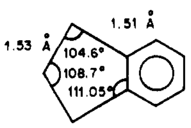
with 10% hydrochloric acid, dried (Na_2CO_3), concentrated, and distilled (Kugelrohr apparatus) to give 36 g (81%) of colorless **3b**.

4,5-Dimethoxyindan (4). 4,5-Dimethoxyindan (**4**) was prepared from 2,3-dimethoxybenzaldehyde (**5**) via the sequence in Scheme II. As shown, the condensation of 8.6 g (0.52 mol) of **5** with 69 g (0.42 mol) of malonic acid in 166 mL of refluxing pyridine containing 4% of piperidine catalyst gave 108 g (98%) of 2,3-dimethoxycinnamic acid (**6**), mp 178–180 °C (lit.[14] 179–180 °C). Acid **6** (103 g, 0.5 mol) was hydrogenated (5% Pd/C in ethyl acetate) at 40 psi and 40 °C to give 82 g (80%) of 2,3-dimethoxyhydrocinnamic acid (**7**). Recrystallization from hexane–toluene gave colorless crystals, mp 65–66 °C (lit.[14] 69–70 °C). Cyclization of 50 g of **7** in PPA[15] at 60 °C gave 29 g (60%) of 4,5-dimethoxy-1-indanone (**8**), mp 73–74 °C (lit.[15] 74–75 °C). A 13.9-g sample of ketone **8** was hydrogenolyzed in the presence of 1 g of 5% Pd/C in 75 mL of acetic acid at 55 °C and 55 psi to give 10.9 g (84%) of distilled **4**, bp 113–114 °C (3.2 mm).[7,16]

MO Calculations. MO calculations were carried out on a PRDDO program supplied by Halgren[3] using an IBM-360 computer. The convergence criteria were set at 10^{-4} root-mean-square change in the density matrix.

The calculations were carried out by using the following distances and angles; C_{ar}–C_{ar} = 1.40 Å, C_{ar}–H = 1.084 Å, C_{ali}–C_{ali} = 1.54 Å, C_{ar}–O = 1.36 Å, O–CH_3 = 1.43 Å, C_{ali}–H = 1.101 Å; sp^3 carbon angles, 109.5°; benzene ring angles, 120°; ether angles, 120°.[17] The zero values for θ and ϕ, as shown in Figure 4, for **3b** are in the plane of the aromatic ring. Rotations around the O–Ar bond are clockwise as viewed from the center of the aromatic ring. All bond rotations in this paper conform to these operations. The other dimensions used for the five-membered ring of indan were as shown.



In the case where R = C_2H_5, the methyl carbon of the alkyl group was placed in the plane of the ring away from the methoxy group. In the case where R = i-C_3H_7, the hydrogen on the branched carbon was placed in the plane of the ring toward the methoxy group so that the methyls in the alkyl group were at the maximum distance from the methoxy group. One of the methyl carbons of the t-C_4H_9 group was placed in the plane of the ring away from the methoxy group because this position proved to be of lower energy than that having the methyl carbon in the plane of the ring toward the methoxy group.

Acknowledgment. We thank Oklahoma State University (Presidential Challenge Grant) for support and the National Science Foundation for Grants GP 17641 and CHE 76-5571, which contributed to acquisition of the NMR instrumentation at Oklahoma State University. We are grateful to Mr. S. Sigle for assistance in the NMR studies.

Registry No. **1a**, 100-66-3; **1b**, 578-58-5; **1c**, 14804-32-1; **1d**, 2944-47-0; **1e**, 2944-48-1; **2a**, 1004-66-6; **2b**, 2944-51-6; **2c**, 2944-52-7; **2d**, 1516-95-6; **3b**, 4463-33-6; **3d**, 71720-27-9; **3e**, 82895-30-5; **4**, 51932-57-1.

Supplementary Material Available: Tables I–V listing PRDDO energies, atomic charges, and dipole moments for compounds **1a**, **1b**, **1c**, **1d**, **1e**, **2a**, **3b**, **3d**, **3e**, and **4** (8 pages). Ordering information is given on any current masthead page.

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[14] Perkin, W. H., Jr.; Robinson, R. *J. Chem. Soc.* **1914**, *105*, 2376.

[15] Koo, J. *J. Am. Chem. Soc.* **1953**, *75*, 1981.

[16] The ^1H and ^{13}C NMR and mass spectra of the compounds cited in this paper were consistent with the cited structures.

