is in accord with Barltrop's experimental and Jug's SINDO1 conclusions concerning cyanopyrrole. Photolysis of 1,5-dimethylpyrazole was also carried out at 77 K in frozen acetonitrile resulting in the formation of imidazoles that are consistent with only the P_4 and P_6 permutation patterns. No P_7 imidazole was detected even after 33% of the reactant had disappeared. These observations are consistent with our calculated results, which suggest that I_2 forms on a relatively flat potential energy surface, such as S_1, and that subsequent reactions occur on the ground-state surface.

Conclusion

MNDO calculations and experimental product distributions are used to provide a qualitative explanation of the phototransposition of pyrazole to imidazole via [1,3]-sigmatropic shift of nitrogen. Initial electrocyclic ring closure of pyrazole and walk of nitrogen occur on the S_1 potential energy surface. The return to the ground state is via a radiationless transition from $I_2(S_1)$ to $TS_2(S_0)$. The second [1,3]-shift of nitrogen may be a biradical process; however, it is difficult to clearly distinguish between concerted and biradical mechanisms at the MNDO level. Kinetic and thermodynamic arguments are in qualitative agreement with the experimentally observed relative product distributions of the P_6 and P_7 imidazoles and support the assignment of the second walk to a ground-state process. Photolysis at decreasing temperature results in increasing P_6 to P_7 product ratios. This is consistent with a ground-state thermal reaction and a smaller barrier for rearomatization than walking as suggested by the theoretical calculations.

Acknowledgment. The authors thank A. E. Johannesen and the staff of the College Computing Center for their assistance during the early stages of this project. We are grateful to Professor M. C. Zerner of the University of Florida for providing a copy of his INDO program. DECstation 3100 and Encore Multimax 520 computers at Worcester Polytechnic Institute were used for the computations.

Registry No. R, 288-13-1; P_6,P_7, 288-32-4; I_1,I_4, 74613-28-8; I_2,I_3, 74613-34-6.

Structures and Lifetimes of 1,4-Biradical Intermediates in the Photochemical Cycloaddition Reactions of *N*-Benzoylindole with Alkenes[1]

David J. Hastings and Alan C. Weedon*

Photochemistry Unit, Department of Chemistry, The University of Western Ontario,
London, Ontario, N6A 5B7, Canada

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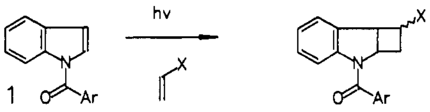
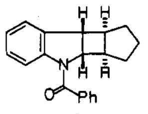
The photochemical cycloaddition reaction of *N*-benzoylindole with 1,6-heptadiene, tetramethylethylene, and vinylcyclopropane has been examined. The structures of the products suggest that the reaction proceeds via a 1,4-biradical intermediate that is formed by bonding between one terminus of the alkene and the 2-position of the indole derivative. This result is used to explain the origin of the previously observed regioselectivity of the photochemical cycloaddition reaction. The biradical intermediates obtained in the photochemical cycloaddition reaction of *N*-benzoylindole with vinylcyclopropane and 1,6-heptadiene can undergo rearrangement reactions whose rate constants can be estimated. Using these rates as clocks, the lifetimes of the intermediate biradicals in the photochemical cycloaddition reaction of *N*-benzoylindole with alkenes are estimated to be of the order of 100 ns. The consequences of this for the potential success of synthetically useful trapping of the intermediate biradicals is discussed.

Introduction

Scheme I



It has been reported[2,3] that indoles possessing a benzoyl substituent on the nitrogen atom form cyclobutane products when irradiated with ultraviolet light in the presence of alkenes. With monosubstituted alkenes the reaction is found[3] to be regioselective, but not normally stereoselective, as indicated in Scheme I. This reaction offers a potential route for the synthesis of substituted indoles if methods for elaboration of the cyclobutane ring can be developed. With this as our motivation, we have been examining the mechanism of this photochemical cycloaddition reaction in order that the factors governing the reaction regiochemistry and stereochemistry can be understood. We have previously obtained[4] steady-state kinetic results that suggest that the reaction proceeds as shown in Scheme II. In this scheme, intersystem crossing of the singlet excited state of *N*-benzoylindole (1) occurs efficiently[5] to yield the triplet excited state, which is intercepted by an alkene such as cyclopentene to give one or more isomeric 1,4-biradical intermediates. The major fates of the biradicals are reversion to the ground-state indole derivative and alkene or closure to the cyclobutane products 2 and 3. The intermediacy of biradicals that partition between product and starting material is sup-



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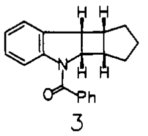

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(1) Contribution no. 440 from the Photochemistry Unit, University of Western Ontario.

