27 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.82, 148.63, 134.86, 59.74, 14.18, 1.03. **(*E*)-Isomer**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (d, 1 H, J = 18.4), 6.28 (d, 1 H, J = 18.4), 4.16 (q, 2 H, J = 7.14), 1.27 (t, 3 H, J = 7.14), 0.18 (s, 27 H).

3-Phenyl-2-[tris(trimethylsilyl)silyl]propenal (Table IV, entry 1): bp 170 °C (5×10^{-2} mbar); GC/MS m/z 378 (M^+), 364 ($M^+ - 15$), 305 ($M^+ - 73$), 174 $(TMS_2Si)^+$, 73 $(TMS)^+$. Anal. Calcd for $C_{18}H_{34}Si_4O$: C, 57.07; H, 9.04. Found: C, 57.18; H, 9.12. **(*Z*)-Isomer**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.71 (s, 1 H), 8.08 (s, 1 H), 7.24–7.27 (m, 5 H), 0.13 (s, 27 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.47 155.01, 142.8, 136.01, 129.71, 129.09, 128.73, 1.48. **(*E*)-Isomer**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.97 (s, 1 H), 7.93 (s, 1 H), 7.34–7.42 (m, 5 H), 0.25 (s, 27 H).

3-Phenyl-2-[tris(trimethylsilyl)silyl]propenenitrile (Table IV, entry 2): bp 150 °C (4×10^{-2} mbar); GC/MS m/z 375 (M^+), 174 $(TMS_2Si)^+$, 73 $(TMS)^+$. Anal. Calcd for $C_{18}H_{33}Si_4N$: C, 57.52; H, 8.85; N, 3.72. Found: C, 57.28; H, 9.02; N, 3.63. **(*Z*)-Isomer**: mp 92 °C (pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (s, 1 H), 7.38 (s, 5 H), 0.21 (s, 27 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.79, 137.14, 129.72, 128.86, 128.80, 123.92 ($J_{(CN-H)}$ = 11.8 Hz), 110.39, 1.78. **(*E*)-Isomer**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25–7.81 (m, 6 H), 0.21 (s, 27 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.64, 135.94, 130.17, 128.79, 128.67, 120.69, 106.28, 0.95; $^3J_{(CN-H)}$ = 17.3 Hz.

1-Phenyl-2-[tris(trimethylsilyl)silyl]-1-heptene (Table IV, entry 3): bp 150 °C (6×10^{-2} mbar); GC/MS m/z 347 ($M^+ - 15$), 289 ($M^+ - 73$), 174 $(TMS_2Si)^+$, 73 $(TMS)^+$. Anal. Calcd for $C_{22}H_{44}Si_4$: C, 62.77; H, 10.53. Found: C, 62.81; H, 10.38. ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.99, 140.10, 132.23, 127.44, 124.98, 123.78, 34.79, 33.53, 32.64, 22.74, 14.22, 0.54. **(*Z*)-Isomer**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.08–7.63 (m, 6 H), 2.63–2.69 (m, 2 H), 1.40–1.57 (m, 6 H), 0.95–0.99 (m, 3 H), 0.16 (s, 27 H). **(*E*)-Isomer**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21–7.37 (m, 5 H), 6.79 (s, 1 H), 2.33–2.38 (m, 2 H), 1.27–1.48 (m, 6 H), 0.89 (t, 3 H, J = 6.9), 0.28 (s, 27 H).

Ethyl (*E*)-2-[tris(trimethylsilyl)silyl]-3-phenylpropenoate (Table IV, entry 4): bp 160 °C (0.8 mbar); mp 47 °C (pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24–7.29 (m, 5 H), 6.86 (s, 1 H), 4.12 (q, 2 H, J = 7.17), 1.16 (t, 3 H, J = 7.18), 0.27 (s, 27 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.54 ($J_{(CO_2Et-H)}$ = 15.5 Hz), 142.25, 137.38, 133.75, 128.27, 127.85, 127.71, 60.51, 13.86, 1.06; MS (EI) m/z 407 ($M^+ - 15$), 349 ($M^+ - 59$), 174 $(TMS_2Si)^+$, 73 $(TMS)^+$. Anal. Calcd for $C_{20}H_{38}Si_4O_2$: C, 56.81; H, 9.05. Found: C, 56.52; H, 9.12.

Bromination Procedure for 1-[Tris(trimethylsilyl)silyl]styrene and Ethyl (*E*)-2-[Tris(trimethylsilyl)silyl]-3-phenylpropenoate. To each vinyl compound (55 mL, 0.05 M in CH_2Cl_2) at −78 °C (acetone, CO_2) was added bromine (1.0 equiv of 0.14 M in CH_2Cl_2) over 1 h. The reaction mixture was stirred for 30 min at −78 °C before being allowed to warm to room temperature. After removal of the solvent under reduced pressure, the product was flash chromatographed (pentane/ether = 9/1).

(*Z*)-Bromostyrene: GC MS m/z 183 $(M)^+$, 103 $(M^+ - Br)$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24–7.34 (m, 5 H), 7.10 (d, 1 H, J = 8.1), 6.46 (d, 1 H, J = 8.1).

Ethyl (*E*)-2-bromo-3-phenylpropenoate: GC MS m/z 256 $(M)^+$, 183 $(M^+ - Br)$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (s, 1 H), 7.26–7.35 (m, 5 H), 4.20 (q, 2 H, J = 7.1), 1.81 (t, 3 H, J = 7.1).

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Registry No. **1a**, 141527-42-6; **1b**, 141527-43-7; **1c**, 131379-56-1; **1d**, 131195-57-8; **1e**, 132162-26-6; **1f**, 141527-44-8; **1g**, 128648-08-8; **1h**, 132182-32-2; **1j**, 141527-45-9; **2a**, 141527-46-0; **2b**, 141527-47-1; **3**, 141527-48-2; **4a**, 141527-49-3; **4b**, 141527-50-6; **5a**, 141527-51-7; **5b**, 132162-25-5; **6**, 127-91-3; **7**, 141527-52-8; **8**, 557-40-4; *cis*-**9**, 141527-53-9; *trans*-**9**, 141527-54-0; **10**, 616-02-4; **11a**, 141527-55-1; **11b**, 141527-56-2; **12**, 5837-78-5; **13a**, 141527-57-3; **13b**, 141527-58-4; **14**, 2418-31-7; **15a**, 141527-59-5; **15b**, 141527-60-8; **16**, 30574-97-1; **17a**, 141527-61-9; **17b**, 141527-62-0; **20a**, 112-30-1; **20c**, 109-78-4; **21** (R = Bu), 693-02-7; **21** (R = cyclohexyl), 931-48-6; **21** (R = *t*-Bu), 917-92-0; **21** (R = Ph), 536-74-3; **21** (R = CO_2Et), 623-47-2; **22** (R = Bu), 141527-63-1; **22** (R = cyclohexyl), 141527-64-2; **22** (R = *t*-Bu), 141527-66-4; **22** (R = Ph), 139526-41-3; **22** (R = CO_2Et), 141527-67-5; **23** (R = Bu), 110577-08-7; **23** (R = cyclohexyl), 141527-65-3; **23** (R = *t*-Bu), 110577-09-8; **23** (R = Ph), 110577-10-1; **23** (R = CO_2Et), 141527-68-6; **26** (Y = CHO), 2579-22-8; **26** (Y = CN), 935-02-4; **26** (Y = pentyl), 14374-45-9; **26** (Y = CO_2Et), 2216-94-6; **27** (Y = CHO), 141527-69-7; **27** (Y = CN), 141527-71-1; **27** (Y = pentyl), 141527-73-3; **27** (Y = CO_2Et), 141527-75-5; **28** (Y = CHO), 141527-70-0; **28** (Y = CN), 141527-72-2; **28** (Y = pentyl), 141527-74-4; **28** (Y = CO_2Et), 141527-76-6; **29**, 588-73-8; **30**, 59106-34-2; tris(trimethylsilyl)silane, 1873-77-4; 1-decene, 872-05-9; styrene, 100-42-5; acrylonitrile, 107-13-1; methyl acrylate, 96-33-3; methyl vinyl ketone, 78-94-4; butyl vinyl ether, 111-34-2; vinyl acetate, 108-05-4; diethyl vinylphosphonate, 682-30-4; phenyl vinyl sulfide, 1822-73-7; α-methylstyrene, 98-83-9; methyl methacrylate, 80-62-6; diethyl fumarate, 623-91-6; crotononitrile, 4786-20-3; ethyl crotonate, 10544-63-5; maleic anhydride, 108-31-6; maleimide, 541-59-3.

