Removable Groups for Activation of Indole Photochemistry[1]

Alan C. Weedon,* Boke Zhang

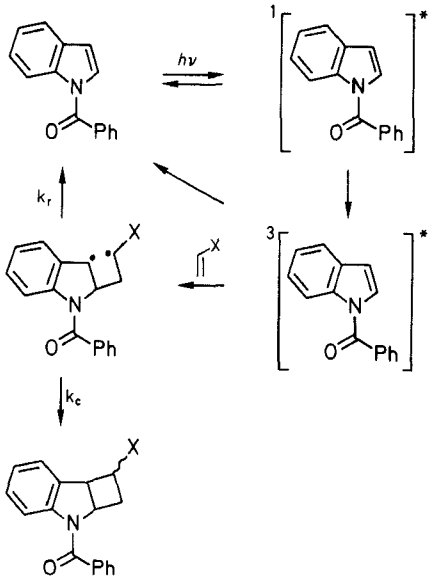
Photochemistry Unit, Department of Chemistry, The University of Western Ontario, London, Ontario, N6A 5B7, Canada

Received 14 August 1991; revised 30 September 1991

The ability of a series of nitrogen-substituents to activate the cycloaddition photochemistry of indoles has been examined; the *N*-substituents were chosen in order to enable their removal following cycloaddition under mild neutral, acidic or basic conditions. *N*-Substituted indoles, **1a–g**, were prepared in which the *N*-substituent is COPh, CO_2Et, $CO_2CH_2CH_2SiMe_3$, $CO_2CH_2CH_2CN$, CO_2Bu-*t*, CO_2Ph, and CO_2CH_2Ph, respectively. Under direct irradiation with ultraviolet light the photochemical cycloaddition reaction of compounds **1a–g** with cyclopentene yields cyclobutane fused indolines resulting from bonding of the alkene termini to the 2- and 3-positions of the indole. The reaction proceeds with chemical yields in the range 32%–80% and photochemical efficiencies in the range 0.00028–0.054. When the reaction is sensitized with acetophenone the chemical yields are raised to 64–95%. This improvement arises from avoidance of competing singlet excited state derived photo-Fries rearrangement. The silylethoxycarbonyl group of photoadducts derived from **1c** can be removed by treatment of the adduct with fluoride ion in dichloromethane, the *tert*-butyloxycarbonyl group of adducts derived from **1e** by treatment with trifluoroacetic acid at room temperature, the benzyloxycarbonyl group of adducts derived from **1g** by hydrogenolysis, and the cyanoethoxycarbonyl group of adducts derived from **1d** with alcoholic carbonate at room temperature. All of these deprotection reactions proceed in very high yield. Removal of the phenoxycarbonyl group of adducts derived from **1f** and the ethoxycarbonyl group of adducts derived from **1b** required treatment with hot concentrated base and the yields were lower, while the benzoyl group of adducts derived from **1a** was stable to hot concentrated acid or base and could be removed only by treatment with lithium aluminum hydride.

Introduction

Ultraviolet light irradiation of *N*-aroylindoles and *N*-acetylindole in the presence of alkenes leads to cyclobutane formation by addition of the alkene terminii to the 2- and 3-positions of the 5-membered ring of the heterocycle.[2,3] The analogous reaction does not proceed for indole.[2–4] We have examined the mechanism of this reaction.[5–11] We have found that lowest singlet excited state of *N*-aroylindoles is a charge-transfer state[5,6] and is not involved in cycloaddition. Direct irradiation of *N*-benzoylindole or *N*-ethoxycarbonylindole results in photo-Fries rearrangement,[7] and production of 3-benzoylindole or 3-ethoxycarbonylindole, respectively, as the major products. If alkenes are present then they react with the triplet excited state[8] of the indole derivative to form biradicals[9] which either ring close to cycloadducts or revert to ground state starting materials.[8,9] For *N*-benzoylindole the biradicals are apparently formed by bonding of the 2-position of the indole to the less substituted end of the alkene (Scheme 1).[10,11]



Scheme 1

Activation of indole photochemistry by *N*-carbonyl substitution allows access to indoline products of potential synthetic utility. Selective cleavage of one of the bonds of the newly formed cyclobutane ring could provide a new route to 2-substituted, 3-substituted, or 2,3-disubstituted indoles. Alternatively, oxidation of the indoline products to indole fused cyclobutenes would provide a new means of generating indole-2,3-quinodimethanes by electrocyclic ring opening. For some applications removal of the activating group from the indoline nitrogen atom would be necessary. The need therefore arises for activating groups which, following the photochemistry, can be removed under mildly acidic, basic or neutral conditions consistent with the survival of other functionality in the rest of the molecule. Described here are the results of a study in which the chemical and photochemical efficiencies with which a variety of groups activate the cycloaddition photochemistry of the indole ring were examined; in addition, the ease and the efficiency with which the activating groups could be removed from the indoline nitrogen atom of the cycloaddition products were investigated.