(2) Julian, D. R.; Foster, R. *J. Chem. Soc., Chem. Commun.* **1973**, 311.

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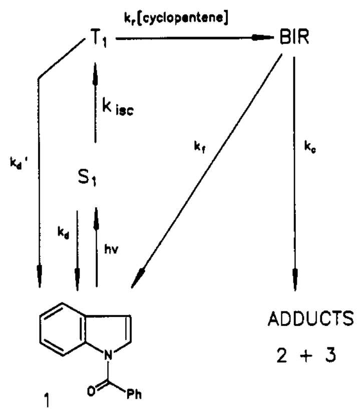
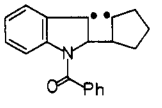
Scheme II



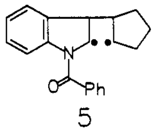
1

ported by the finding[6] that the same mixture of stereoisomeric cyclobutane products is obtained when either *cis*-2-butene or *trans*-2-butene is used as the alkene and by the fact that Schenk isomerization of the alkene is observable.[6] The purpose of the work described here was to find additional evidence for the intermediacy of these biradicals and to obtain information about their lifetimes and structures. As will be explained, a knowledge of the structures of the biradicals can cast light on the origins of the regioselectivity of the reaction. In addition, an estimate of the biradical lifetimes could lead to the development of synthetically useful trapping procedures.

For the reaction of *N*-benzoylindole with cyclopentene the intermediate biradicals could, in principle, have structures 4 or 5; these correspond to initial bonding to



4



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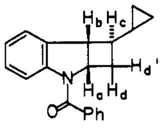
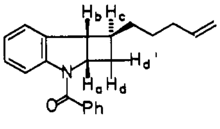
the 2-position or 3-position of the indole, respectively. If this reaction were to be performed using alkenes that yield biradicals that can undergo a rearrangement, in competition with ring closure or bond homolysis, to form alternative products, then the rearrangement reaction could be used as a probe of both the structure of the biradical and, if the rate of the rearrangement reaction is known, as a clock to measure its lifetime. Alkenes that fulfill this requirement are tetramethylethylene, 1,6-heptadiene, and vinylcyclopropane.

Scheme III shows the anticipated outcome of the reaction between *N*-benzoylindole and vinylcyclopropane. Interaction of the triplet excited *N*-benzoylindole with the alkene can, in principle, lead to biradicals 6–9, although 6 and 9 would be expected to dominate over 7 and 8 if it is assumed that the primary radical centers present in 7 and 8 inhibit their rate of formation. Biradicals 6 and 7 can cyclize to stereoisomers of 10 while 8 and 9 can close to stereoisomers of 11. The intermediates 6 and 9 contain a cyclopropylalkyl radical that is known[7-10] to ring open rapidly to a homoallylic radical yielding intermediates 12 and 13, respectively. If the double-bond geometry is *Z* in 12 and 13 then they can close to give 14 and 15, respectively. The ring opening is, in principle, reversible, but the homoallylic radical is heavily favored thermodynamically. Since the rate of the rearrangement of the cyclopropylalkyl radical to a homoallylic radical is known,[7-10] the quantities of 14 and 15 formed relative to the amounts of 10 and 11 can be used to estimate the lifetimes of 6 and 9. In addition, since 14 is only produced from 6, and 15 only from 9, the identity of the products formed yields information about the structures of the intermediate biradicals and the position of the first bond made between the indole and the alkene.



11a



21a

In Scheme IV, the expected outcome of the reaction between *N*-benzoylindole and 1,6-heptadiene is shown. The expected biradicals are 16–19, although 16 and 19 should dominate since 17 and 18 contain primary radical centers and would be expected to be formed more slowly. Cyclization of 16 and 17 gives 20 while cyclization of 18 and 19 gives 21. However, 16 and 19 contain derivatives of 1-hexenyl radicals that can cyclize to cyclopentylmethyl radicals. If this occurs then species 22 and 23 are formed, which can proceed to give various stereoisomers of 24. The rate of cyclization of 1-hexenyl radicals to cyclopentylmethyl radicals is known,[11] and so the proportions of 20 and 21 relative to 24 formed can be used to define the lifetime of the biradicals 16 and 19.

In Scheme V, the expected outcome of the reaction between *N*-benzoylindole and tetramethylethylene is shown. Here, only the two biradicals 25 and 26 are possible, and both may cyclize to give 27. However, by analogy with the products obtained in the photochemical 2 + 2 cycloaddition reaction between 2-cyclohexenones and methyl-substituted alkenes,[12] it is possible for disproportionation of the 1,4-biradicals to occur so the "ene" products 28 and 29 can be produced. The structures of 28 and 29, if formed, can be used to infer the site of initial bonding between the indole and the alkene.