Supplementary Material Available: ORTEP plots and full details of crystal data of compounds **27** (Y = CN) and **28** (Y = CO_2Et) (12 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Photoreactions of Isoindoline-1-thiones with Alkenes: Unusual Formation of Tricyclic Isoindolines

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Photochemical cycloaddition reactions of cyclic thioamides and alkenes have been examined. Irradiation of 2-arylisoindoline-1-thiones **1** in the presence of alkenes **2** gave the unexpected tricyclic isoindolines **3–18**. The formation of tricyclic isoindolines can best be explained in terms of the intermediacy of aminospirothietane **27**, formed by [2 + 2] photocycloaddition of the C=S double bond of **1** to the C=C double bond of **2**. Ring cleavage of the resultant amino thietane, assisted by the participation of the nitrogen lone-pair electrons, produced zwitterions **28** and **29** or 1-mercaptoethylisoindole (**30**). Subsequent nucleophilic attack of the thiol anion on the iminium carbon of **29** or attack of the thiol group on C-3 of **30** gave the final products. Irradiation of isobenzofuran-1-thione (**22**) and isobenzothiophene-1-thione (**23**) in the presence of tetramethylethylene (**2a**) gave the corresponding spirothietanes **24** and **25**.

Interest in the photochemistry of thiocarbonyl compounds has been growing in recent years. The majority of the reported reactions involve thioketones, which undergo cycloaddition with alkenes, allenes, ketenes, imines, or alkynes, intramolecular or intermolecular hydrogen abstraction, and photooxidation.[1] Relatively few reports

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Scheme I

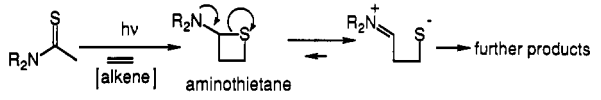


Table I. Yield of Tricyclic Isoindolines 3–18 (Irradiation Was Carried Out in Benzene unless Otherwise Stated)

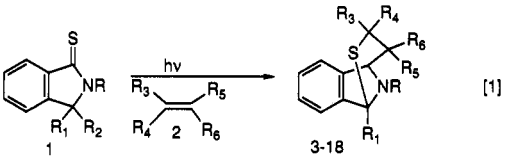
run	isoindoline-1-thione 1	alkene 2	yield[a] (%) product 3–18	yield[a] (%) rec. 1
1	1a	2a	3, 91	trace
2[b]	1a	2a	3, 19	45
3[c]	1a	2a	3, 25	68
4[d]	1a	2a	3, 18	71
5	1a	2b	4, 95	trace
6	1a	2c	5, 32	55
7	1a	2d	6, 65 (1/1)[e]	trace
8	1a	2e	7, 49 (6/7)[e]	trace
9	1a	2f	8, 70 (6/4)[e]	trace
10	1b	2a	9, 81	10
11	1b	2c	10, 30	50
12	1b	2d	11, 49 (5/8)[e]	trace
13	1c	2a	12, 92	trace
14	1c	2c	13, 60	trace
15	1c	2d	14, 21 (4/3)[e]	trace
16	1d	2a	15, 70	10
17	1e	2a	16, 86	trace
18	1f	2a	17, 49	30
19	1g	2a	18, 80	19

[a] Isolated yield. [b] Irradiation was carried out in MeOH. [c] At 366 nm. [d] At >400 nm (halogen lamp). [e] Ratio of stereoisomers.

have dealt with the photochemical reactions of thioamides, and the majority of these reports deal with intra- or intermolecular cycloaddition to alkenes.[2] Aminothietanes are believed to be intermediates in these reactions. However, they have not yet been isolated,[3] probably because the nitrogen-lone-pair-assisted cleavage of the C–S bond of the thietane ring facilitates formation of a zwitterion (Scheme I). In contrast, thietanes have been isolated from photochemical cycloadditions of alkenes and thioimides,[4] which have a cross-conjugated carbonyl system. Thioparabanates[5] and thiouracils,[6] in which the effect of the lone-pair electrons on nitrogen is reduced by conjugation with the second carbonyl group, also behave in a similar way to form corresponding thietanes. de Mayo and his co-workers used low-temperature NMR spectroscopy to confirm the formation of an aminothietane in the photochemical reaction of *N*-(*o*-vinylphenyl)thioamide.[2g] However, these processes are not fully understood. We set out to investigate the effect of heteroatoms adjacent to the thiocarbonyl group on the formation of a thietane ring. We now present a full report of our studies on the intermolecular photoaddition of alkenes **2** and isoindoline-1-thiones **1** and related thiones **22** and **23**.

Results and Discussion

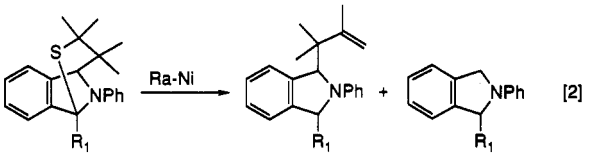
Irradiation of a benzene solution of 2-phenylisoindoline-1-thione (**1a**) with a high-pressure mercury lamp through a Pyrex filter under argon resulted in the recovery of unchanged starting material. However, when a solution of **1a** in benzene was irradiated in the presence of tetramethylethylene (**2a**), an electron-rich alkene, until the yellow color of the solution disappeared, a 1:1 adduct of **1a** and **2a** (**3**) was obtained in 91% isolated yield. The



1	R	R_1	R_2
a	Ph	H	H
aD	Ph	D	D
b	p-MeC_6H_4	H	H
c	p-$MeOC_6H_4$	H	H
d	Ph	Me	H
e	Ph	Ph	H
f	p-MeC_6H_4	Me	H
g	p-ClC_6H_4	Me	H
h	Ph	Me	Me
i	Me	H	H
j	i-Bu	H	H
k	Allyl	H	H
l	H	H	H