Results and Discussion

Selection and Preparation of *N*-Substituted Indoles

The photochemical cycloaddition reaction of *N*-benzoylindole (**1a**) and *N*-ethoxycarbonylindole (**1b**) with cyclopentene has previously been studied by us in some detail.[5-11] These compounds were therefore selected as standards for comparison with the other *N*-carbonyl substituted indoles to be investigated. They were readily prepared from indole by the method of Illi in which the indolyl anion is generated in the presence of ethyl chloroformate or benzoyl chloride by phase-transfer catalysis.[9,12]

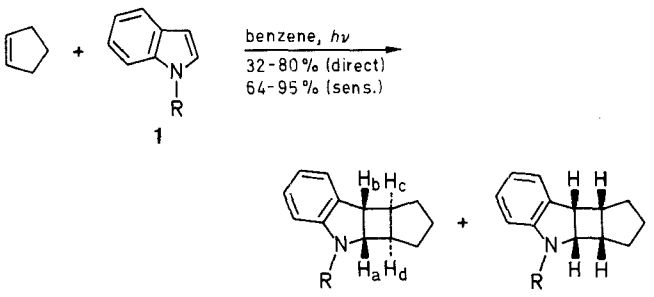
The compounds *N*-[(2-trimethylsilylethoxy)carbonyl]indole, (**1c**), *N*-[(2-cyanoethoxy)carbonyl]indole (**1d**), *N*-*tert*-butoxycarbonylindole (**1e**), *N*-phenoxycarbonylindole (**1f**), and *N*-benzyloxycarbonylindole (**1g**) were chosen as substrates because of the anticipated ease of removal of the *N*-substituent from the indoline following the photochemistry.

Indoles in which the nitrogen atom is protected by a 2-(trimethylsilyl)ethoxycarbonyl group are reported to be converted to the parent indole by treatment with fluoride ion under anhydrous conditions,[13] while urethanes containing the *N*-(2-cyanoethoxy)carbonyl function present in **1d** regenerate the parent amine upon treatment with carbonate.[14] The *tert*-butoxycarbonyl group is widely used as a nitrogen protecting group in amino acid chemistry and has also been reported for protection of the indole nitrogen;[13,15] it is removed by thermolysis,[16] base hydrolysis,[16] or by treatment with trifluoroacetic acid at room temperature.[13] Similarly, the benzyloxycarbonyl group was chosen because of its ready removal from the nitrogen of amino acids by hydrogenolysis.[17] Compound **1f** was chosen because it was anticipated that the phenoxy group would be more easily removed under basic conditions than the ethoxy group of **1b**; compound **1f** was also required as a starting material for the preparation of *N*-[(2-trimethylsilylethoxy)carbonyl]indole (**1c**).

Phenoxycarbonylindole **1f** and benzyloxycarbonylindole **1g** were prepared in a similar manner to **1a** and **1b** by reaction of either phenyl chloroformate or benzyl chloroformate with indole in the presence of a phase transfer catalyst and base.[12] *N*-[(2-Cyanoethoxy)carbonyl]indole (**1d**) was prepared by alcoholysis of indole-1-carboxylic acid anhydride[18] with 2-cyanoethanol. *N*-[(2-Trimethylsilylethoxy)carbonyl]indole was prepared by ester exchange of phenoxycarbonylindole **1f**, with 2-(trimethylsilyl)ethanol catalyzed by triethylamine.

Photochemical Cycloaddition Reaction of 1a–g with Cyclopentene

We have previously reported that ultraviolet light irradiation of **1a** with cyclopentene in benzene solution yields mainly the cis-anti-cis adduct **2a** and minor amounts of the cis-syn-cis adduct **3a**.[9] Similarly, **1b** yields mainly adduct **2b** and minor amounts of the stereoisomer **3b**.[9] At room temperature the cyclobutane methine H_a in these adducts generally appears in the ^1H NMR spectrum recorded at 200 MHz as a multiplet below $\delta = 4$ which is broadened due to slow rotation of the carbonyl group on the adjacent nitrogen atom. Methine H_a is coupled to H_b (J_{ab} = ca. 8 Hz) and also to H_d; the magnitude of J_{ad} allows assignment of stereochemistry to the adducts since it is smaller (ca. 2 Hz) for the anti adducts **2a** and **2b**, and larger (ca. 7–8 Hz) for the syn adducts **3a** and **3b**.



1 R	2 R	3 R
a COPh	**a** COPh	**a** COPh
b CO_2Et	**b** CO_2Et	**b** CO_2Et
c $CO_2CH_2CH_2SiMe_3$	**c** $CO_2CH_2CH_2SiMe_3$	**c** $CO_2CH_2CH_2SiMe_3$
d $CO_2CH_2CH_2CN$	**d** $CO_2CH_2CH_2CN$	**d** $CO_2CH_2CH_2CN$
e CO_2Bu-*t*	**e** CO_2Bu-*t*	**e** CO_2Bu-*t*
f CO_2Ph	**f** CO_2Ph	**f** CO_2Ph
g CO_2CH_2Ph	**g** CO_2CH_2Ph	**g** CO_2CH_2Ph
	h H	**h** H
	i CH_2Ph	**i** CH_2Ph

Direct ultraviolet light irradiation of each of the *N*-carbonyl substituted indoles **1c–g** in benzene solution containing cyclopentene gave in all cases the corresponding anti adducts **2c–g** along with small amounts of the corresponding syn adducts **3a–g**. The anti adducts **2c–g** were isolated in pure form by crystallization from the mixture of adducts **2c–g** and **3c–g** obtained by chromatography of the reaction mixture. The structures of the anti adducts **2c–g** were readily determined by compa-

rison of their ^{1}H NMR spectra with those of **2a** and **2b**, and were confirmed by mass spectroscopy as well as by removal of the *N*-carbonyl substituent (see below) which yields the previously characterized anti amine **2h**. The syn adducts **3c–g** were not obtained in pure form; their structures were assigned by inspection of the ^{1}H NMR spectra of the mixture of syn and anti adducts (enriched in the syn adducts) obtained from the mother liquors after crystallization of the anti adducts. The structures of the syn adducts were confirmed by removal of the *N*-substituent which yields the previously characterised syn amine **3h**.