Results

Irradiation of *N*-Benzoylindole with Tetramethylethylene. Ultraviolet light irradiation of a benzene solution of *N*-benzoylindole and tetramethylethylene, under conditions such that 1 absorbed all of the light, gave a single major product that was identified as the 2 + 2 cycloadduct 27 on the basis of its mass spectrum and ^{1}H NMR spectrum. In the latter, the four methyl groups were seen as the expected high field singlets and the two cyclobutane methine protons were observed at 4.60 and 3.56 ppm, which is characteristic for alkene adducts of *N*-benzoylindole.[6] The signal at 4.60 ppm was broadened and its splitting pattern unresolved and is assigned to H_a in 27. This broadening is associated with slow rotation of the *N*-benzoyl group and has been seen in other *N*-benzoylindole adducts and characterized by variable-temperature NMR spectroscopy.[6,13] The signal at 3.56 ppm was a doublet coupled to H_a and is therefore assigned to H_b. The coupling constant of 8 Hz is typical of the cis-fused indole–cyclobutane ring system.[6] Inspection of the reaction mixture by ^{1}H NMR spectroscopy or coupled gas chro-

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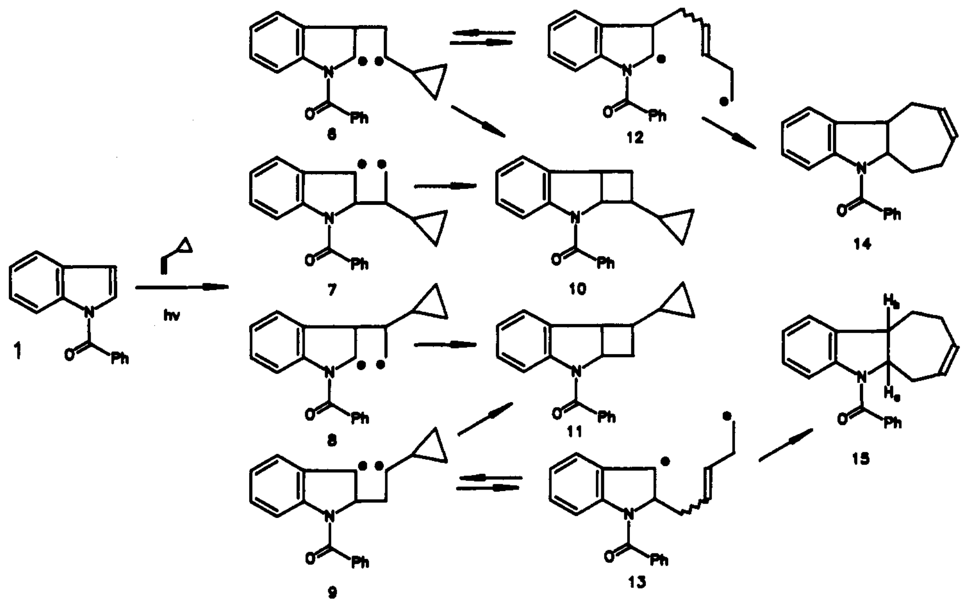
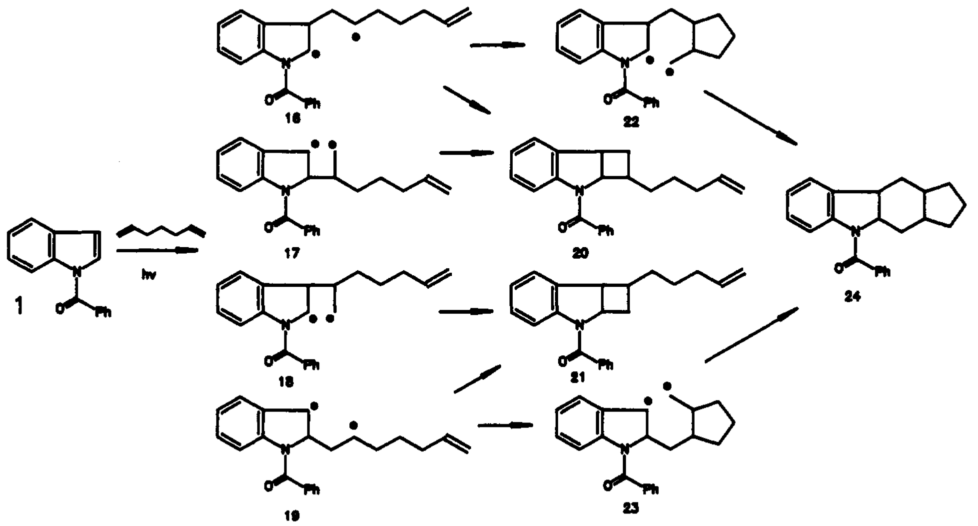
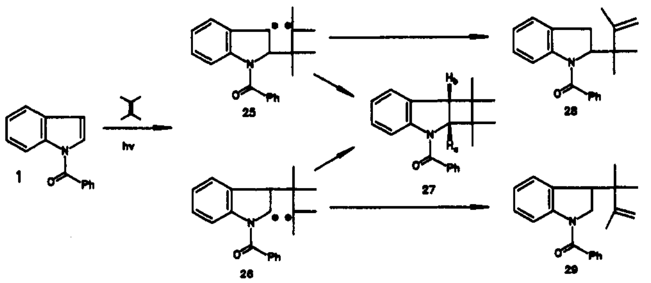
Scheme III