2	R_3	R_4	R_5	R_6
a	Me	Me	Me	Me
b	Me	H	Me	Me
c	H	H	Me	Me
d	H	H	Me	CN
e	Me	H	Me	CN
f	H	H	Me	CO_2Me

structure of **3** was confirmed on the basis of spectroscopic data and elemental analysis. The microanalysis and mass spectrum of photoproduct **3** were consistent with the proposed structure. The ^{1}H-NMR spectrum of **3** showed four singlets assignable to methyl protons, two singlets assignable to methine protons, and aromatic proton signals. The ^{13}C-NMR spectrum of **3** showed four methyl carbons, two tertiary carbons, two quaternary carbons, and aromatic carbon signals. The thiocarbonyl and secondary carbon signals disappeared. Photoproduct **3** was treated with Raney-nickel in methanol to give isoindoline derivatives **20a** and **21a**. The formation of **20a** and **21a** is further



3	R_1=H	20a	40%	21a	43%
15	R_1=Me	20d	8%	21d	5%

evidence for the tricyclic isoindoline structure. Irradiation of **1a** in methanol in the presence of **2a** also gave tricyclic isoindoline **3**, but in lower yield (19%).[11]

In a similar manner, irradiation of isoindoline-1-thiones **1b–c** and **2a** in benzene yielded the corresponding tricyclic isoindolines **9** and **12** in high yields. Photoreactions of isoindoline-1-thiones **1a–c** with electron-rich alkenes such as 1,1,2-trimethylethylene (**2b**) and isobutene (**2c**) gave the tricyclic isoindolines **4**, **5**, **10**, and **13** in 30–95% yields.

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(3) Quite recently, we succeeded in isolation of an amino thietane from photochemical cycloaddition of 1,3,3-trimethylindoline-2-thione and isobutene, but in low yield.[2n]

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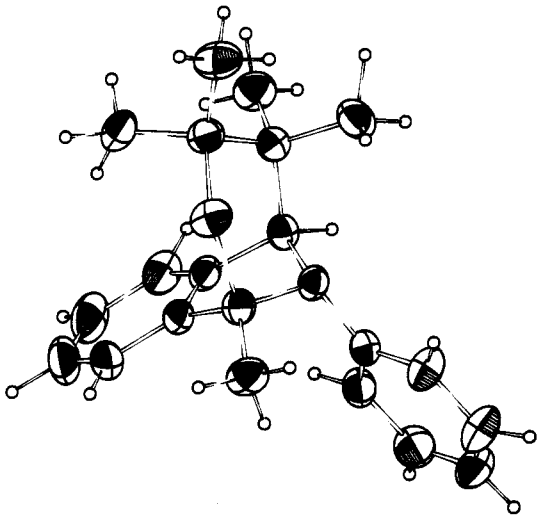
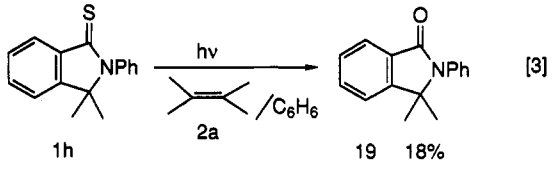


Figure 1. Stereographic view of tricyclic isoindolin **15**.

In order to determine the mechanism for the formation of tricyclic isoindolines, we carried out the photochemical reactions of 3-substituted 2-arylisoindoline-1-thiones **1d–g** with tetramethylethylene (**2a**). Irradiation of a benzene solution of 3-methyl-2-phenylisoindoline-1-thione (**1d**) in the presence of **2a** gave tricyclic isoindoline **15** in 70% yield.

The structure of **15** was determined on the basis of spectroscopic data and elemental analysis. The ^{1}H-NMR spectrum of **15** displayed five singlets assignable to methyl protons, a singlet due to a methine proton, and aromatic proton signals. The ^{13}C-NMR spectrum of **15** showed five methyl carbons, a tertiary carbon, three quaternary carbons, and aromatic carbons. Further, evidence for the structure of **15** was obtained by comparing the chemical shifts of **15** with those of tricyclic isoindoline **3** as shown in eq 1. Compound **15** was treated with Raney-nickel to give 1,3-disubstituted isoindoline **20d** and 1-methyisoindoline (**21d**). The structure of **15** was also confirmed by X-ray structural analysis (Figure 1).[7] Irradiation of 3-substituted 2-arylisoindoline-1-thiones **1e–g** in the presence of **2a** yielded the corresponding tricyclic isoindolines **16–18** in 49–86% yields. However, irradiation of 3,3-dimethyl-2-phenylisoindoline-1-thione (**1h**) in benzene in the presence of **2a** gave oxidation product 3,3-dimethyl-2-phenylisoindolin-1-one (**19**) in 18% yield as the only



[3]

isolable product,[9] along with unchanged starting material.

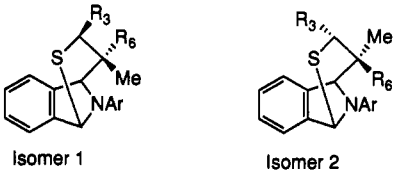


Figure 2. Stereoisomers of **6–8**, **11**, and **14**.

The tricyclic isoindoline was not formed because the reaction site at C-3 was substituted by two methyl groups. Although the photoreaction of isoindoline-1-thione **1a** and tetramethylethylene (**2a**) was not sensitized efficiently by the addition of the triplet sensitizer thioxanthone (E_T = 65–66 kcal/mol), the addition of a triplet quencher such as *trans*-stilbene (E_T = 50 kcal/mol) or 2,5-dimethyl-2,4-hexadiene decreased the reaction rate and the yield of tricyclic isoindoline **3**. Irradiation of **1a** and **2a** in benzene in the n–π^* region using a halogen lamp gave **3** in 18% yield. These results suggest that the formation of **3** proceeds mainly via the n–π^* triplet state of **1a**, although the possibility of the intermediacy of an n–π^* singlet state or a higher singlet state[1c] can not be ruled out completely.

To investigate the scope and limitations of this reaction, photocycloadditions of isoindoline-1-thiones **1** were carried out with various alkenes. Irradiation of isoindoline-1-thiones **1a–c** in benzene in the presence of electron-poor alkenes such as methacrylonitrile (**2d**), 2-butene-2-nitrile (**2e**), and methyl methacrylate (**2f**) gave the corresponding tricyclic isoindolines **6–8**, **11**, and **14** as mixtures of two stereoisomers. The structure of the photoproducts was elucidated on the basis of spectroscopic properties and elemental analyses. The stereochemistry was tentatively assigned as shown in Figure 2 on the basis of NMR data. The signals of the methyl protons of isomer 1 of **6**, **8**, **11**, and **14** appeared as a singlet at lower field (δ 1.41–1.55) than those of isomer 2 (δ 1.23–1.41) because of the anisotropic effect of the fused benzene ring. When a benzene solution of isoindoline-1-thione **1a** was irradiated in the presence of cyano alkenes such as acrylonitrile and crotononitrile, which have no substituent at the α-position, several products were detected by TLC, but separation and isolation of pure components proved difficult. Isoindoline-1-thione **1a** did not react photochemically with electron-rich alkene ethyl vinyl ether, with electron-neutral aromatic alkenes such as styrene, stilbene, and 1,1-diphenylethylene, or with alkyne phenylacetylene. Compound **1a** was recovered almost quantitatively. No photoproducts were obtained when *N*-alkyl- or *N*-allylisoindoline-1-thiones **1i–l** were irradiated in the presence of alkenes **2a,c**; unchanged starting materials were recovered.