The chemical yields of the adducts were determined at high conversions by gas chromatographic analysis of the crude reaction mixtures using a calibrated internal standard and also by weighing of the mixture of syn and anti adducts following isolation by liquid chromatography. The yields are shown in Table 1 and vary from 32% for **1a** to 80% for **1e**. The quantum yields for formation of adducts **2** and **3** from each of the acylindoles **1a–g** were also measured and these are shown in Table 1. The quantum yields were determined at low conversions, in order to avoid secondary photochemistry of the products, and at high alkene concentrations. We have previously shown that the cycloaddition reaction of *N*-benzoylindole and *N*-ethoxycarbonylindole is a triplet excited state process;[8] at sufficiently high alkene concentrations all of the triplet excited states produced are intercepted so that the quantum yield measured is governed by the efficiency of intersystem crossing of the indole derivative and the degree to which the intermediate biradicals formed proceed to products instead of reverting to the ground state starting materials (Scheme 1).[8] More quantitatively, this quantum yield is equal to $\Phi_{isc}[k_c/(k_c + k_r)]$, where Φ_{isc} is the quantum yield of intersystem crossing and k_c and k_r are defined in Scheme 1 such that $k_c/(k_c + k_r)$ is the fraction of the biradicals which proceed to the products. The quantum yields shown in Table 1 are all very low and correspond to formation of products from less than 5% of the excited states initially produced by light absorption. In the case of **1b** the quantum yield of the reaction sensitized by acetophenone was also measured under conditions where all of the incident light was absorbed by the sensitizer, all of the sensitizer triplet excited states were quenched by the indole derivative and essentially all of the indole triplet excited states were intercepted by cyclopentene. The sensitized quantum yield of adduct formation was 0.019, which corresponds to $k_c/(k_c + k_r)$. In the absence of sensitizer the corresponding quantum yield at high alkene concentration was 0.0061 and the difference can be used to derive an approximate value of the quantum yield of intersystem crossing , Φ_{isc} of 0.32. This is similar to the value previously measured for **1a** in the same solvent by the triplet counting procedure.[8]

We have previously shown for **1a** and **1b** that photo-Fries rearrangement to yield, predominantly, 3-acylindoles competes with cycloaddition of the indole with alkenes.[7] Inspection of the reaction mixtures obtained by irradiation of **1c–g** in the presence of cyclopentene by coupled gas chromatography mass spectroscopy (GC-MS) indicated that photo-Fries rearrangement also occurred for **1d, 1e** and **1g**, but apparently not for **1c** and **1f**. The photo-Fries products were not isolated or fully characterized in this work. However, the chemical yields of the photo-Fries products, as estimated by uncalibrated GC analysis, were comparable in many cases to that of the cycloaddition product. Consequently, interference from this reaction would appear to be the main cause of the lower chemical yields of cycloadduct formation seen for some of the indole derivatives in Table 1.

Table 1. Chemical and Quantum Yield Data for Photochemical Cycloaddition of Indoles **1a–g** with Cyclopentene

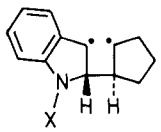
Substrate	λ_{irrad}[a] (nm)	Φ_{adduct}[b]	Yield (%)[c] (conversion)	Yield (%)[d] (conversion)	Yield (%)[e] (conversion)	Ratio **2/3**
1a	313	0.0540	32 (95)	32 (94)	95 (68)	2.9
1b	295	0.0061	64 (61)	47 (86)	95 (81)	6.9
1c	295	0.0039	74 (88)	75 (85)	92 (69)	8.8
1d	295	0.0028	66 (58)	68 (58)	95 (58)	4.3
1e	295	0.0037	80 (59)	61 (68)	64 (82)	5.7
1f	300	0.0038	52 (61)	58 (58)	75 (81)	3.2
1g	295	0.0043	44 (77)	46 (76)	88 (89)	4.5
1g	310	0.0057				
1g	320	0.0078				

[a] Wavelength of light used for quantum yield determination. The monochromator bandwidth was 5 nm.
[b] Quantum yield of formation of the adducts **2a–g** and **3a–g**.
[c] Calibrated GC yield of adducts **2a–g** and **3a–g** formed under direct irradiation of **1a–g** on a 1 g scale. Yields are based upon converted **1a–g**, as estimated by calibrated GC.
[d] Isolated yield of adducts **2a–g** and **3a–g** formed under direct irradiation of **1a–g** on a 1 g scale. Yields are based on converted **1a–g** as estimated from the weight of recovered **1a–g**.
[e] Calibrated GC yield of adducts **2a–g** and **3a–g** formed under sensitized irradiation of **1a–g** on a 25 mg scale. Yields are based on converted **1a–g** as estimated by calibrated GC. For **1a**, **1b** and **1d** the yields shown represent lower limits.