[17] Goodwin, T. H.; Drzybylska, M.; Robertson, J. M. *Acta Crystallogr.* **1950**, *3*, 279.

[18] Korp, J. D.; Thummel, R. P.; Bernal, I. *Tetrahedron* **1977**, *33*, 3069.

Experimental Evidence for an Electron-Transfer Mechanism in the Reaction between 2-Phenyl-3-(phenylimino)-3*H*-indole and Grignard Reagents: Application of the Marcus Theory

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2-Phenyl-3-(phenylimino)-3*H*-indole reacts with 5-hexenylmagnesium bromide to give products of 1,2- and 1,4-addition and reduction. For both addition modes, the products are mixtures of 5-hexenyl- and cyclopentylmethyl-substituted derivatives. Since the 5-hexenyl radical undergoes cyclization to the cyclopentylmethyl radical, the reaction is interpreted on the basis of an electron-transfer mechanism. This is also supported by estimates of electron-transfer rate constants according to the Marcus theory.

Previously, one of us[1] studied the reaction between 2-phenyl-3-(arylimino)-3*H*-indole and organolithium reagents. On the basis of the composition of the reaction products (of 1,2- and 1,4-addition and reduction), the reaction mechanism was suggested to involve competition between nucleophilic attack and nonbonded electron transfer (the term "nonbonded" is to be preferred over "outer-sphere" in connection with organic electron-transfer processes).[2,3] 2-Phenyl-3-(phenylimino)-3*H*-indole has now been found to react with Grignard reagents under conditions slightly different from those used for reaction with RLi,[1] which gives another possibility to probe the reaction

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[1] Berti, C.; Greci, L.; Marchetti, L. *J. Chem. Soc., Perkin Trans 2* **1977**, 1032.

[2] Littler, J. S. *Spec. Publ. Chem. Soc.* **1970**, *no. 24*, 383.

[3] Eberson, L. *Adv. Phys. Org. Chem.* **1982**, *18*, 79.

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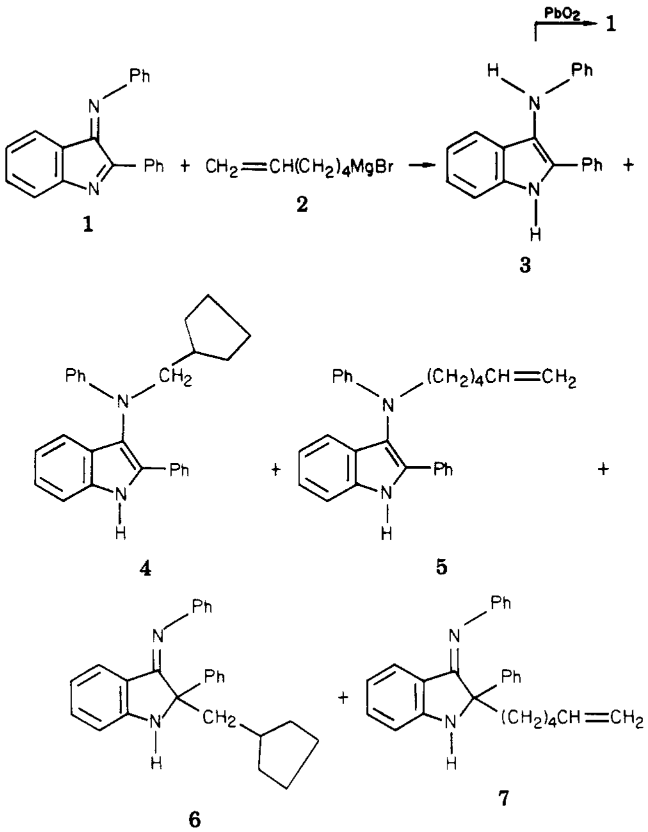
Scheme I



mechanism. The 5-hexenyl radical or derivatives thereof are known to undergo rapid cyclization ($k \approx 10^5$ s^{-1}) to the cyclopentylmethyl radical[4] and can be used as a "radical clock" to diagnose and calibrate rates of different types of radical reactions.[5] We have therefore decided to study the reaction between 2-phenyl-3-(phenylimino)-3*H*-indole and 5-hexenylmagnesium bromide in order to obtain further evidence for the postulated electron-transfer step. The results, in combination with theoretical calculations based on the Marcus theory of electron-transfer reactions,[6] give a consistent view of the mechanism as being governed by initial electron transfer between substrate and RMgX.