A plausible mechanism for the formation of tricyclic isoindolines **3–18** is presented in Scheme II. Amino thietane **27** is formed through the photochemical [2 + 2] cycloaddition of isoindoline-1-thione **1** and alkene **2**. The intermediacy of the amino thietane **27** (R_1 = H, R′ = Me) was indicated by an NMR experiment.[10] The ^{1}H-NMR spectrum of the photolysate of **1a** and **2a** in $CDCl_3$ showed four singlets (δ 1.31, 1.34, 1.36, and 1.84) and a double doublet [δ 5.0 (J = 11.5, 17.5 Hz)] due to amino thietane **27**, along with the signals of **3** and **1a**. After the photolysate was kept at room temperature for several hours, these signals of the thietanes disappeared, and the signals of **3** increased. Amino thietane **27** is unstable and undergoes thietane ring cleavage assisted by the lone-pair

(7) Formula: 323.51, monoclinic, a = 8.559 (1) Å, b = 28.605 (5) Å, c = 7.321 (6) Å, β = 92.13 (0)°, V = 1791.1 Å, D_c = 1.209 g/cm^3. Intensities were measured at room temperature on Enraf-Nonius CAD 4 computer-controlled κ axis diffractometer equipped with a graphite crystal, incident beam monochromator (Mo Kα, λ = 0.709 30 Å). Of the 1681 reflections measured, 1176 independent reflections with $I > 3.0\sigma(I_o)$ were used in the refinement. The structure was solved by direct method[8] and refined by full-matrix least-squares analysis. The refinement converged at R = 0.031, Rw = 0.038.

(8) Frenz, B. A. The Enraf-Nonius CAD 4 SDP-A Real-time System for Concurrent X-Ray Data Collection and Crystal Structure Determination. In *Computing in Crystallography*; Schenk, H.; Olthof-Hazekamp, R.; van Konoingsveld, H.; Bassi, G. C., Eds.; Delft University Press; Delft, Holland, 1978; pp 64–71.

(9) Although the mechanism for the formation of 3,3-dimethylisoindolin-2-one (**19**) is not clear, **1h** is presumably oxidized by a trace of oxygen dissolved in solvent.

(10) A solution of **1a** and **2a** in benzene was irradiated at ~10 °C for 6 h. After removal of the solvent at ~10 °C, the ^{1}H-NMR spectra of the reaction mixture were recorded in $CDCl_3$.

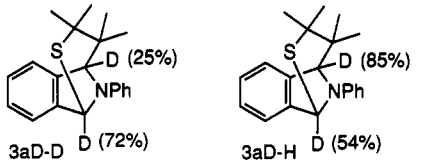
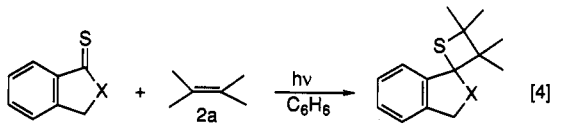


Figure 3.

electrons on nitrogen to yield zwitterion **28**.[11] Zwitterion **28** may be in equilibrium with its tautomer (**29**), formed by 1,3-hydrogen transfer, and with mercaptoisoindole **30**, formed by 1,6-hydrogen transfer. Finally, either intramolecular nucleophilic attack of the thiol anion of **29** on the iminium carbon or attack of the thiol group of **30** on the C=C double bond yields tricyclic isoindolines **3-18**. In this mechanism, the formation of tricyclic isoindolines must be accompanied by 1,3-hydrogen migration from C-3 to C-1 of the isoindoline-1-thiones (**1**).

In order to investigate this mechanism in more detail, 3,3-dideuteriated 2-phenylisoindoline-1-thione (**1aD**) was prepared, and photochemical reactions of **1aD** and tetramethylethylene (**2a**) were examined. When a benzene solution of **1aD** and **2a** was irradiated, 1,3-dideuteriated tricyclic isoindoline **3aD-D** was obtained. The deuterium content of **3aD-D**, shown in parenthesis in Figure 3, suggests that partial 1,3-hydrogen migration took place.[12] The 1,3-dideuteriated tricyclic isoindoline **3aD-H** was also obtained when a solution of 2-phenylisoindoline-1-thione (**1a**) and **2a** in methanol-d_1 was irradiated. This result suggests that 1-mercaptoethylisoindole **30**, in which the hydrogen atom of the mercapto group can be easily exchanged with deuterium, is the reactive intermediate. The regiochemistry of [2 + 2] photocycloaddition of **1** and **2** is in accord with the expected formation of the more stable diradical (**26**).[2-6]

To determine the role of the nitrogen lone-pair electrons in the thietane ring cleavage, the photocycloadditions of 1,3-dihydroisobenzofuran-1-thione (**22**) and 1,3-dihydroisobenzothiophene-1-thione (**23**) with tetramethylethylene (**2a**) were compared with the reaction of **1a** and **2a**. Irradiation of **22** and **23** in benzene in the presence of **2a** gave spirothietanes **24** and **25** in 80% and 66% yields, respectively. These spirothietanes were stable; rearrangement



22 X=O
23 X=S

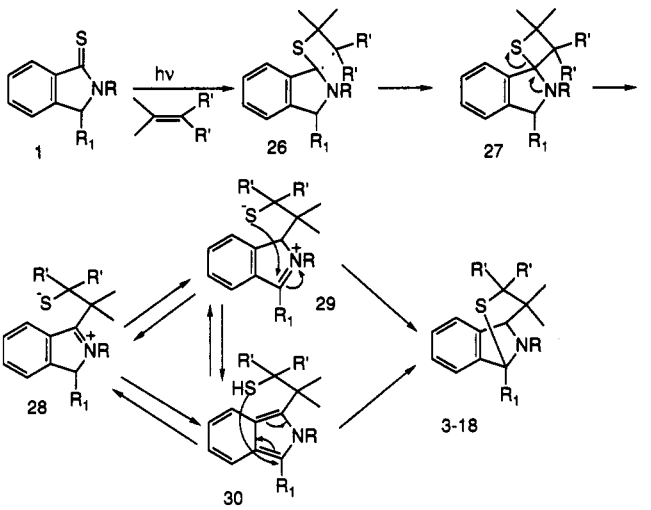
24 X=O 80%
25 X=S 66%

to tricyclic dihydroisobenzofuran or dihydroisobenzothiophene was not observed even when the spirothietanes were heated in refluxing benzene for ca. 12 h. These reactivity differences can be rationalized in terms of the participation of the heteroatom lone-pair electrons that facilitates the ring cleavage of the thietane. The lone-pair electrons on nitrogen have more effect than those on oxygen or sulfur. The greater effectiveness of the nitrogen lone-pair electrons parallels the greater electronic influence of nitrogen substituents (reflected by their σ^+ values in the Hammet equation) on the rate and course of a reaction.[13]

(11) Irradiation of isoindoline-1-thione **1a** in the presence of tetramethylethylene (**2a**) in methanol was carried out in the hope of trapping zwitterion intermediates **28** and **29**; however, this attempt was unsuccessful.

(12) Although dry solvent was used and care was taken to exclude water from the reaction mixture, the low incorporation of deuterium was probably due to D–H exchange in the equilibrium state by a trace of water in the solvent.