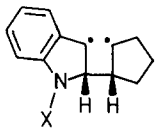
In our previous study of the photo-Fries rearrangement of **1a** and **1b** we found that the reaction is wavelength dependent.[7] This was also found to be the case for **1g**; as the wavelength of the excitation light was increased the proportion of the photo-Fries product formed decreased. This was reflected in an increased quantum yield of cycloaddition product formation, as shown in Table 1. The wavelength effect suggests that the photo-Fries rearrangement proceeds from an upper excited state or from a vibrationally hot lowest excited state which could, in principle, be of singlet or triplet multiplicity. In fact, when benzene solutions containing cyclopentene and each of the indoles **1a–g** were sensitized with acetophenone, little or no photo-Fries products were observed and cycloaddition was the dominant reaction.[19] This suggests that whereas the cycloaddition reaction proceeds from the lowest triplet excited state, the photo-Fries reaction must proceed from an upper singlet excited state or a vibrationally hot form of the lowest singlet excited state, although it is also possible that it could proceed from an upper triplet excited state of energy intermediate between that of the singlet excited state of the indole derivatives (*circa* 98 kcal/mol from absorption spectra) and the triplet energy of the sensitizer (74 kcal/mol). Most importantly, for

synthetic applications, this observation implies that the photo-Fries reaction can be suppressed in favor of the cycloaddition reaction by sensitization. This was indeed found to be the case; when the indoles **1a–g** were sensitized with acetophenone the chemical yield of the cycloadducts rose dramatically, in some cases doubling as shown in Table 1, and little or no photo-Fries rearrangement products were observed.

The ratio of anti to syn products **2** to **3** was found to vary somewhat with the nature of the nitrogen substituent. This variation is shown in Table 1 and presumably reflects the effect of the nitrogen substituent on either the relative rates of formation of the diastereoisomeric biradical intermediates **4** and **5**, or on the relative efficiencies with which these two biradicals proceed to products rather than reverting to the starting materials.



4



5

Table 2. Deprotection of Cycloadducts **2a–g** and **3a–g** to give **2h** and **3h**

Cycloadduct	Reaction Conditions	Yield[a] (%)
2a + **3a**	$LiAlH_4/Et_2O$	41
2b	$KOH/MeOH–H_2O$ (2 : 1) reflux, 3 h	57
2c	Bu_4NF/THF, r.t. 107 min	92
2d	1. MeOH/10% aq K_2CO_3 r.t., 40 min; 2. 1 N HCl, Δ	81
2e	TFA, r.t., 90 min	75
2f + **3f**	1. NaOH/THF-H_2O (1 : 1), reflux, 5 h; 2. conc HCl, Δ	56
2g	10% Pd-C/1,4-cyclohexadiene/EtOH	97

[a] Isolated yields **2h**, or of **2h** and **3h**. The yield for **2a** and **3a** is taken from reference 9.

Removal of Activating Groups from 2a–g and 3a–g

The cycloadducts **2a–g** and **3a–g** were converted to the corresponding free amines **2h** and **3h** using the mildest procedure possible. The optimum procedures and the yields of **2h** and **3h** obtained are shown in Table 2. It was possible to deprotect the indoline nitrogen under neutral conditions in high yield by treatment of a mixture of **2c** and **3c** with fluoride ion and by hydrogenolysis of a mixture of **2g** and **3g**. The mildest acidic condition found was treatment of **2e** and **3e** with trifluoroacetic acid at room temperature and the mildest basic condition was treatment of **2d** and **3d** with aqueous methanolic potassium carbonate at room temperature; both of these result in deprotection in good yield. Deprotection of **2b** and **3b**, and **2f** and **3f** was more difficult and required treatment with hot concentrated base; the harsher conditions also led to lower yields. As reported previously, **2a** and **3a** are resistant to acid or base hydrolysis;[9] treatment with lithium aluminum hydride does, however, yield the free amines **2h** and **3h** in low yield along with the corresponding *N*-benzylamines **2i** and **3i**.[3,9]

Conclusions

A variety of *N*-acyl substituents activate the photochemical cycloaddition reaction of indoles with alkenes. The yields are good if the reaction is sensitized so that competing photo-Fries rearrangement can be avoided. Use of the appropriate *N*-acyl substituent allows removal of the activating group from the product under mild neutral, acidic or basic conditions.

Unless otherwise specified, reagents were commercial samples (Aldrich Chemical Co.) and were used as received. All irradiations were performed using spectroscopic grade benzene as the solvent. *N*-Ethoxycarbonylindole (**1b**),[12] *N*-benzoylindole (**1a**),[12] and 1-indolecarboxylic acid anhydride[18] were prepared by the literature procedures.