Scheme IV



Scheme V



matography mass spectroscopy (gc–ms) revealed no evidence for the presence of products with the structures 28 or 29.

Irradiation of *N*-Benzoylindole with 1,6-Heptadiene. Ultraviolet light irradiation of a benzene solution of N-benzoylindole and 1,6-heptadiene under conditions such that only 1 absorbed light gave one major and three very minor products in a ratio of 0.3:99.4:0.2:0.1 as indicated by GC. Analysis by GC-MS indicated that all four products were 1:1 adducts of 1 and the diene. The four compounds were not separable; however, the minor components were present in such small amounts that they were not discernable in the ^{1}H NMR spectrum of the purified mixture and so did not interfere with the assignment of structure 21a to the major isomer by ^{1}H NMR spectroscopy. This structure is based upon the observation of the expected aromatic signals as well as signals corresponding to the pentenyl side chain and cyclobutane protons. The regiochemistry and stereochemistry were determined by analysis of the coupling pattern of the cyclobutane protons. Decoupling of the H_a resonance, which appeared at 4.60 ppm and showed characteristic broadening by the adjacent *N*-benzoyl group,[6] caused a two-proton multiplet at 2.52 ppm to collapse to an AB quartet. The multiplet at 2.52 ppm is therefore assigned to H_d and $H_{d'}$, which establishes the regiochemistry of the photoadduct. Proton H_b was seen at 3.58 ppm as a double doublet coupled to H_a (J = 8 Hz) and H_c (J = 2 Hz). Small vicinal coupling constants between protons on cyclobutane rings in indole–alkene adducts has been found indicative of a trans relationship[6] so that the value of J_{bc} found suggests the stereochemistry shown in 21a, which corresponds to exo addition of the alkene to 1.

Hydrogenation of the mixture of cycloadducts resulted in reduction of three of them to give new products in the ratio 0.3:99.5:0.2, which were shown by GC–MS to have increased in mass by two units. The third minor product (0.1% of the mixture) was unchanged. Based upon this evidence, two of the minor photoaddition products possess a single double bond and so may be stereoisomers of **21a** or **20**. The failure of the third minor component to undergo hydrogenation indicates it to be saturated; consequently, it is possible that it may be a stereoisomer of the expected rearrangement product **24**.

Irradiation of *N*-Benzoylindole with Vinylcyclopropane. Ultraviolet light irradiation of a benzene solution of *N*-benzoylindole and vinylcyclopropane gave a mixture of three 1:1 adducts of these compounds in the ratio 5:31:64, as determined by GC, GC–MS, and ^{1}H NMR spectroscopy.

The adducts comprising 64% and 31% of the mixture were separated in pure form by chromatography and were assigned structures **15** and **11a**, respectively.

The structure of **15** was assigned on the basis of the appearance of its ^{1}H NMR spectrum. In the spectrum H_a appeared at 4.9 ppm and H_b at 3.7 ppm. As in other adducts of **1** and alkenes, the signal assigned to H_a exhibited broadening attributed to slow rotation of the *N*-benzoyl substituent.[6] Irradiation of H_a resulted in partial decoupling of a methylene multiplet at 2.40 ppm, which in turn was also decoupled by irradiation of the two olefinic protons that appeared superimposed on one another at 5.6 ppm. Irradiation of H_b resulted in decoupling of a methylene multiplet at 2.0 ppm; however, the latter was not affected by irradiation of the olefinic protons. This pattern allows unambiguous assignment of structure **15** and rules out the alternative, **14**. The value of J_{ab} was 8 Hz, which suggests cis ring fusion stereochemistry in **15**.