Scheme II



Experimental Section

Melting and boiling points are uncorrected. UV spectra were recorded on a JASCO UVIDEC-505 spectrophotometer, and IR spectra were recorded on a Hitachi 260-30 spectrophotometer. ^1H and ^{13}C NMR spectra were run on JEOL FX 100 (100-MHz) or FX 90Q (90-MHz) spectrometers with $CDCl_3$ as solvent and tetramethylsilane as an internal standard. Mass spectra were measured with a Hitachi M-80 spectrometer. Isoindoline-1-thiones **1a–c,h–l** were prepared by thionation of the corresponding isoindolin-1-ones with 2,4-bis(*p*-methoxyphenyl)-1,3-dithiaphosphetane 2,4-disulfide (Lawesson reagent: LR). Isoindoline-1-thiones **1d–g** were prepared according to the method described in the literature.[14]

General Procedure for the Thionation of the Isoindolin-1-ones with LR. A solution of the isoindolin-1-one (10 mmol) and LR (6 mmol) in toluene or 1,2-dimethoxyethane (80 mL) was heated to reflux under argon for 5–60 min. After removal of the solvent, the residue was chromatographed on a silica gel column with benzene–hexane (1:1–9:1) as eluent to yield the corresponding isoindoline-1-thiones **1a–c,h–l**. Satisfactory microanalyses for all new compounds were obtained: C ± 0.31, H ± 0.16, N ± 0.07.

2-Phenylisoindoline-1-thione (1a): mp 167–168 °C (lit.[15] mp 168 °C); UV (EtOH) 264 (ε 15900), 323 nm (9100); UV (hexane) 256 (ε 15800), 330 nm (8400); IR (KBr) 1295, 1200 cm^{-1}; ^1H NMR δ 5.01 (2 H, s), 7.25–7.70 (8 H, m), 8.05–8.20 (1 H, m); ^{13}C NMR δ 60.2 (t), 193.7 (s), and aromatic carbon peaks.

2-(*p*-Tolyl)isoindoline-1-thione (1b): mp 127–128 °C; IR (KBr) 1295, 1275, 1200 cm^{-1}; ^1H NMR δ 2.38 (3 H, s), 4.98 (2 H, s), 7.20–7.70 (7 H, m), 8.00–8.20 (1 H, m); ^{13}C NMR δ 21.2 (q), 60.3 (t), 193.6 (s), and aromatic carbon peaks.

2-(*p*-Anisyl)isoindoline-1-thione (1c): mp 99–100 °C; IR (KBr) 1300, 1285, 1240, 1200 cm^{-1}; ^1H NMR δ 3.28 (3 H, s), 4.96 (2 H, s), 6.96 (2 H, d, J = 9.3 Hz), 7.30–7.70 (5 H, m), 8.00–8.15 (1 H, m); ^{13}C NMR δ 55.4 (q), 60.4 (t), 193.5 (s), and aromatic carbon peaks.

2-Phenyl-3,3-dimethylisoindoline-1-thione (1h): mp 189–190 °C; IR (KBr) 1310, 1255 cm^{-1}; ^1H NMR δ 1.53 (6 H, s), 7.15–7.30 (2 H, m), 7.35–7.60 (6 H, m), 8.05–8.20 (1 H, m), ^{13}C NMR δ 25.8 (q), 72.1 (s), 194.1 (s), and aromatic carbon peaks.

2-Methylisoindoline-1-thione (1i): mp 168–170 °C; UV (EtOH) 253 (ε 11300), 304 nm (10000); UV (hexane) 249 (ε 10700), 310 nm (8200); IR (KBr) 1310, 1285 cm^{-1}; ^1H NMR δ 3.54 (3 H, s), 4.62 (2 H, s), 7.30–7.65 (3 H, m), 7.90–8.05 (1 H, m); ^{13}C NMR δ 34.5 (q), 59.2 (t), 193.1 (s), and aromatic carbon peaks.

2-Isobutylisoindoline-1-thione (1j): bp 180 °C (2 mmHg); IR (film) 1290, 1255, 1215, 1200 cm^{-1}; ^1H NMR δ 0.95 (6 H, d, J = 6.8 Hz), 2.05–2.45 (1 H, m), 3.83 (2 H, d, J = 7.8 Hz), 4.65 (2 H, s), 7.25–7.60 (3 H, m), 7.90–8.10 (1 H, m); ^{13}C NMR δ 20.2 (q), 27.7 (d), 54.3 (t), 58.0 (t), 193.4 (s), and aromatic carbon peaks.

(13) Lowry, T. H.; Richardson, S. *Mechanism and Theory in Organic Chemistry*; Harper & Row: New York, 1976; p 57.

(14) Nishio, T.; Okuda, N.; Mori, Y.; Kashima, C. *Synthesis* **1989**, 396.

(15) Prey, V.; Kerres, B.; Berballa, H. *Monatsh. Chem.* **1960**, *91*, 319.

2-Allylisoindoline-1-thione (1k): mp 81–82 °C; IR (KBr) 1640, 1295, 1260, 1200 cm^{-1}; ^1H NMR δ 4.60 (2 H, s), 4.69 (2 H, d, J = 5.9 Hz), 5.15–5.35 (2 H, m), 5.70–6.15 (1 H, m), 7.35–7.65 (3 H, m), 7.95–8.10 (1 H, m); ^{13}C NMR δ 49.5 (t), 56.7 (t), 118.9 (t), 139.5 (d), 193.8 (s), and aromatic carbon peaks.

Isoindoline-1-thione (1l): mp 163–154 °C; UV (EtOH) 248 (ϵ 9900), 307 nm (10 000); IR (KBr) 3150, 1305, 1260, 1215 cm^{-1}; ^1H NMR δ 4.66 (2 H, d, J = 1.5 Hz), 7.40–7.70 (3 H, m), 8.05–8.15 (1 H, m), 9.4 (1 H, br s); ^{13}C NMR δ 52.6 (t), 196.3 (s), and aromatic carbon peaks.

2-Phenyl-3,3-dideuterioisoindoline-1-thione (1aD). Compound **1aD** (D content >95% estimated by ^1H NMR) was prepared by direct thionation with LR of the corresponding 3,3-dideuterioisoindolin-1-one, which was obtained by the reduction of *N*-phenylphthalimide with zinc powder in CH_3CO_2D.

General Procedure for the Photochemical Reactions of Isoindoline-1-thiones 1 with Alkenes 2. A solution of isoindoline-2-thione **1** (200 mg) and a large excess of alkene **2** (~1 mL) in benzene or methanol (70 mL) in a Pyrex vessel was degassed with argon for 15 min and then irradiated with a high-pressure mercury lamp (300 W) at room temperature for 5–15 h until the yellow color of the solution disappeared. After removal of the solvent, the residue was chromatographed on a silica gel column with benzene–hexane (1:1–1:10) as eluent to yield the photoproducts and unchanged thioamide. Satisfactory microanalyses for all new compounds were obtained: C ± 0.34, H ± 0.16, N ● 0.13.