Table 3. Physical and Spectroscopic Data for Cycloadducts **2**

Compound	mp (°C)	HRMS, M^+		^1H NMR ($CDCl_3$, 200 MHz) δ, J (Hz)
		Calc.	Found	
2a	124–126	289.14665	289.14653	1.17–1.79 (m, 6H), 2.66 (H_c, dt, J_{cd} = 6.8, J_{bc} = 2.8), 2.85 (H_d, dt, J_{cd} = 6.8, J_{ad} = 2.8), 3.33 (H_b, dd, J_{ab} = 7.8, J_{bc} = 2.8), 3.92 (H_a, dd, J_{ab} = 7.8, J_{ad} = 2.8), 7.05–7.24 (3H, m), 7.45 (5H, m), 8.29 (1H, m)
2b	44–45	257.14157	257.14250	1.29 (3H, t, J = 7), 1.40–1.64 (2H, m), 1.78–1.98 (4H, m), 2.64 (H_c, dt, J_{cd} = 6.8, J_{bc} = 2.8), 2.80 (H_d, m), 3.26 (H_b, dd, J_{ab} = 7.7, J_{bc} = 2.8), 4.16 (H_a, dd, J_{ab} = 7.7, J_{ad} = 2.5), 4.25 (2H, q, J = 7), 6.95 (1H, m), 7.09–7.22 (2H, m), 7.88 (1H, m)
2c	58.5–60	329.18110	329.18175	0.02 (9H, s), 0.99 (2H, m), 1.48 (2H, m), 1.78 (4H, m), 2.64 (H_c and H_d, m), 3.22 (H_b, dd, J_{ab} = 8, J_{bc} = 2.7), 4.14 (H_a, dd, J_{ab} = 8, J_{ad} = 2.7), 4.2 (2H, m), 6.9 (1H, m), 7.04–7.16 (2H, m), 7.84 (1H, m).
2d	101–102	282.13682	282.13714	1.54 (2H, m), 1.77–1.95 (4H, m), 2.68 (H_c and H_d, m), 2.75 (2H, m), 3.3 (H_b, dd, J_{ab} = 7.6, J_{bc} = 2.6), 4.20 (H_a, dd, J_{ab} = 7.6, J_{ad} = 2.5), 4.33–4.53 (2H, m), 7.00 (1H, m), 7.12–7.20 (2H, m), 7.85 (1H, m)
2e	88–90	285.17287	285.17288	1.53 (9H, s), 1.77–1.90 (6H, m), 2.65–2.70 (H_c and H_d, m), 3.23 (H_b, dd, J_{ab} = 7.9, J_{bc} = 2.8), 4.08 (H_a, dd, J_{ab} = 7.9, J_{ad} = 1.9), 6.90–7.3 (3H, m), 7.86 (1H, m)
2f	90–92	305.14157	305.14120	1.53 (2H, m), 1.80–2.16 (4H, m), 2.74 (H_c, dt, J_{bc} = 3, J_{cd} = 7), 2.98 (H_d, dt, J_{cd} = 7, J_{ad} = 2), 3.36 (H_b, dd, J_{ab} = 8, J_{bc} = 3), 4.40 (H_a, dd, J_{ab} = 8, J_{ad} = 2), 7.02 (1H, m), 7.15–7.28 (5H, m), 7.39 (2H, m), 7.90 (1H, m)
2g	72–73	319.15722	319.15679	1.49 (2H, m), 1.71–1.90 (4H, m), 2.65 (H_c, dt, J_{cd} = 7.0, J_{bc} = 2), 2.74 (H_d, dt, J_{cd} = 7.0, J_{ad} = 2.2), 3.27 (H_b, dd, J_{ab} = 8, J_{bc} = 2), 4.20 (H_a, dd, J_{ab} = 8, J_{ad} = 2.2), 5.14–5.31 (2H, m), 6.96 (1H, m), 7.10–7.36 (7H, m), 7.91 (1H, m)

General Irradiation Procedures for Indole Derivatives 1a–g:

(a) Direct Irradiations. The indole derivative (1 g), an inert internal standard (0.1 g) and freshly distilled cyclopentene (20 mL) were dissolved in benzene (220 mL) which had previously been purged with nitrogen gas. This concentration of the alkene was chosen so as to ensure that the triplet excited state of the indole derivative was efficiently intercepted. For this to be so k_r[alkene] must be greater than k_d, where k_r is the rate constant for reaction of the triplet excited state with alkene and k_d is the rate constant for decay of the triplet excited state to the ground state. Values of these rate constants were estimated from data in references 8 and 9. The concentration of the indole derivative used was chosen in order to ensure that the optical density of the solution at the irradiating wavelengths was greater than unity. In MeOH solution compounds **1b–e** and **1g** had values of ε_{300} of *ca.* 50, while for **1a** ε_{300} was *ca.* 6000 and for **1f** ε_{300} was *ca.* 140. The internal standard used was tetracosane in the cases of **1a, 1f,** and **1g**, docosane in the cases of **1b, 1c,** and **1d**, and eicosane in the case of **1e**. The mixture was stirred under nitrogen and irradiated with light from a 450 Watt Hanovia medium pressure mercury lamp housed in a Pyrex water jacket which was immersed in the solution to be irradiated. The progress of the reaction was monitored by GC; when the conversion of starting material became slow (typically this occured after 25–100 h at conversions in the range 58–95%) the irradiation was terminated and the solvent removed under reduced pressure to yield an oil. Purification by liquid chromatography on silica gel (eluent Et_2O/hexanes) allowed recovery of the unconverted indole derivative and yielded a mixture of the syn and anti cycloadducts **2** and **3**. GC yields were calibrated against pure **1** and the isolated mixture of **2** and **3**. Isolated yields were determined by weighing **1** and the mixture of **2** and **3** following their isolation by chromatography. The yields are shown in Table 1. The anti adducts **2** were obtained in pure form (homogeneous by TLC and GC) by crystallization of the mixture of **2** and **3** obtained from chromatography of the reaction mixture. The mother liquors contained the syn adduct **3** in concentrated form contaminated by the anti adduct **2**. Physical and spectroscopic data for **2** are given in Table 3. The syn adduct **3** was characterized by ^{1}H NMR spectroscopy of the samples obtained by evaporation of the mother liquors remaining from crystallization of **2**, by GC-MS, and by conversion to the known[9] indoline **3h** (see below). The ^{1}H NMR spectra (in $CDCl_3$), of **3a–g** were very similar to those of **2a–g**, the major difference being in the appearance and chemical shifts of the protons H_a, H_b, H_c and H_d. The latter were as follows: **3a** 3.04 (H_c and H_d, m), 4.03 (H_b, t, $J_{ab} = J_{bc}$ = 8.4 Hz), 4.64 (H_a, **t**, $J_{ab} = J_{ad}$ = 8.4 Hz); **3b** 3.05 (H_c, m), 3.09 (H_d, m), 4.00 (H_b, t, $J_{ab} = J_{bc}$ = 8.3 Hz), 4.83 (H_a, t, $J_{ab} = J_{ad}$ = 8.3 Hz); **3c** 3.09 (H_c and H_d, m), 4.01 (H_b, t, $J_{ab} = J_{bc}$ = 8.3 Hz), 4.82 (H_a, t, $J_{ab} = J_{ad}$ = 8.3 Hz); **3d** 3.27 (H_c and H_d, m), 4.03 (H_b, t, $J_{ab} = J_{bc}$ = 8.7 Hz), 4.87 (H_a, t, $J_{ab} = J_{ad}$ = 8.7 Hz); **3e** 3.05 (H_c and H_d, m), 3.98 (H_b, t, $J_{ab} = J_{bc}$ = 8.0 Hz), 4.77 (H_a, t, $J_{ab} = J_{ad}$ = 8.0 Hz); **3f** 3.16 (H_c and H_d, m), 4.11 (H_b, t, $J_{ab} = J_{bc}$ = 8.2 Hz), 5.07 (H_a, t, $J_{ab} = J_{ad}$ = 8.2 Hz); **3g** 2.90 (H_c and H_d, m), 3.89 (H_b, t, $J_{ab} = J_{bc}$ = 8.5 Hz), 4.76 (H_a, t, $J_{ab} = J_{ad}$ = 8.5 Hz). In the cases of **2a–g** and **3a–g** the signal assigned to H_a was broadened because of slow rotation of the *N*-acyl group.[9,10] The signal was sharpened in order to allow measurement of the coupling constants by rerecording the spectrum at higher temperatures, although this necessitated a change of solvent to DMSO-d_6. The coupling constants were also measured in $CDCl_3$ by rerecording the spectra at lower temperatures; under these conditions the broad signal assigned to H_a was resolved into two separate, sharp signals corresponding to the syn and anti conformations of the *N*-acyl substituent.