The structure of **11a** was also deduced from the ^{1}H NMR spectrum. The monosubstituted cyclopropyl group gave rise to a characteristic pattern of signals consisting of a methine multiplet at 0.86 ppm, and methylene multiplets at 0.52 and 0.14 ppm. For the cyclobutane protons a broad signal at 4.60 ppm assigned to H_a was coupled to signals at 3.70 (assigned to H_b) and 2.50 and 2.20 ppm (H_d and $H_{d'}$), while H_b was weakly coupled to a signal at 1.95 ppm (H_c). This pattern is consistent with the regiochemistry in **11a** but not for its regioisomer **10** (Scheme III). The trans relationship of H_b and H_c shown in **11a** is assigned on the basis of the small value[6] of J_{bc} and corresponds to exo addition of the alkene to the indole. A cis arrangement of H_b and H_c would lead to a coupling constant of the order of 8 Hz as observed for J_{ab}.

The minor component of the mixture (i.e., that comprising 5% of the adducts) was not isolated in sufficiently pure form to allow characterization. However, the presence of cyclopropyl protons in the ^{1}H NMR spectrum of the impure material suggest that it is either the stereoisomer of **11a** or one of the stereoisomers of the regioisomer **10**.

Discussion

The isolation of **27** as the exclusive product in the irradiation of *N*-benzoylindole with tetramethylethylene implies that disproportionation of the putative biradicals **25** and **26** to give products **28** and **29** is slower than their alternative fates, closure to **27** or reversion to **1** and the alkene. Since **28** and **29** are not products, irradiation of **1** with tetramethylethylene yields no information about the point of initial bonding between the alkene and the indole.

With vinylcyclopropane the major product **15** accounts for 64% of the adducts and must have its origins in the biradicals **13** and **9** (Scheme III); thus, it can be concluded that for this product the first bond formed between the indole and the alkene is to the 2-position of the indole. In addition, the second most prevalent product **11a**, accounting for 31% of the adducts, must have its origins in either biradical **8** or biradical **9**. The addition of radicals to monosubstituted alkenes results in bonding to the less hindered alkene terminus and the formation of a secondary radical at a much faster rate than bonding to the more substituted alkene terminus and formation of primary radicals;[14] thus, if radicals are accepted as satisfactory models for the triplet excited state, then it can be argued that the biradical **9** should be formed preferentially over biradical **8** and therefore that the addition of vinylcyclopropane to **1** to give **11a** also proceeds by initial bonding between the alkene and the 2-position of the indole. The argument that the regiochemistry of addition of radicals to alkenes is a good model for the expected orientation of addition of triplet excited states to alkenes is supported by the outcome of the addition of 2-methylpropene to triplet excited 2-cyclohexenones[15] as outlined by us previously.[16]

The rate constant for rearrangement of secondary cyclopropylalkyl radicals to the corresponding open chain homoallylic radical has been estimated[9,10] to be 2×10^7 s^{-1}. Using this value for the rearrangement of biradical **9** to biradical **13** and assuming that formation of **11a** is proceeding exclusively from biradical **9** and hence competitively with rearrangement, the sum of the rate constants for closure of **9** to **11a** and reversion of **9** to **1** plus alkene can be estimated to be of the order of 1×10^7 s^{-1}. This translates into a biradical lifetime of 100 ns for **9**. The product of addition of 1,6-heptadiene to **1**, compound **21a**, can be formed from closure of either of biradicals **18** or **19**; using the same arguments as above, formation of **21a** via **19** is likely to be the favored pathway. Thus, the isolation of **21a** as the almost exclusive product of addition suggests that with this alkene also, the position of initial bonding of the alkene is to the 2-position of the indole. In addition, the fact that **21a** accounts for more than 99% of the adducts formed from **1** and 1,6-heptadiene, and the fact that compounds with structure **24** form at most 0.1% of the adduct mixture, indicate that closure of biradical **19** to **21a** is 100 to 1000 times faster than rearrangement of **19** to **23**. The rate constant for the latter rearrangement can be estimated from the rate constant measured[11] for closure of hexenyl radical to cyclopentylmethyl radical, which is 1×10^5 s^{-1}. This leads to a rate constant for closure of **19** of 10^7–10^8 s^{-1}, which is similar to that estimated above using vinylcyclopropane as the radical clock precursor.