Results

The reaction of 2-phenyl-3-(phenylimino)-3*H*-indole (1) with 5-hexenylmagnesium bromide, carried out at room temperature under nitrogen with the reagents in a 1:2 ratio, yielded the products shown in Scheme I. Since the 3-(phenylamino)indole 3 (isolated and identified in one run by comparison with an authentic sample)[7a] undergoes autoxidation in solution on exposure to air and reverts to the starting material 1, the reaction mixture was oxidized with lead dioxide to transform 3 completely to 1. A portion of this reaction mixture was analyzed by HPLC.

Table I. Yields of Products for the Reaction of 1 with 2

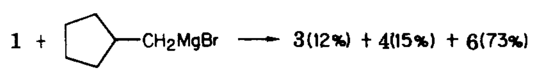
compd	yield, %
3[a]	16
4 + 5	13
6 + 7	70
4	55[b]
5	45[b]
6	28[c]
7	72[c]

[a] Isolated in the form of compound 1. [b] Percentage referred to the mixture 4 plus 5. [c] Percentage referred to the mixture 6 plus 7.

Since the products of 1,4-addition (4 and 5) have the same electronic structure, they will also have approximately the same extinction coefficient; the same assumption can be made for the products of 1,2-addition (6 and 7). Thus, from the peak heights of the chromatogram, we can calculate the 4/5 and the 6/7 ratios (Table I).

The reaction mixture was chromatographed on an SiO_2 column using benzene for elution and gave mixtures 4 plus 5 and 6 plus 7, as well as compound 1; the yields are reported in Table I.

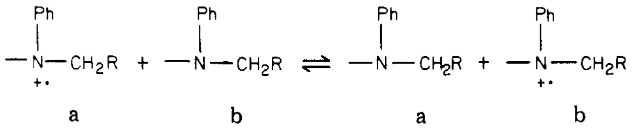
Since the products of 1,4-addition (4 and 5) and 1,2-addition (6 and 7) cannot be separated completely by chromatography,[7b] we performed the reaction of 1 with (cyclopentylmethyl)magnesium bromide (8) to isolate products 4 and 6 in a pure state in order to obtain samples for identification (eq 1). The mass spectra of compounds



(1)

4 and 6, with respect to the molecular ion peaks, clearly show two peaks at −69 and at −83, which correspond to loss of cyclopentyl and cyclopentylmethyl, respectively. The ^{1}H NMR and the IR spectra of 4[3] and 6[1] agree with those already described in the literature for similar compounds. In particular, the ^{1}H NMR spectra of compounds 4 and 6 permitted the analysis of the ^{1}H NMR spectra of the mixtures 4 plus 5 and 6 plus 7. In the spectrum of the mixture 4 plus 5, there is a clear superposition of the doublet of the N-CH_2 of 4 and the triplet of the N-CH_2 of 5 at δ ~3.6; furthermore, the signal of the allylic group of compound 5 is clearly visible (see Experimental Section).

The mixture of 4 plus 5 undergoes autoxidation in solution on exposure to air, yielding traces of the corresponding radical cation. Then the signals from the CH_2 groups of the NCH_2R groups cannot be observed in the NMR spectrum from $CDCl_3$ solution owing to the equilibrium shown in eq 2. If, however, the equilibrium was



$$\underset{\mathbf{a}}{-\overset{\text{Ph}}{\underset{+\cdot}{\text{N}}}-CH_2R} + \underset{\mathbf{b}}{-\overset{\text{Ph}}{\text{N}}-CH_2R} \rightleftharpoons \underset{\mathbf{a}}{-\overset{\text{Ph}}{\text{N}}-CH_2R} + \underset{\mathbf{b}}{-\overset{\text{Ph}}{\underset{+\cdot}{\text{N}}}-CH_2R} \quad (2)$$

destroyed by adding traces of phenylhydrazine, the peaks mentioned could be observed. This phenomenon has already been described.[8-11] To confirm the tendency of compounds 4 and 5 to give the corresponding radical cations and to have further information about their structure, we oxidized the mixture of 4 plus 5 and com-

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(4) Lal, D.; Griller, D.; Husband, S.; Ingold, K. U. *J. Am. Chem. Soc.* **1974**, *96*, 6355.