(b) Sensitized Irradiations. The indole derivative (25 mg), freshly distilled cyclopentene (0.2 mL), acetophenone (0.008 mL) and an internal standard (see (a) above, 10 mg) were dissolved in benzene (1 mL) and placed in a Pyrex tube. The tube was flushed with nitrogen, sealed and placed alongside a 400 Watt Hanovia medium pressure mercury lamp housed in a water cooled Pyrex jacket. The reaction was monitored by GC and terminated when product formation had reached a maximum. The conversion of **1** and the yields of **2** and **3** were determined by GC using the internal standard as in (a) above. The results are given in Table 1.

(c) Quantum Yield Determintions. A sample (3.0 mL) of a benzene solution containing **1** (0.01–0.03 M), cyclopentene (2 M) and a known weight of an internal standard (see (a) above) was degassed by several freeze-pump-thaw cycles to a residual pressure of 1.5×10^{-4} mbar. This solution was irradiated for a known time with a monochromatic light source of known intensity.[20] Conversions of **1** were limited to < 5% to avoid light absorption by the products. The absolute amounts of the adducts formed were determined by GC using the internal standard as in (a) above.

***N*-[(2-Trimethylsilylethoxy)carbonyl]indole (1c):**

An alternative procedure to that described in the literature was used.[13] A solution of **1f** (1.01 g, 4.26 mmol) and 2-(trimethylsilyl)ethanol (0.72 g, 6.1 mmol) in dry Et_3N (10 mL) was heated to reflux (90 °C) under N_2 for 72 h. After cooling to r.t., Et_2O (50 mL) was added and the solution was washed with water (2 × 100 mL). Drying ($MgSO_4$) and evaporation of the ether gave crude **1c** as an oil (1.23 g). Pure **1c** (0.73 g, 66%) was obtained after purification of the crude material on a silica gel column eluted with hexanes/Et_2O (9:1).

^{1}H NMR (200 MHz): δ = 0.09 [s, 9 H, $Si(CH_3)_3$], 1.26 (t, J = 8 Hz, 2 H, $SiCH_2$, 4.51 (t, J = 8 Hz, 2 H, OCH_2), 6.56 (d, J = 4 Hz, 1 H, H-3_{indole}), 7.18–7.35 (m, 2 H), 7.53–7.61) (m, 2 H), 8.19 (d, J = 8 Hz, 1 H, H-7_{indole}).

IR (neat): ν = 1742 (C=O), 1244 cm^{-1} (C–O–C).

HRMS: M^+, $C_{14}H_{19}NO_2Si$, calcd 261.11847, found 261.11821.

***N*-[(2-Cyanoethoxy)carbonyl]indole (1d):**

A solution of 1-indolecarboxylic acid anhydride (2.02 g, 6.64 mmol) in 2-cyanoethanol (2.08 g, 29.3 mmol) containing octadecane (0.084 g) as an internal standard was stirred and heated at 75 °C under N_2. After 1 h, GC indicated that the reaction was complete. The solution was diluted with water (100 mL) and extracted with CH_2Cl_2 (3 × 30 mL). Drying (Na_2SO_4) and evaporation of the CH_2Cl_2 gave crude **1d** (2.86 g) which was purified by liquid chromatography on a silica gel column eluted with hexanes/Et_2O (5:5) to give pure **1d** (0.88 g, 62%) as an oil.

^{1}H NMR (200 MHz): δ = 2.84 (t, J = 6 Hz, 2 H, CH_2CN), 4.57 (t, J = 6 Hz, 2 H, OCH_2), 6.18 (d, J = 4 Hz, 1 H, H-3_{indole}), 7.22–7.39 (m, 2 H), 7.55–7.58 (m, 2 H), 8.16 (d, J = 8 Hz, 1 H, H-7_{indole}).