The value of 100 ns estimated for the lifetime of the 1,4-biradical produced in the cycloaddition of *N*-benzoylindole to vinylcyclopropane is similar to the lifetimes reported for other 1,4-biradicals such as those generated via the Norrish Type II reaction,[17] the 2 + 2 photocycloaddition reaction between cyclic enones and olefins,[16,18] the Paterno-Buchi reaction,[17c,19] and the photochemical dimerization of 2-cyclopentenone.[20] The general

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similarity reflects the fact that the lifetimes of these biradicals at room temperature largely depend on the rate of intersystem crossing from the triplet biradical to the singlet biradical, and not so much on the structural effects in the biradical.[21] For synthetic purposes it is attractive to consider the possibility of trapping the 1,4-biradical intermediates in these indole cycloaddition reactions. The biradical lifetimes estimated here suggest that for this to be successful, species capable of reacting with radical centers with rate constants of at least 10^8 M^{-1} s^{-1} would be required.

The conclusion that adduct formation between triplet excited 1 and alkenes occurs via initial bonding between one terminus of the alkene and the 2-position of 1 can be used to rationalize the generally observed regiochemistry of addition of monosubstituted alkenes to 1. As noted in the Introduction, the addition is normally regioselective and does not depend upon the nature of the alkene substituent. This is in contrast to the situation found for photochemical cycloaddition of alkenes to cyclic enones, where the regiochemistry is apparently governed by the polarity of the group attached to the alkene.[12] With the indole system the regiochemistry can be understood and predicted if it is assumed that initial bonding occurs between the 2-position and the indole and the terminus of the alkene less able to stabilize a radical center. We are currently examining this idea by investigating the regiochemical outcome for the addition of polysubstituted alkenes.

Experimental Section

N-Benzoylindole was prepared from indole and benzoyl chloride using the method of Illi.[22] Vinylcyclopropane was most easily prepared in larger quantities by Bamford–Stevens reaction of the tosylhydrazone of cyclopropyl methyl ketone using the modified method of Rudolf and Weedon.[16] The samples so obtained contained variable amounts of the 1-methylcyclobutene as byproduct. The 1,6-heptadiene and tetramethylethylene used were commercial samples from Baker and Aldrich, respectively, and their purities were checked by gas chromatography and ^{1}H NMR spectroscopy. They were used as received. High-performance liquid chromatography (HPLC) was performed using a Waters automatic gradient controller with dual Waters Model 510 pumps and a Waters 490 programmable multiwavelength detector. This was equipped with a Varian normal-phase silica semipreparative steel column, and fractions were collected with a Gilson 201 collector. The ^{1}H NMR spectra were recorded at 200 MHz in $CDCl_3$ on a Varian XL200 instrument. Coupled GC–MS was performed using a Varian 3400 GC attached to a Finnegan-MAT 8230 mass spectrometer. The ^{13}C NMR spectra were recorded at 75 MHz in $CDCl_3$ on a Varian XL300 instrument. Routine GC was performed on a Hewlett-Packard 5880 instrument with a 30 meter DB-5 methyl silicone capillary column maintained at a temperature of 250 °C.

Irradiation of *N*-Benzoylindole with Tetramethylethylene. *N*-Benzoylindole (26 mg, 0.118 mmol) and tetramethylethylene (0.8 g, 9.5 mmol) were dissolved in benzene (2 mL). The solution was purged with nitrogen, sealed, and irradiated with Pyrex- and water-filtered light from a medium-pressure mercury lamp. After 87 h, GC indicated that a single product had been formed in 61% yield. The solvents were removed in vacuo, and preparative TLC (25% ether/75% hexanes) was performed on the irradiation mixture. Two bands were isolated and characterized. The first band (R_f = 0.5) was identified as *N*-benzoylindole by GC coinjection and ^{1}H NMR spectroscopy. The second band (R_f = 0.35) was identified as 27: ^{1}H NMR δ 8.36 (br s, 1 H), 7.45 (m, 5 H), 7.08 (m, 3 H), 4.60 (br s, 1 H), 3.56 (d, *J* = 8.0 Hz, 1 H), 1.61 (s, 3 H), 1.20 (br s, 3 H), 0.81 (s, 3 H), 0.79 (s, 3 H) ppm; *m/e* 305 (M^+, 1.0), 221 (44), 105 (100), 77 (28); calcd M^+ 305.17794, found 305.1777.

