointed out by a number of workers,[1] if data acquistion commences immediately following the ^{13}C $\pi/2$ pulse, a CH resonance appears as a −1:1 doublet, CH_2 resonance as a −1:0:1 "doublet", and a CH_3 resonance as a −1:−1:1:1 quartet. Consequently, if broad-band decoupling is employed, mutual cancellations occur, and no signal is observed. We note, however, that if a delay period (Δ) is introduced, the signal components will undergo *different* intensity cycles, depending on the carbon type. Since J is approximately constant for most CH, CH_2, and CH_3 carbons (in the range 130–150 Hz), broad-band decoupling

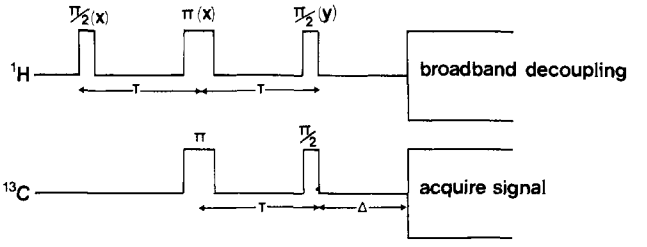

Figure 1. Polarization transfer pulse sequence, $\tau = (4J)^{-1}$. Δ is the decay before proton decoupling and data acquisition. Phase alternation of the final ^1H $\pi/2$ pulse was used.

(21) R. Srinivason and K. L. Carlough, *J. Am. Chem. Soc.*, **89**, 4932 (1967); R. S. Liu and G. S. Hammond, *ibid.*, **89**, 4936 (1967).

(22) Compound **10**: NMR ($CDCl_3$, 100 MHz) δ 0.59 (s, 3 H), 1.20 (s, 3 H), 1.42 (s, 3 H), 2.24 (ddd, 1 H, J = 9.0, 5.0, and 2.0 Hz), 2.34 (dd, 1 H, J = 12.0, 2.0 Hz), 2.98 (dd, 1 H, J = 12.0, 9.0 Hz), 3.30 (d, 1 H, J = 5.0 Hz), and 6.4–7.3 (m, 9 H). The alternative mode of photocyclization of **9** would lead to a structure having an NMR spectrum quite different from that observed. A detailed analysis of the spectral data will be provided in a later publication.

(23) Compound **14**: NMR ($CDCl_3$, 270 MHz) δ 0.84 (s, 3 H), 1.00 (s, 3 H), 1.60 (s, 3 H), 2.12 (d, 1 H, J = 11.7 Hz), 2.27 (dd, 1 H, J = 8.8, 5.1 Hz), 2.35 (dd, 1 H, J = 11.7, 8.8 Hz), 3.63 (d, 1 H, J = 5.1 Hz), and 7.03–7.36 (m, 9 H).

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