(5) For examples of applications, see: (a) Garst, J. F.; Barton II, F. E. *J. Am. Chem. Soc.* **1974**, *96*, 523. (b) Ashby, E. C.; DePriest, R. N.; Goel, A. B. *Tetrahedron Lett.* **1981**, *22*, 1763. (c) Ashby, E. C.; Goel, A. B.; DePriest, R. N. *J. Org. Chem.* **1981**, *46*, 2429. (d) Ashby, E. C.; Bowers, J. R. *J. Am. Chem. Soc.* **1981**, *103*, 2242. (e) Kitching, W.; Olszowy, H. A.; Harvey, K. *J. Org. Chem.* **1982**, *47*, 1893. (f) Rilalt, J. A.; Kitching, W. *Organometallics* **1982**, *1*, 1089. (g) Ashby, E. C.; DePriest, R. *J. Am. Chem. Soc.* **1982**, *104*, 6144.

(6) Marcus, R. A. *Annu. Rev. Phys. Chem.* **1964**, *15*, 155.

(7) (a) Marchetti, L.; Greci, L.; Tosi, G. *Gazz. Chim. Ital.* **1970**, *100*, 770. (b) A small amount of 7 was obtained by preparative TLC, eluting with petroleum ether/ethyl acetate (9:1), and extracting the lower part of the large yellow spot with chloroform.

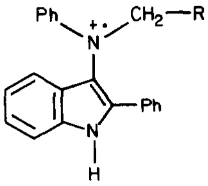
(8) Colonna, M.; Greci, L.; Marchetti, L. *Ann. Chim. (Rome)* **1973**, *63*, 785.

(9) Griffin, R. G.; Van Willigen, H. *J. Chem. Phys.* **1972**, *57*, 86.

(10) Johnson, Jr., C. S. *J. Chem. Phys.* **1963**, *39*, 2111.

(11) Jones, G. T.; Murret, J. N. *J. Chem. Soc., Chem. Commun.* **1965**, *2*, 28.

pound 4 with $I_2/AgClO_4$ in the ESR cavity. In both cases, the same signal for the radical cations **9a** and **9b** was recorded.



9a, R = $c\text{-}C_5H_9$
b, R = $(CH_2)_3CH{=}CH_2$

It showed five lines, with relative intensities 1:3:4:3:1, due to one nitrogen (a^N = 6.25 G) and two hydrogens (a^H = 6.25 G). These results agree with those described in the literature for similar compounds.[12] The ^1H NMR spectrum of mixture **6** plus **7** shows a strong signal for the allylic group and a doublet at δ 2.46 for the CH_2-cyclopentyl, which is absent in the NMR spectrum of pure **7**.

All analytical and spectroscopic data are reported in the Experimental Section.

Discussion

Although the reactions of Grignard reagents with ketones,[5d,13] quinones and quinone diimines,[14] azo compounds,[13,15] nitrosoarenes,[16] and nitroarenes[17] are of great importance in organic chemistry, the mechanistic details are still in considerable dispute. The most significant question that remains to be answered is whether the reaction proceeds by a heterolytic or an electron-transfer mechanism. In the last decade the mechanistic problem has been extensively studied by several authors, and the results have been reviewed by Dagonneau.[18] In spite of the fact that a large amount of experimental data have accumulated over this period, the topic has only recently attracted the interest of theoreticians. Thus, a 1982 ab initio SCF MO study[19] of the model reaction CH_2O plus MgH_2 has shown that electron transfer would be favored in cases of Grignard reagents with high HOMO energy levels (tertiary R in RMgX) and/or ketones with low LUMO levels, as is indeed expected on the basis of simple thermodynamic arguments. Holm[13] used a different approach in interpreting his data on the reactions between RMgX and azobenzene and benzophenone, in that the Marcus theory could be applied with encouraging results. We have here used the later approach to discuss our experimental results because of its conceptual and mathematical simplicity.[3]

The Marcus theory treats the reactants of an electron-transfer reaction as two spherical species (A = acceptor and D = donor), embedded in a continuous medium (dielectric constant ϵ). The species first form a collision complex from which the transition state for electron transfer is reached by bond reorganization (requiring expenditure of bond reorganization energy = λ_i) within the reactants and solvent reorganization energy (requiring expenditure of solvent reorganization energy = λ_0) around the reactants (eq 3). The sum of λ_i and λ_0 is called the reorganization energy and is commonly denoted λ. It can either be calculated from simple assumptions about the two spherical reactants or estimated from experimental data regarding the two self-exchange reactions involved (eq 4 and 5). The rate constants of these processes can

$$\underset{\text{collision complex}}{A + D \rightleftharpoons (A{-}D)} \rightleftharpoons \underset{\text{transition state}}{[A{-}D \leftrightarrow A^{-}\cdot\ D^{+}\cdot]^{\ddagger}} \rightleftharpoons A^{-}\cdot + D^{+}\cdot \quad (3)$$