Tricyclic isoindoline 3: mp 101–103 °C; ^1H NMR δ 0.37 (3 H, s), 0.99 (3 H, s), 1.05 (3 H, s), 1.17 (3 H, s), 4.57 (1 H, s), 5.83 (1 H, s), 6.65–6.95 (4 H, m), 7.35–7.10 (5 H, m); ^{13}C NMR δ 22.1 (q), 26.9 (q), 28.9 (q), 29.9 (q), 39.7 (s), 49.1 (s), 65.8 (d), 71.3 (d), and aromatic carbon peaks; MS m/z 309 (M^+), 225 ($M^+ - C_6H_{12}$), 193 ($M^+ - C_{13}H_{11}N$).

Tricyclic isoindoline 4: mp 111–112 °C; ^1H NMR δ 0.91 (3 H, d, J = 6.8 Hz), 0.99 (3 H, s), 1.05 (3 H, s), 2.33 (1 H, q, J = 6.8 Hz), 4.68 (1 H, s), 5.80 (1 H, s), 6.60–6.95 (3 H, m), 7.15–7.35 (6 H, m); ^{13}C NMR δ 14.3 (q), 20.1 (q), 24.7 (q), 37.3 (s), 41.6 (d), 65.3 (d), 70.4 (d), and aromatic carbon peaks.

Tricyclic isoindoline 5: mp 136–137 °C; ^1H NMR δ 0.99 (3 H, s), 1.14 (3 H, s), 2.09 (2 H, AB q), 4.66 (1 H, s), 5.81 (1 H, d, J = 1.0 Hz), 6.65–6.95 (3 H, m), 7.10–7.35 (6 H, m); ^{13}C NMR δ 14.8 (q), 17.8 (q), 32.6 (s), 36.2 (t), 63.6 (d), 68.6 (d), and aromatic carbon peaks.

Tricyclic Isoindoline 6. Isomer-1 (**6-1**): mp 152–155 °C; IR (KBr) 2220 cm^{-1}; ^1H NMR δ 1.54 (3 H, s), 2.54 (2 H, AB q), 5.18 (1 H, br s), 5.83 (1 H, br s), 6.75–7.00 (3 H, m), 7.20–7.45 (5 H, m), 7.50–7.65 (1 H, m); ^{13}C NMR δ 21.0 (q), 32.5 (t), 33.8 (s), 64.2 (d), 64.9 (d), 119.1 (s), and aromatic carbon peaks; MS m/z 292 (M^+), 264 ($M^+ - CH_2S$), 225 ($M^+ - C_4H_5N$), 193 ($M^+ - C_4H_5NS$). Isomer-2 (**6-2**): IR ($CHCl_3$) 2240 cm^{-1}; ^1H NMR δ 1.41 (3 H, s), 2.19 (1 H, A of AB q), 2.61 (1 H, B of AB q), 4.99 (1 H, d, J = 1.0 Hz), 5.90 (1 H, br s), 6.75–7.05 (3 H, m), 7.20–7.45 (6 H, m); ^{13}C NMR δ 24.5 (q), 33.6 (s), 33.6 (t), 64.6 (d), 66.8 (d), 120.1 (s), and aromatic carbon peaks.

Tricyclic Isoindoline 7. Isomer-1 (**7-1**): mp 180–183 °C; IR (KBr) 2200 cm^{-1}; ^1H NMR δ 1.22 (3 H, d, J = 6.8 Hz), 1.49 (3 H, s), 2.28 (1 H, q, J = 6.8 Hz), 5.03 (1 H, s), 5.91 (1 H, s), 6.70–7.10 (3 H, m), 7.15–7.45 (6 H, m); ^{13}C NMR δ 15.7 (q), 22.1 (q), 39.9 (d), 40.5 (s), 66.1 (d), 67.9 (d), 120.2 (s), and aromatic carbon peaks. Isomer-2 (**7-2**): mp 116–118 °C; IR (KBr) 2220 cm^{-1}; ^1H NMR δ 1.06 (3 H, d, J = 6.8 Hz), 1.33 (3 H, s), 2.64 (1 H, q, J = 6.8 Hz), 5.30 (1 H, s), 5.84 (1 H, s), 6.70–6.95 (3 H, m), 7.10–7.50 (5 H, m), 7.55–7.65 (1 H, m); ^{13}C NMR δ 15.8 (q), 16.5 (q), 38.1 (d), 39.3 (s), 65.1 (d), 66.2 (d), 121.9 (s), and aromatic carbon peaks.

Tricyclic Isoindoline 8. Isomer-1 (**8-1**): mp 112–113 °C; IR (KBr) 1720 cm^{-1}; ^1H NMR δ 1.41 (3 H, s), 2.28 (1 H, A of AB q), 2.66 (1 H, B of AB q), 3.74 (3 H, s), 5.50 (1 H, br s), 5.83 (1 H, s), 6.70–7.40 (9 H, m); ^{13}C NMR δ 21.3 (q), 30.0 (t), 43.4 (s), 52.0 (q), 63.9 (d), 64.6 (d), 175.0 (s), and aromatic carbon peaks. Isomer-2 (**8-2**): mp 195 °C (sublim); IR (KBr) 1700 cm^{-1}; ^1H NMR δ 1.23 (3 H, s), 2.07 (1 H, A of AB q), 2.91 (1 H, B of AB q), 3.51 (3 H, s), 5.12 (1 H, br s), 5.81 (1 H, s), 6.70–7.50 (9 H, m); ^{13}C NMR δ 24.6 (q), 30.4 (t), 43.5 (s), 51.8 (q), 65.1 (d), 68.6 (d), 174.1 (s), and aromatic carbon peaks.

Tricyclic isoindoline 9: mp 98–99 °C; ^1H NMR δ 0.36 (3 H, s), 1.00 (3 H, s), 1.04 (3 H, s), 1.20 (3 H, s), 2.22 (3 H, s), 4.47 (1 H, s), 5.77 (1 H, s), 6.75–7.40 (8 H, m); ^{13}C NMR δ 20.4 (q), 22.1 (q), 26.9 (q), 28.8 (q), 29.9 (q), 39.6 (s), 48.9 (s), 66.4 (d), 72.3 (d), and aromatic carbon peaks.

Tricyclic isoindoline 10: bp 190 °C (2 mmHg); ^1H NMR δ 0.95 (3 H, s), 1.13 (3 H, s), 2.06 (2 H, AB q), 2.23 (3 H, s), 4.56 (1 H, d, J = 1.0 Hz), 5.74 (1 H, d, J = 1.0 Hz), 6.70–6.86 (2 H, m), 6.95–7.35 (6 H, m); ^{13}C NMR δ 20.4 (q), 24.8 (q), 27.8 (q), 32.5 (s), 36.1 (t), 64.1 (d), 69.1 (d), and aromatic carbon peaks.

Tricyclic Isoindoline 11. Isomer-1 (**11-1**); mp 144–146 °C; IR (KBr) 2240 cm^{-1}; ^1H NMR δ 1.52 (3 H, s), 2.25 (3 H, s), 2.32 (1 H, A of AB q), 2.69 (1 H, B of AB q), 5.09 (1 H, s), 5.76 (1 H, s), 6.81 (2 H, d, J = 8.8 Hz), 7.07 (2 H, d, J = 8.8 Hz), 7.25–7.65 (4 H, m); ^{13}C NMR δ 20.3 (q), 21.0 (q), 32.4 (t), 33.5 (s), 64.5 (d), 65.2 (d), 128.4 (s), and aromatic carbon peaks. Isomer-2 (**11-2**): IR ($CHCl_3$) 2250 cm^{-1}; ^1H NMR δ 1.40 (3 H, s), 2.17 (1 H, A of AB q), 2.25 (3 H, s), 2.60 (1 H, B of AB q), 4.89 (1 H, d, J = 1.0 Hz), 5.85 (1 H, d, J = 1.0 Hz), 6.85–7.40 (9 H, m); ^{13}C NMR δ 20.5 (q), 24.5 (q), 33.4 (t), 33.7 (s), 65.1 (d), 67.6 (d), 122.6 (s), and aromatic carbon peaks.