Irradiation of *N*-Benzoylindole with 1,6-Heptadiene. A solution of *N*-benzoylindole (53 mg, 0.24 mmol) and 1,6-heptadiene (124 mg, 1.28 mmol) in benzene (6 mL) was deoxygenated by purging with nitrogen and irradiated at room temperature using water- and Pyrex-filtered light from a medium-pressure mercury lamp for 68 h, after which time GC indicated ca. 75% conversion of the *N*-benzoylindole. Four products were observed in relative percent amounts in order of increasing retention times of 0.3:99.4:0.2:0.1. The solvent was removed under reduced pressure to yield a yellow oil (60 mg), which was chromatographed on preparative TLC plates doubly eluted with 30% ether/70% hexanes to give two fractions. The least polar fraction was identified as *N*-benzoylindole (12 mg), and the second fraction (47 mg) was identified as cycloadduct **21a** ^{1}H NMR δ 8.26 (br s, 1 H), 7.44 (m, 5 H), 7.16 (m, 3 H), 5.79 (m, 1 H), 4.98 (m, 2 H), 4.60 (br s, 1 H), 3.58 (br d, *J* = 8, 2 Hz, 1 H), 2.52 (m, *J* = 12, 1–2 Hz, 2 H), 2.26 (m, *J* = 1–2 Hz, 1 H), 2.08 (m, 6 H) ppm; GC–MS calcd M^+ 317.17796, found 317.1781, *m/e* 317 (3), 221 (40), 105 (100). The other three adducts were undetectable by ^{1}H NMR. However, GC–MS gave mass spectral data in order of increasing retention times: first minor product *m/e* 317 (M^+, 1.0), 221 (49), 105 (100); second minor product *m/e* 317 (M^+, 6.0), 221 (4), 105 (57), 91 (100); third minor product *m/e* 317 (M^+, 21), 221 (6), 105 (96), 91 (100). The mixture of adducts was dissolved in benzene (2 mL) and hydrogenated over PtO_2 at 1 atm for 1 h. GC showed four product peaks, three of them with retention times slightly slower than that of the starting mixture. GC coinjection confirmed that three new products had formed in a percent ratio of 0.3:99.4:0.2 and that the one minor product (0.1%) remained unchanged. GC–MS showed the new products to have M^+ at *m/e* 319 and the unchanged minor product to have M^+ at *m/e* 317.

Irradiation of *N*-Benzoylindole with Vinylcyclopropane. *N*-Benzoylindole (1.0 g, 4.5 mmol) was dissolved in benzene (4 mL), and the solution was purged with nitrogen. Vinylcyclopropane (2.2 mL, 1.54 g, 22.6 mmol; the sample contained 5% 1-methylcyclobutene) was added, and the solution was sealed and irradiated at room temperature using water- and Pyrex-filtered light from a medium-pressure mercury lamp for 122 h at which time GC indicated approximately 10% conversion of the *N*-benzoylindole. The GC also indicated that seven products were formed. Removal of the solvent afforded 0.8 g of a yellow oil, which was not characterized further. This crude irradiation mixture was treated with 5 mL of concentrated KOH in methanol/water (3:1 by vol) to hydrolyze unreacted 1. The hydrolyzed mixture was extracted into ether and dried (Na_2SO_4), and solvent was removed to yield 352 mg of yellow oil. GC showed the seven products still intact, the absence of 1, and a new peak assigned to indole (confirmed by coinjection). The oil was steam distilled for 45 min to remove indole. The stillpot was extracted with ether and dried (Na_2SO_4), and solvent was removed to give 130 mg of an oily brown solid. GC indicated five major products in a ratio of 7:15:4:24:50, accounting for 99% of the total products, and two minor peaks accounting for less than 1%. GC–MS showed all peaks to possess M^+ at *m/e* 289, consistent with the formation of 1:1 adducts.

A portion of this mixture of five adducts (35 mg) was separated by HPLC to yield three product-containing fractions, which were analyzed by GC, GC–MS, and ^{1}H NMR. Fractions are described in order of increasing retention times.

Fraction 1 yielded 3.5 mg of a colorless oil, which by GC showed three peaks with retention times identical with the first three peaks in the starting mixture. GC–MS revealed all three peaks to have M^+ with *m/e* 289. The ^{1}H NMR spectrum of the mixture indicated that the two major components were adducts of *N*-benzoylindole and 1-methylcyclobutene, the latter being a contaminant present in the vinylcyclopropane. The third component in the mixture showed cyclopropyl signals at 0.50 and 0.86 ppm and was tentatively assigned to an isomer of **10** or **11**.

Fraction 2 yielded 2 mg of a clear colorless oil, which GC showed to be a single species (99% pure) with a retention time identical with that of the component that comprised 24% of the original mixture. This was identified as **11a** and had M^+ at *m/e* 289: *m/e*

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289 (2), 221 (20), 105 (100); ^{1}H NMR δ 7.5–6.7 (m, 9 H), 4.60 (br s, 1 H), 3.70 (br dd, J = 8, 2.5 Hz, 1 H), 2.50 (m, 1 H), 2.2 (m, 1 H), 1.95 (m, 1 H), 0.86 (m, 1 H), 0.52 (m, 2 H), 0.14 (m, 2 H) ppm.