$$A + A^{-}\cdot \rightleftharpoons A^{-}\cdot + A \quad (4)$$

$$D^{+}\cdot + D \rightleftharpoons D + D^{+}\cdot \quad (5)$$

be measured and converted to the corresponding activation free energies, $\Delta G^{\ddagger}(0)$ (the zero refers to the fact that the free energy change of a self-exchange reaction is zero). From this energy term the Marcus treatment defines the reorganization energy $\lambda(0)$ of the self-exchange reaction as $4\Delta G^{\ddagger}(0)$ and the reorganization energy λ of any heteronuclear electron-transfer reaction as the mean value of the $\lambda(0)$'s of the two self-exchange reactions that it can be dissected into.

The Marcus treatment eventually gives $\Delta G^{\ddagger}$ for an electron-transfer process as in eq 6, where $\Delta G^{\circ\prime}$ is the

$$\Delta G^{\ddagger} = W + \frac{\lambda}{4}\left(1 + \frac{\Delta G^{\circ\prime}}{\lambda}\right)^2 \quad (6)$$

standard free energy change, if necessary corrected by an electrostatic term due to charge change upon electron transfer in the transition state, and W is an electrostatic free energy term due to electrostatic interactions developing as the reagents approach each other to form the collision complex. From this expression and the Eyring equation, log k_{el} (k_{el} is the rate constant for the electron transfer step) can be calculated.

The Marcus treatment has previously been applied to organometallic reactions in a number of cases, most prominently in the discussion of oxidative cleavage of alkyl metals by Fe(III) complexes[20] and the reaction between RMgX and benzophenone or azobenzene.[13] An extended discussion[21] of available data on possible ET reactions of carbanions, carbanionoid species, and certain anionic nucleophiles shows that the Marcus treatment can be used to give a consistent view of such processes. Most importantly, it provides a simple sorting devise for classifying reactions as possible candidates for an ET mechanism. For all species treated in these studies,[13,20,21] a common feature is a high or very high value of $\lambda(0)$.

For the reaction at hand, $W = 0$, and $\lambda G^{\circ\prime}$ can be estimated from the reduction potential of **1** (−0.67 V vs. NHE[22]) and the oxidation potential of **2**. The latter has not been determined explicitly, but a value is available for butylmagnesium bromide (−0.53 V)[13] and can be used as a good approximation of the oxidation potential of **2**. This gives a ΔG° of 23.36 × 0.14 = 3.2 kcal mol^{-1} for electron transfer, but this value must be corrected for the electrostatic free energy change in the transition state upon electron transfer (eq 7). With ϵ equal to 4.3 and r (the

$$[1\ XMgR \leftrightarrow 1^{-}\cdot\ XMg^{+}\ R\cdot] \quad (7)$$

distance between the reacting centers in the transition state) equal to 5 Å, this amounts to −9.0 kcal mol^{-1}, giving a $\Delta G^{\circ\prime}$ of −5.8 kcal mol^{-1}.

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[12] Bruni, P.; Colonna, M.; Greci, L. *Tetrahedron* **1971**, *27*, 5893.

[13] Holm, T. *Acta Chem. Scand., Ser. B* **1983**, *37*, 567.

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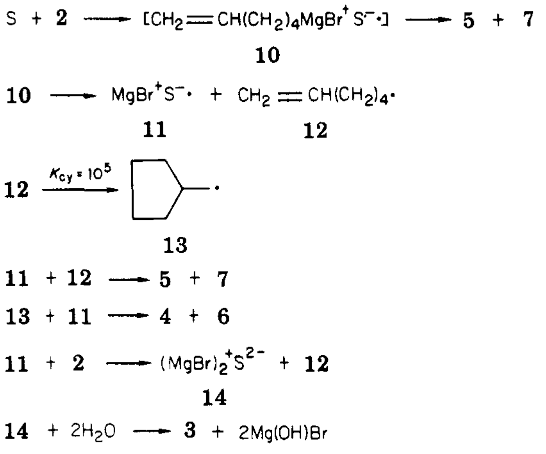
[22] Andruzzi, R.; Trazza, A.; Bruni, P.; Greci, L. "Quaderni della Facolta"; Facolta di Ingegneria, Universita di Ancona, 1978; 97.

Scheme II[a]



[a] S = 2-phenyl-3-(phenylimino)-3*H*-indole (1).