Tricyclic isoindoline 12: mp 102–103 °C; ^1H NMR δ 0.36 (3 H, s), 1.01 (3 H, s), 1.03 (3 H, s), 1.25 (3 H, s), 3.70 (3 H, s), 4.30 (1 H, s), 5.68 (1 H, s), 6.70–6.90 (4 H, m), 7.10–7.40 (4 H, m); ^{13}C NMR δ 22.2 (q), 26.9 (q), 28.8 (q), 29.8 (q), 39.5 (s), 48.7 (s), 55.5 (q), 67.4 (d), 74.0 (d), and aromatic carbon peaks.

Tricyclic isoindoline 13: bp 150 °C (2 mmHg); ^1H NMR δ 0.96 (3 H, s), 1.17 (3 H, s), 2.06 (2 H, AB q), 3.71 (3 H, s), 4.46 (1 H, d, J = 1.0 Hz), 5.69 (1 H, d, J = 1.0 Hz), 6.82 (4 H, s), 7.15–7.40 (4 H, m); ^{13}C NMR δ 24.9 (q), 27.9 (q), 32.4 (s), 36.0 (t), 55.6 (q), 65.1 (d), 70.6 (d), and aromatic carbon peaks.

Tricyclic Isoindoline 14. The two isomers could not be completely separated: IR ($CHCl_3$) (a mixture of two isomers) 2240 cm^{-1}; ^1H NMR δ [for isomer-1 (**14-1**)] 1.55 (3 H, s), 2.35 (1 H, A of AB q), 2.57 (1 H, B of AB q), 3.69 (3 H, s), 4.97 (1 H, s), 5.69 (1 H, s), 6.75–7.00 (4 H, m), 7.25–7.60 (4 H, m); δ [for isomer-2 (**14-2**)] 1.39 (3 H, s), 2.11 (1 H, A of AB q), 2.66 (1 H, B of AB q), 3.73 (3 H, s), 4.73 (1 H, s), 5.75 (1 H, s), 6.75–7.00 (4 H, m), 7.25–7.40 (4 H, m); ^{13}C NMR δ (for **14-1**) 20.9 (q), 32.2 (t), 33.5 (s), 55.3 (q), 65.5 (d), 66.3 (d); δ (for **14-2**) 24.3 (q), 33.1 (t), 34.3 (s), 55.5 (q), 66.1 (d), 69.1 (d), and aromatic carbon peaks.

Tricyclic isoindoline 15: mp 113–114 °C; ^1H NMR δ 0.29 (3 H, s), 0.99 (6 H, s), 1.04 (3 H, s), 1.84 (3 H, s), 4.42 (1 H, s), 6.80–7.05 (1 H, m), 7.10–7.50 (8 H, m); ^{13}C NMR δ 21.4 (q), 22.1 (q), 26.7 (q), 28.8 (q), 29.4 (q), 38.1 (3 H, s), 50.1 (s), 73.7 (s), 76.1 (d), and aromatic carbon peaks.

Tricyclic isoindoline 16: mp 135–137 °C; ^1H NMR δ 0.33 (3 H, s), 0.88 (3 H, s), 1.02 (6 H, s), 5.03 (1 H, s), 6.55–6.80 (2 H, m), 6.80–7.50 (12 H, m); ^{13}C NMR δ 22.3 (q), 27.4 (q), 29.3 (q), 29.7 (q), 37.7 (s), 50.4 (s), 73.7 (d), 77.8 (s), and aromatic carbon peaks.

Tricyclic isoindoline 17: mp 115–116 °C; ^1H NMR δ 0.30 (3 H, s), 1.00 (3 H, s), 1.01 (3 H, s), 1.10 (3 H, s), 1.79 (3 H, s), 2.56 (3 H, s), 4.29 (1 H, s), 7.02 (3 H, s), 7.10–7.40 (5 H, m); ^{13}C NMR δ 20.8 (q), 21.3 (q), 22.1 (q), 26.7 (q), 28.8 (q), 29.4 (q), 38.2 (s), 50.1 (s), 74.2 (s), 76.6 (d), and aromatic carbon peaks.

Tricyclic isoindoline 18: mp 129–130 °C; ^1H NMR δ 0.28 (3 H, s) 0.99 (6 H, s), 1.83 (3 H, s), 4.40 (1 H, s), 7.05–7.45 (8 H, m); ^{13}C NMR δ 21.3 (q), 22.1 (q), 26.9 (q), 28.8 (q), 29.3 (q), 38.2 (s), 50.1 (s), 73.3 (s), 76.1 (d), and aromatic carbon peaks.

Desulfurization of Tricyclic Isoindolines 3 and 15 with Raney-Nickel. A mixture of tricyclic isoindoline (200 mg) and Raney-Ni (800 mg) in methanol (15 mL) was stirred at room temperature for 1 h. The catalyst was filtered off, the solvent was evaporated, and the residue was chromatographed on a silica gel column with benzene–hexane (1:5) to give isoindolines **20** and **21**. Satisfactory microanalyses were obtained: C ● 0.34, H ● 0.11, N ± 0.1.

1-(1′,1′,2′-Trimethyl-2′-propenyl)-2-phenylisoindoline (20a): bp 100 °C (3 mmHg); ^1H NMR δ 0.74 (3 H, s), 1.14 (3 H, s), 2.01 (3 H, s), 4.48 (1 H, A of AB q), 4.67 (1 H, d, J = 1.0 Hz), 4.84 (1 H, B of AB q), 4.88–4.94 (1 H, m), 5.41 (1 H, d, J = 2.4 Hz), 6.60–6.90 (3 H, m), 7.10–7.35 (6 H, m); ^{13}C NMR δ 20.4 (q), 21.6 (q), 26.9 (q), 48.2 (s), 58.1 (t), 67.4 (d), 112.6 (t), 150.2 (s), and aromatic carbon peaks.

2-Phenylisoindoline (21a): mp 165 °C (sublim); ^1H NMR δ 4.63 (4 H, s), 6.60–6.80 (3 H, m), 7.15–7.50 (6 H, m); ^{13}C NMR δ 53.7 (t), and aromatic carbon peaks.

1-(1′,1′,2′-Trimethyl-2′-propenyl)-2-phenyl-3-methylisoindoline (20d): ^{1}H NMR δ 0.80 (3 H, s), 1.16 (3 H, s), 1.76 (3 H, d, J = 6.6 Hz), 2.11 (3 H, s), 4.78 (1 H, q, J = 6.6 Hz), 4.82 (1 H, s), 4.99 (1 H, s), 5.38 (1 H, br s), 6.75–6.80 (1 H, m), 7.00–7.05 (2 H, m), 7.10–7.20 (3 H, m), 7.20–7.30 (3 H, m); ^{13}C NMR δ 20.8 (q), 22.9 (q), 23.4 (q), 27.1 (q), 45.9 (s), 65.5 (d), 68.4 (d), 112.8 (t), 151.6 (s), and aromatic carbon peaks; MS m/z 291 (M^+), 276 ($M^+ - CH_3$), 208 ($M^+ - C_6H_{11}$); HRMS calcd for $C_{21}H_{25}N$ 291.199 30, found 291.144 01.