IR (neat): ν = 1743 (C=O), 2255 (CN), 1211 cm^{-1} (C–O–C).

HRMS: M^+, $C_{12}H_{10}N_2O_2$, calcd 214.07422, found 214.07423.

***N*-*tert*-Butoxycarbonylindole (1e):**

To indole (1.20 g, 10.2 mmol) in toluene (40 mL) was added 50% aq NaOH (17 mL) and $(Bu)_4NBr$ (1.00 g, 3.1 mmol). The two-phase system was stirred under N_2 in an ice bath while di-*tert*-butyl carbonate (4.36 g, 25 mmol) in toluene (12 mL) was added over 30 min. After further stirring (2 h) the organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with H_2O (2 × 200 mL), dried (Na_2SO_4) and evaporated to give crude **1e** (2.8 g). The crude product was purified by liquid chromatography on a short silica gel column eluted with hexanes/EtOAc (9:1) to yield pure **1e** (2.03 g, 91%) as an oil.

^{1}H NMR (200 MHz): δ = 1.67 [s, 9 H, $C(CH_3)_3$], 6.56 (d, J = 4 Hz, 1 H, H-3_{indole}), 7.14–7.34 (m, 2 H), 7.53–7.60 (m, 2 H), 8.14 (d, J = 8 Hz, 1 H, H-7_{indole}).

IR (neat): ν = 1743 (C=O), 1252 cm^{-1} (C–O–C).

HRMS: M^+, $C_{13}H_{15}NO_2$, calcd 217.11027, found 217.10991.

***N*-Phenoxycarbonylindole (1f):**

To an ice cooled, stirred suspension of indole (2 g, 17.1 mmol), powdered NaOH (2 g, 0.050 mmol) and Bu_4NBr (0.16 g, 0.50 mmol) in dry CH_2Cl_2 (25 mL) was added over a period of 1 h a solution of phenyl chloroformate (4.19 g, 0.027 mol) in CH_2Cl_2 (25 mL). After further stirring (2 h), water (50 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 30 mL). The combined CH_2Cl_2 layers were washed with H_2O (2 × 50 mL) and dried (Na_2SO_4). Removal of

the solvent gave pink crystals which were recrystallized from Et_2O to yield white crystals of **1f** (3.05 g, 75%): mp 94–95 °C (lit.[18] mp 95–96 °C).

^1H NMR (200 MHz): δ = 6.69 (d, J = 4 Hz, 1 H, H-3_{indole}), 7.24–7.36 (m, 5 H), 7.40–7.52 (m, 2 H), 7.61 (m, 1 H), 7.75 (m, 1 H), 8.24 (d, J = 8 Hz, 1 H, H-7_{indole}).

HRMS: M^+, $C_{15}H_{11}NO_2$, calcd 237.07897, found 237.07845.

***N*-Benzyloxycarbonylindole (1 g):**

To a stirred, ice cooled suspension of indole (12.0 g, 0.102 mol), Bu_4NBr (1.16 g, 3.6 mmol) and powdered NaOH (5.24 g, 0.13 Mol) in CH_2Cl_2 (100 mL) was added over a period of 50 min, a solution of benzyl chloroformate (15 mL, 0.11 mol) in CH_2Cl_2 (50 mL). The mixture was stirred for a further 10 min, diluted with H_2O (200 mL) and extracted with CH_2Cl_2 (2 × 100 mL). The combined extracts were dried (Na_2SO_4) and evaporated to give crude **1 g** as an oil (25.7 g) which solidified on cooling in ice. Recrystallization of a portion (16.50 g) of this solid from Et_2O gave pure **1 g** (13.86 g, 84%); mp 44–45 °C).

^1H NMR (200 MHz): δ = 5.45 (s, 2 H, OCH_2), 6.59 (d, J = 4 Hz, 1 H, H-3_{indole}), 7.18–7.65 (m, 9 H), 8.15 (d, J = 8, 1 H, H-7_{indole}).

IR (Nujol): ν = 1746 (C=O), 1240, 1211 cm^{-1} (C–O–C).

HRMS: M^+, $C_{16}H_{13}NO_2$, calcd 251.09462, found 251.09443.

***cis-anti-cis*- and *cis-syn-cis*-1,2,3,3a,3b,4,8b,8c-Octahydrocyclopenta[3,4]cyclobuta[1,2-b]indole (2 h and 3 h):**

By Hydrolysis of anti-Adduct **2b**. A solution of **2b** (56.0 mg, 0.22 mol) in MeOH/H_2O (2:1 by volume, 3.0 mL) saturated with KOH was heated to reflux for 3 h. After cooling to r.t., conc. HCl (5 mL) was added and the solution was briefly heated to effect decarboxylation. H_2O (10 mL) was added and the cooled acidic solution was extracted with Et_2O (2 × 30 mL). The aqueous solution was neutralized with sat. aq $NaHCO_3$ and extracted with Et_2O (3 × 20 mL). The combined ether extracts were dried ($MgSO_4$) and evaporated to the yield known[9] indoline **2 h** (23.0 mg, 57%), homogeneous by TLC and GC.