λ(0)'s of the two self-exchange reactions are not known from direct measurements but can be estimated by considering λ's of similar species (for a list, see ref 3) or looking at previous theoretical treatments. The well-behaved electrochemistry of 1 points to a rather low λ(0); therefore, λ(0) was taken to be 10 kcal mol^{-1}. Holm[13] estimated high λ(0)'s for RMgX (~70 kcal mol^{-1}) in his analysis of kinetic data for reaction between Ph_2CO and RMgX, in keeping with the character expected of this particular transition state (charge localized in one bond, extensive lengthening of the R–Mg bond).[21] Thus, we have used a λ value for the 1 plus 2 reaction of 0.5 (10 + 70) = 40 kcal mol^{-1}.

With these parameters, k_{el} for electron transfer between 1 and 2 comes out as $\sim 2 \times 10^5$ M^{-1} s^{-1}, assuming a simple kinetic collision model, i.e., a very fast reaction. For comparison, benzophenone (reduction potential = −1.48 V) reacts with BuMgX with an experimental rate constant of 10.4 M^{-1} s^{-1}, a result that can be reproduced by eq 6 by assuming that λ is ~40 kcal mol^{-1}. Application of eq 6 to the just reported[17] electron-transfer reaction between 2-methoxy-1-nitronaphthalene (reduction potential estimated[23] to be ≈ −0.8 V) and BuMgBr gives a rate constant of $\sim 2.5 \times 10^4$ M^{-1} s^{-1}, somewhat lower than that of the reaction with 1.

A final remark regarding the use of Marcus' treatment for judging the feasibility of electron-transfer steps is in order. The fact that the estimated electron-transfer rate constant of a certain reaction is compatible with experimental evidence is not in itself *proof* that the reaction actually proceeds via electron transfer, only that it may do so. Only experiments will then tell which mechanistic possibility is the correct one. Contrarily, if the estimated electron-transfer rate constant is much lower than the experimental one, we can be reasonably sure that nonbonded electron transfer is not a viable alternative. One example of this situation is the reaction between RMgX and pyrazine (reduction potential = −1.84 V), for which k_{el} is estimated to be $\sim 8 \times 10^{-7}$ M^{-1} s^{-1} with the same assumptions regarding the electrostatic correction term and λ as above. There is ESR evidence[24] for rapid formation of organomagnesium complexes of pyrazine anion radical in this reaction, and it is then reasonable to assume that this is formed in a polar addition–homolytic cleavage reaction sequence and not via direct electron transfer.

Returning to the mechanism of the reaction between 1 and 2, we have found that an initial electron-transfer process is eminently feasible and propose that Scheme II, entirely analogous to that suggested for the reaction between 5-hexenylmagnesium bromide and nitroarenes,[18] constitutes a good representation of our data. Following electron transfer ($k \approx 2 \times 10^5$ M^{-1} s^{-1}), the 5-hexenyl radical can either diffuse apart from the ($1^{-}\cdot MgBr^+$) ion pair (10) or undergo coupling with the $1^{-}\cdot$ within 10, the first-formed radical pair. Since both diffusion and coupling[18] are expected to be very fast processes ($k > 10^9$ s^{-1}), coupling within the radical pair most likely leads to unrearranged products (5 and 7) only.

Any 5-hexenyl radical that escapes from the radical pair 10 can either react with 11 to give 5 and 7 or rearrange ($k \approx 10^5$ s^{-1}) to give the cyclopentylmethyl radical (13) and then react with 11. Assuming that the steady-state concentration of 11 is lower than 10^{-4} M, practically all of the free 5-hexenyl radical will undergo rearrangement before coupling with 11; thus, we conclude that 4 and 6 originate solely via this pathway.

The formation of the reduction product, 3, can be easily explained by a second electron-transfer reduction of $1^{-}\cdot$ to give 1^{2-} (this step is a feasible one, although, of course, slower than the first) as its complex with two $MgBr^+$ (see Scheme II). The fact that the products of 1,2-addition are the main products of the reaction shows that coordination between magnesium and the endocyclic nitrogen may be involved due to its higher electron density with respect to that of the exocyclic nitrogen. This is confirmed by HMO calcations (see Experimental Section). This assumption is in agreement with the fact that the highest spin densities for radical 11 are on C-2 and the exocyclic nitrogen as the reaction products require and also explains why C-3 is never involved in the reaction.