The last (third) fraction yielded 10 mg of an oil whose GC indicated it to be the major product of the mixture (i.e., that comprising 50% of the adducts). This was identified as **15**: M$^+$ 289.1462, calcd 289.1466; ^{1}H NMR δ 7.5–6.7 (m, 9 H), 5.6 (br, 2 H), 4.88 (br s, 1 H), 3.71 (ddd, J = 4, 8, 11 Hz, 1 H), 2.4 (m, 2 H), 2.3 (m, 2 H), 2.0 (m, 2 H) ppm.

Registry No. **1**, 1496-76-0; **11g**, 135733-81-2; **15**, 135733-80-1; **21a**, 135733-79-8; **27**, 135733-78-7; $Me_2C{=}CMe_2$, 563-79-1; $H_2C{=}CH(CH_2)_3CH{=}CH_2$, 3070-53-9; vinylcyclopropane, 693-86-7.

Effects of Metal Ions on the Equilibria of Methanol and Methoxide Ion Addition to Benzaldehydes. Effect of a Poly(oxyethylene) Side Arm

Giancarlo Doddi,* Gianfranco Ercolani,* Paolo Mencarelli,* and Carlo Scalamandrè

Centro CNR di Studio sui Meccanismi di Reazione and Dipartimento di Chimica, Università "La Sapienza", 00185 Roma, Italy

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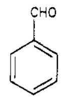
The effect of added alkali (Na, K) and alkaline-earth (Sr, Ba) metal bromides on the equilibria for the addition of methanol and methoxide ion to 2-(1,4,7,10,13-pentaoxatetradecyl)benzaldehyde (2) has been studied in methanol at 25 °C. Whilst alkali cations do not significantly perturb the above equilibria, alkaline-earth metal ions cause a dramatic increase of the equilibrium constant for the addition of methoxide ion (ca. 420 and 150 times in the presence of 0.1 M $SrBr_2$ and $BaBr_2$, respectively). A detailed study of the system afforded equilibrium constants for associations of metal ions with all of the species involved in the process. An analogous set of equilibrium measurements was carried out for comparison purposes with benzaldehyde (1). All of the added salts did not affect both the addition of methanol and methoxide ion to 1, thus indicating that a substantial contribution to the ligand ability of the hemiacetal anion of 2 arises from interaction of metal ions with at least some of the donor sites of the polyether side arm.

A large number of organic reactions are carried out in the presence of either alkali or alkaline-earth metal ions whose effects on reaction rates and equilibria are very often neglected or underestimated at best.[1] The principal obstacle to a detailed analysis of metal ion effects on organic reactions is due to the formation of aggregates of unknown composition and structure, which becomes important in solvents of low dielectric constant. On the other hand, in more polar solvents, associations with metal ions are weaker and not always recognizable. A possible approach to overcome this difficulty is to modify the substrate structure by adding a number of suitable coordinating sites capable of holding the metal ion in close proximity to the reaction center. Hopefully, the information gained about the interaction between metal ion and reaction zone will contribute also to the understanding of some of the many facets of supramolecular reactivity and catalysis.

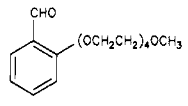
Table I. Equilibrium Constants for the Formation of the Hemiacetals (K_{SH}) and Hemiacetal Anions (K_{S^-}) of Benzaldehydes 1 and 2 in MeOH at 25 °C

aldehyde	K_{SH}	K_{S^-}, mol^{-1} L
1	0.055	0.20
2	0.068	0.060

To date, only a limited number of reaction types have been studied in detail by this approach, namely, nucleophilic substitution,[2] base-induced methanolysis of esters,[3] and acid–base equilibria.[4] Here, we report a study of the effects of alkali (Na, K) and alkaline-earth (Sr, Ba) cations on the equilibria for the addition of methanol and methoxide ion to benzaldehyde (1) and to a substituted benzaldehyde bearing in ortho position a polyether chain (2).



1



2

Results and Discussion

Equilibria in the Absence of Metal Ions. Benzaldehydes (a) in neutral and alkaline methanolic solutions undergo the reversible addition of methanol (eq 1) and methoxide ion (eq 2) to yield the corresponding hemiacetals (h) and hemiacetal anions (ha).[5,6] The formation

$$\underset{\text{a}}{\text{ArCHO}}\ \text{(+ MeOH)} \xrightleftharpoons{K_{SH}} \underset{\text{h}}{\text{ArCH(OMe)OH}} \tag{1}$$

$$\underset{\text{a}}{\text{ArCHO}} + \text{MeO}^- \xrightleftharpoons{K_{S^-}} \underset{\text{ha}}{\text{ArCH(OMe)O}^-} \tag{2}$$

of acetals, rather than hemiacetals, is known to occur in

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