1-Methyl-2-phenylisoindoline (21d): bp 140 °C (3 mmHg); mp 74–75 °C; ^{1}H NMR δ 1.48 (3 H, d, J = 6.7 Hz), 4.48 (1 H, A of AB q), 4.77 (1 H, B of AB q), 4.95–5.20 (1 H, m), 6.45–6.80 (3 H, m), 7.15–7.60 (6 H, m); ^{13}C NMR δ 20.5 (q), 54.0 (t), 59.1 (d), and aromatic carbon peaks.

Sensitizing and Quenching Experiments. A benzene solution of **1a** (112.5 mg) and **2a** (0.5 mL) in the presence of thioxanthone (in such a ratio that the sensitizer absorbs >95% of the incident light) was degassed with argon and then irradiated at 366 nm for 3 h. Workup gave **3** in 22% yield. In the absence of thioxanthone, **3** was produced 25% yield. A Pyrex filter and methanol solution of naphthalene (5 g/L) were used to isolate the 366-nm light, and a 300-W high-pressure mercury lamp was used as an irradiation source. A benzene solution of **1a** (112.5 mg) and **2a** (0.5 mL) containing 10 molar equiv of a quencher was irradiated under the same conditions. Yield of **3**: 5% (*trans*-stilbene); 3% (2,5-dimethyl-2,4-hexadiene).

Photochemical Reactions of 1,3-Dihydroisobenzofuran-1-thione (22) and 1,3-Dihydroisobenzothiophene-1-thione (23) in the Presence of Tetramethylethylene (2a). A solution of the thione **22** or **23** (200 mg) and tetramethylethylene (~1 mL) in benzene (70 mL) was irradiated. Usual workup gave the thietane derivatives **24** and **25**. Satisfactory microanalyses for **24** and **25** were obtained.

1:1-Adduct 24: mp 104–105 °C; ^{1}H NMR δ 1.05 (3 H, s), 1.35 (3 H, s), 1.40 (3 H, s), 1.82 (3 H, s), 5.08 (2 H, AB q), 7.10–7.40 (3 H, m), 7.50–7.65 (1 H, m); ^{13}C NMR δ 20.2 (q), 24.4 (q), 26.3 (q), 30.4 (q), 49.5 (s), 58.0 (s), 72.1 (t), 100.7 (s), and aromatic carbon peaks; MS m/z 234 (M^+), 160 ($M^+ - C_3H_6S$), 145 ($M^+ - C_3H_5OS$).

1:1-Adduct 25: bp 165 °C (2 mmHg); ^{1}H NMR δ 1.08 (3 H, s), 1.36 (3 H, s), 1.49 (3 H, s), 1.81 (3 H, s), 3.80 (1 H, A of AB q), 4.17 (1 H, B of AB q), 7.15–7.35 (3 H, m), 7.55–7.70 (1 H, m); ^{13}C NMR δ 23.8 (q), 25.0 (q), 26.3 (q), 30.2 (q), 37.3 (t), 49.7 (s), 56.7 (s), 72.3 (s), and aromatic carbon peaks.

Remote Oxidation of Perhydrophenanthrenes by Template-Directed Hydrogen Atom Abstraction[1]

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The use of Breslow's remote functionalization paradigm for installation of an axial C-7 hydroxy group into a perhydrophenanthrene nucleus, with a view toward synthesis of bruceantin (1), has been investigated. The substrates that were evaluated were **9a–c**, **11**, **17**, **18**, and **20**. Substrates **9a–c** all undergo preferential functionalization at C-12. After oxidative cleavage of the initial photoproduct, ketones **18a–c** were obtained in yields of 18–26% (36–41%, based on unrecovered starting material). Unsaturated substrate **11** undergoes remote functionalization exclusively at the secondary allylic position (C-12); enone **20** is obtained in 83% overall yield after oxidative cleavage of the initial photoadduct, **19a,b**. Thus, in this system, C-12 appears to be the preferred site of intramolecular functionalization. Attempts to block reaction at this position by the use of saturated ketone **18**, the derived ketal **17**, or enone **20**, were all unsuccessful. In the case of **18** the only photoproduct was the intramolecular pinacol. Enone **20** gave an exceedingly complex mixture, consisting of many products. Ketal **17** afforded the unusual macrocyclic lactone **21** in 33% yield. The main conclusion of this study is that it is difficult to extrapolate from the excellent regioselectivity observed by Breslow in the steroid system to the trans-anti-trans perhydrophenanthrene system, which is only slightly less rigid. A second factor which we believe is important in the system we have studied is the apparently minor perturbation of having an equatorial substituent at C-4. We postulate that this substituent, which was not present in the model steroidal systems investigated previously by Breslow, disfavors functionalization at C-7.

Biological syntheses of highly functionalized natural products typically involve enzymes that oxidize unactivated carbon positions with exquisite regio- and stereocontrol. Synthetic chemists strive for the level of selectivity exemplified by these biological systems. More than 20 years ago, Breslow reported his group's attempts to mimic the selectivity of enzymatic transformations by employing covalently-attached, benzophenone-containing templates to direct the remote oxidation of steroid substrates.[2] We have evaluated the Breslow remote functionalization strategy for a key step in the synthesis of the quassinoid group of terpenoid natural products.[3] We sought to explore the possibility of employing these template-directed remote functionalization reactions on substrates lacking the steroid D-ring, namely perhydrophenanthrenes. We focused on the benzophenone-mediated reactions because of our interest in functionalization of unactivated methylene positions.[4] In particular, we sought to use the technology of Breslow to introduce the oxygen functionality at position 7 of bruceantin (1).

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(1) Taken in part from the Ph.D. Thesis of Sean M. Kerwin, University of California, Berkeley, 1989.

(2) For a recent review see: Breslow, R. *ChemTracts* **1988** *1*, 333. Breslow, R. *Acc. Chem. Res.* **1980**, *13*, 170.

(3) For a review of quassinoid synthesis work see: Kawada, K.; Kim, Moonsun; Watt, D. S. *Org. Prep. Proc. Int.* **1989**, *21*, 521. For our previous work in the quassinoid area see: Kerwin, S. M.; Paul, A. G.; Heathcock, C. H. *J. Org. Chem.* **1987**, *52*, 1686.

(4) Although the radical-relay remote functionalization reactions are in general more efficient than the benzophenone-mediated remote functionalization reactions, the former are quite specific for methine hydrogen atom abstraction, while the later are much less so. Breslow, R.; Corcoran, R. J.; Snider, B. B.; Doll, R. J.; Khanna, P. L.; Kaleya, R. *J. Am. Chem. Soc.* **1977**, *99*, 905. A recently developed alternative to the benzophenone-mediated functionalization of remote methylene positions utilizes a oxometaloporphyrin-containing template: Grieco, P. A.; Stuk, T. L. *J. Am. Chem. Soc.* **1990**, *112*, 7799.

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