An interesting feature of the reaction between 1 and 2 is that the ratios of 1,2- and 1,4-addition are different for the products containing the 5-hexenyl group (i.e., 7 and 5, formed by cage recombination within the initial radical pair 10) from that of the products incorporating the cyclopentylmethyl group (i.e., 6 and 4, formed by coupling of free radicals), the 7/5 and 6/4 ratios being 8.6 and 2.7, respectively. Garst and Smith[25] found a similar phenomenon in the Wittig rearrangement of benzhydryl 5-hexenyl ether and ascribed it to differences in reaction geometries in the two cases. Here the radical pair is formed by R–O bond homolysis and, thus, has a well-defined intial geometry. Little systematic knowledge is available about the geometrical requirements for electron transfer between two molecules,[26] but it has been established that rate constants for self-exchange even between different enantiomeric forms of radical ions and their parent hydrocarbons can differ appreciably, e.g., by a factor of ~6 in the case of hexahelicene.[27] Thus, there is no inherent difficulty in assuming that the steric requirement for electron transfer between 1 and 2 is reflected in a well-defined initial geometry of 10.

Experimental Section

IR and UV spectra were recorded on Perkin-Elmer Models 257 and 402 spectrophotometers, respectively. ^1H NMR spectra were recorded on a Varian XL-100 spectrometer. The ESR spectra were recorded with a Varian E spectrometer. Mass spectra were recorded on a Varian 112 S apparatus. The liquid chromatography was performed on a Perkin-Elmer series 2. Compound 1 and cyclopentylmethyl bromide were prepared as described.[25,28]

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5-Hexenyl bromide was purchased from Fluka AG, Buchs SG, Switzerland.

Reaction of Compound 1 with 5-Hexenylmagnesium Bromide. The Grignard reagent was prepared by the usual method starting from freshly distilled 5-hexenyl bromide (3 g in 10 mL of THF) and magnesium (0.45 g in 10 mL of THF), under nitrogen. The Grignard solution was added to a solution of **1** (3.3 g in 100 mL of THF) at room temperature under stirring. After 1 h, the reaction mixture was poured onto 10% aqueous NH_4Cl (300 mL) and extracted with benzene (150 mL). The separated benzene layer was washed with water (2 × 50 mL).

The benzene solution was dried with Na_2SO_4, 1 mL of it was evaporated to dryness, and the residue was kept under vacuum (0.5 mmHg) for 1 h at 70 °C. The small residue was dissolved in 5 mL of pure methanol, and the solution was injected into the HPLC apparatus (see below). The main benzene solution was treated with PbO_2 (1.5 g) under stirring. After 1 h, the mixture was filtered, and the filtrate, reduced to a small volume, was chromatographed on an SiO_2 column eluting with benzene. As the first eluate was obtained the fluorescent mixture of **4** and **5**, after the yellow fraction of the mixture of **6** and **7**, and finally the starting material. The yields are reported in Table I.

Compound 4: UV (EtOH) λ_{max} 225 nm (S), 255, 319; IR (Nujol) ν 3400, 1600, 1500 cm^{-1}; NMR ($CDCl_3$) δ 2.6–1.7 (8 H, cyclopentyl), 1.9–2.43 (1 H, m, cyclopentyl), 3.5 (2 H, d, CH_2-cyclopentyl), 6.7–7.7 (14 H, m, arom), 8.54 (1 H, br s, NH); mass spectrum calcd for $C_{26}H_{26}N_2$, m/e 366.48; found, m/e 366; m/e (relative intensity) 366 (M^+, 84), 297 (100), 284 (31).

Compound 5: for UV and IR spectra, see compound 4; NMR $CDCl_3$) δ 0.85–2.05 [6 H, m, $(CH_2)_3$], 3.6 [2 H, t, $CH_2(CH_3)_3$], 4.9 (1 H, s, CH=CH_2), 5.02 (2 H, d, CH=CH_2), 5.74 (1 H, m, CH=CH_2), 6.74–7.8 (14 H, m, arom), 8.37 (1 H, br s, NH); mass spectrum calcd for $C_{26}H_{26}N_2$, m/e 366.48; found, m/e 366; m/e (relative intensity) 366 (M^+, 3), 297 (87), 284 (67), recorded on the mixture **4** plus **5**.