By Hydrolysis of anti-Adduct **2c**. To a stirred solution of **2c** (56.0 mg, 0.170 mmol) in dry THF (1 mL) was added a solution of Bu_4NF (0.17 mL of a 1.0 M solution in THF). The mixture was stirred at r.t. for 107 min. H_2O (20 mL) was added and the solution obtained was extracted with Et_2O (3 × 20 mL). The combined extracts were dried ($MgSO_4$) and evaporated to give **2 h** (29.0 mg, 92%), homogeneous by TLC and GC. The *syn*-adduct **3h** was obtained from hydrolysis of the mixture of adducts **2c** and **3c**. Separation of **2h** and **3h** was achieved on a silica gel column (hexanes/Et_2O = 75:25).

By Hydrolysis of anti-Adduct **2d**. To a solution of **2d** (37 mg, 0.13 mmol) in MeOH (2 mL) was added a 10% aq K_2CO_3 (1 mL). The mixture was stirred for 40 min at r.t., acidified with 1 N HCl solution and briefly heated to effect decarboxylation. The solution was made basic by addition of sat. aq $NaHCO_3$ and extracted with Et_2O (4 × 10 mL). The combined extracts were dried ($MgSO_4$) and evaporated to yield **2 h** (20 mg, 81 %), homogeneous by TlC and GC.

By Hydrolysis of anti-Adduct **2e**. The adduct **2e** (25.0 mg, 0.088 mmol) was dissolved in trifluoroacetic acid (2 mL). After 90 min, H_2O (5 mL) was added. The acidic solution was extracted with Et_2O (2 × 10 mL) and neutralized with sat. aq. $NaHCO_3$. The basic solution was extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic phases were washed with H_2O (50 mL) and dried (Na_2SO_4). Evaporation of the solvent yielded **2h** (12.2 mg, 75%), homogeneous by TLC and GC. Hydrolysis of a mixture of the *anti* and *syn* adducts under the same conditions yielded a mixture of **2h** and **3h** which could be separated by chromatography (Et_2O/hexanes).

By Hydrolysis of anti-Adducts **2f** *and* **3f**. A sample (58.0 mg, 0.190 mmol) of a mixture of **2f** and **3f** was dissolved in aq THF (1:1, 4 mL) saturated with NaOH and refluxed for 5 h. The mixture was cooled and acidified with conc. HCl. Following brief heating to effect decarboxylation the cooled solution was neutralized by addition of sat. aq $NaHCO_3$ and extracted with Et_2O (3 × 20 mL). The combined extracts were dried ($MgSO_4$) and evaporated to give a solid (40 mg). Chromatography (Et_2O/hexanes) gave **2h** (17.5 mg, 50%) and **3h** (2.0 mg, 6%), both homogeneous by TLC and GC.

By Hydrolysis of anti-Adducts **2f** *and* **3f**. A sample (58.0 mg, 0.190 mmol.) of a mixture of **2f** and **3f** was dissolved in aq THF diene (0.68 g, 8.46 mmol) and 10% Pd-C (0.10 g). After 25 min, GC indicated that the reaction was complete. The solution was filtered, the catalyst was washed with Et_2O (100 mL) and the combined filtrates evaporated to yield **2h** (101.0 mg, 97%) homogeneous by TLC and GC.

(1) Contribution number 443 from the Photochemistry Unit, University of Western Ontario
(2) Julian, D.R.; Foster, R. *J. Chem. Soc., Chem. Commun.* **1973**, 311.
(3) Ikeda, M.; Ohno, K.; Mohri, S.; Takahashi, M.; Tamura, Y. *J. Chem. Soc., Perkin Trans. 1*, **1984**, 405.
(4) Yamasali, K.; Matsuura,T.; Saito, I. *J. Chem. Soc., Chem. Commun.* **1974**, 944.
(5) Disanayaka, B.W.; Weedon, A.C. *Can. J. Chem.* **1987**, *65*, 245.
(6) Weedon, A.C.; Wong, D.F. *J. Photochem. Photobiol.* **1991**, *61*, 27.
(7) Oldroyd, D.L.; Weedon, A.C. *J. Photochem. Photobiol.* **1991**, *57*, 207.
(8) Disanayaka, B.W.; Weedon, A.C. *Can. J. Chem.* **1990**, *68*, 1685.
(9) Hastings, D.J.; Weedon, A.C. *Can. J. Chem.* **1991**, *69*, 1171.
(10) Hastings, D.J.; Weedon, A.C. *J. Org. Chem.* **1991**, *56*, 6326.
(11) Hastings, D.J.; Weedon, A.C. *Tetrahedron Lett.* **1991**, *32*, 4107.
(12) Illi, V.O. *Synthesis* **1979**, 387.
(13) Dhanak, D.; Reese, C.B. *J. Chem. Soc., Perkin Trans. 1*, **1986**, 2181.
(14) Misra, P.K.; Hashmi, S.a.N.; Haq, W.; Katti, S.B. *Tetrahedron Lett.* **1989**, *30*, 3569.
(15) Grehn, L.; Ragnarsson, U. *Angew. Chem.* **1984**, *96*, 291; *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 296.
(16) Rawal, V.H.; Cava, M.P. *Tetrahedron Lett.* **1985**, *26*, 6141.
(17) Boissonnas, R.A. *Adv. Org. Chem.* **1963**, *3*, 159.
(18) Boger, D.L.; Patel, M. *J. Org. Chem.* **1987**, *52*, 3934.
(19) The triplet energies of **1a–1g** were determined at 77K in hexanes from the position of th 0-0 band in the phosphorescence spectra. They were all in the range 68–71 kcal/mol, which is lower than the triplet energy of acetophenone (74 kcal/mol).
(20) A Quantacount apparatus, marketed by Photon Technology International, Princeton, New Jersey, was used. The instrument was calibrated using azoxybenzene as an actinometer.