Compound 6: This is the only compound isolated in a crystalline state, mp 125 °C, from n-pentane, and its microanalysis was satisfactory: C, –0.03; H, +0.03; N, –0.12. UV (EtOH) λ_{max} max 250 nm, 270 (s), 380; IR (Nujol) ν 3420, 1650, 1610, 1595 cm^{-1}; NMR ($CDCl_3$) δ 1.0–2.0 (9 H, m, cyclopentyl), 2.46 (2 H, d, CH_2-cyclopentyl), 4.84 (1 H, br s, NH), 6.46 (2 H, d, arom), 6.8–7.0 (3 H, m, arom), 7.1–7.5 (7 H, m, arom), 7.68–7.91 (2 H, m, arom); mass spectrum calcd for $C_{26}H_{26}N_2$, m/e 366.48; found, m/e 366; m/e (relative intensity) 366 (M^+, 3), 297 (8), 284 (100).

Compound 7: for UV and IR spectra, see compound **6**; NMR ($CDCl_3$) δ 1.23–1.7 [4 H, m, $CH_2(CH_2)_2CH_2$), 1.97–2.46 [4 H, m, $CH_2(CH_2)_2CH_2$), 4.9 (1 H, br s, NH), 4.97 [1 H, s, $(CH_2)_4CH$=CH_2], 5.1 [1 H, d, $(CH_2)_4CH$=CH_2], 5.9 [1 H, m, $(CH_2)_4CH$=CH_2], 6.48 (2 H, d, arom), 6.85–7.0 (3 H, m, arom), 7.17–7.57 (7 H, m, arom), 7.7–7.9 (2 H, m, arom); mass spectrum calcd for $C_{26}H_{26}N_2$, m/e 366.48; found, m/e 366; m/e (relative intensity), 366 (M^+, 15), 284 (100).

HPLC. The liquid chromatography carried out on the reaction mixture (see above) was performed on a Sephadex C-18 column, eluting with water/methanol (1:4) and working at λ 254 nm and at 55 °C with a flow rate of 1.2 mL/min. The elution order of the compounds was **1**, **7**, **6**, **5**, and **4**.

Reaction of Compound 1 with (Cyclopentylmethyl)magnesium Bromide. The Grignard reagent, prepared starting from cyclopentylmethyl bromide (1.6 g in 10 mL of THF) and magnesium (0.24 g in 5 mL of THF), was added to the solution of **1** (0.8 g in 30 mL of THF). The products shown in eq 1 were isolated by working up the reaction as described above.

HMO Calculations. The calculations were carried out with the aid of a computer program, using the following parameter set:[29,30] $h_N = 0.5$, $K_{CC} = 1.0$, $K_{C\text{-}C} = 0.9$, $K_{C=N} = 1.06$, $K_{C\text{-}N} = 0.8$. Calculated electron densities for N (endocyclic), C-2, C-3, and N (exocyclic) were 1.263, 0.882, 0.889, and 1.089, respectively.

Reaction in the ESR Cavity. Acetonitrile solutions of **4** plus **5** or **4** (10^{-1} M) and the corresponding quantities of I_2 and $AgClO_4$ in acetonitrile solution were placed in one of the two arms of an inverted cell similar to that described by Russell[31] and degassed with nitrogen at room temperature. The mixed materials were transferred into ESR cavity.

Registry No. 1, 23073-34-9; 2 (alkyl bromide), 2695-47-8; 4, 89031-91-4; 5, 89031-92-5; 6, 89031-93-6; 7, 89031-94-7; cyclopentylmethyl bromide, 3814-30-0.

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Acylphosphonates. 4.[1] Synthesis of Dithymidine Phosphonate: A New Method for Generation of Phosphonate Function via Aroylphosphonate Intermediates

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Dithymidine phosphonate (**10**) was synthesized by a new method via dithymidine aroylphosphonates (**3**) in which the aroyl group served as a protecting group for O=P—H functions. In a way analogous to the phosphotriester method, **3** was prepared by successive condensation of an aroylphosphonic acid with two kinds of thymidine derivatives. In the last step, the aroyl group was easily removed from **3** by n-butylamine in the presence of a catalytic amount of DBU to generate the O=P—H function. In enzymatic hydrolysis dithymidine phosphonate (**10**) was resistant to phosphodiesterases. On oxidation and sulfurization of **10** via silylation **10** was successfully converted to the corresponding phosphate and phosphorothioate derivatives, respectively.

During the past 15 years a number of oligonucleotide analogues in which the internal phosphate oxygen (O=P—OH) was altered by other elements have been synthesized and their physical properties and biological activities have been studied.

They are classified in two groups according to their replacement modes: (i) replacement of the internucleotidic P=O by P=S,[2-4] P=Se[3], and P=NR;[3] (ii) replacement

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