

PHOTOREACTIONS OF PHTHALIMIDE-THIETANES:

FISSION OF THE THIETANE RING AND FORMATION OF 1,2-DITHIANES¹

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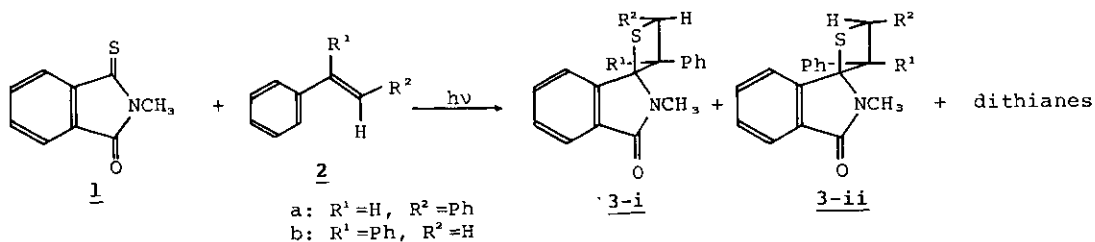
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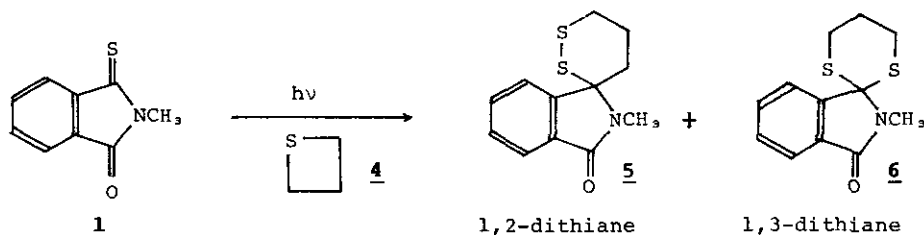
Abstract— Photolysis of N-methylmonothiophthalimide (**1**) in the presence of thietane (**4**) gave 1,2-dithiane (**5**) and 1,3-dithiane (**6**). The formation of 1,2-dithianes in the photoreaction of **1** with styrene derivatives (**2**) is explained in terms of the intermediacy of the phthalimide-thietanes. Photolysis of the thietane ring is also described.

In a previous paper² of this series, we reported that in the photocycloaddition of N-methylmonothiophthalimide (**1**) with styrene derivatives (**2**) certain dithianes were obtained in addition to thietanes (**3**), often in comparable yields (Scheme 1). The dithianes were assumed to be formed by subsequent photochemical fission of the thietanes followed by addition of the aromatic monothioimide. We now wish to report that the fission of the thietane rings in fact leads to formation of 1,2-dithianes.



Scheme 1

The dithianes formed in the photoreactions of 1 with phenyl derivatives of styrene (2) were determined to be consisting of two molecules of 1 and one molecule of the styrene derivative (2) on the basis of their spectral data. Therefore, to confirm a possible reactivity of *N*-methylmonothioimide (1) toward thietanes, a simple thietane (4) was selected and irradiation of a solution of 4 and 1 in benzene was examined. After irradiation for 20 h, 1,2-dithiane (5) and 1,3-dithiane (6) were isolated in 22 and 12% yields, respectively, together with recovery of 1 (28%).

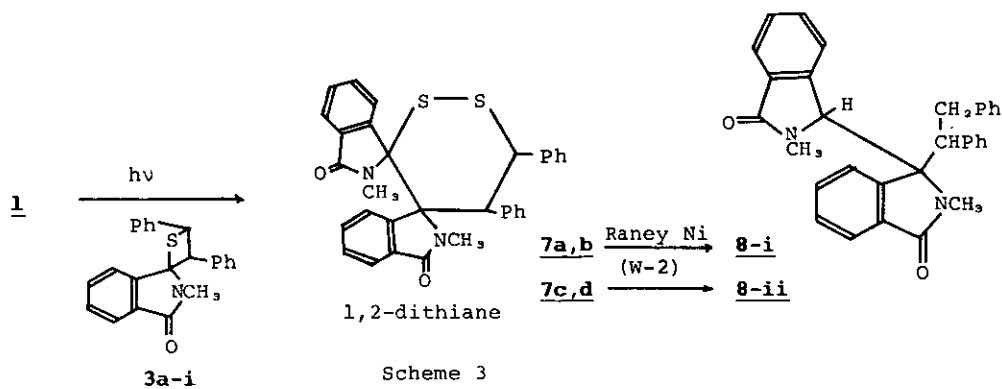


Scheme 2

The mass spectra of the products 5 and 6 showed the molecular ion peak at m/z 251, consistent with the molecular weight of addition product of 1 with 4. The IR spectra indicated the presence of lactam moiety. In the ¹³C-NMR spectra of the adducts, the presence of a spiro-carbon was suggested on the basis of generation of a new quaternary carbon instead of disappearance of a thiocarbonyl. The structures of the products (5 and 6) were inferred to be consisting of dithianes, and were easily discriminated on the basis of the ¹H-NMR and ¹³C-NMR spectra. In the ¹H-NMR spectrum of 6, a four-protons triplet at δ 3.20 with a coupling constant of 6 Hz suggested the presence of two magnetically equivalent methylenes adjacent to a sulfur atom. In addition, the ¹³C-NMR spectrum of 6 showed two peaks (t) at δ 22.1 and 27.9, and the latter peak is due to two magnetically equivalent carbons. As contrasted, in ¹H-NMR spectrum of 5, three methylene protons appeared as multiplets at δ 2.1-2.6 and 3.1-3.4 regions. The ¹³C-NMR spectrum showed three peaks at δ 31.6 (t), 35.3 (t), and 41.6 (t), indicating the presence of three magnetically nonequivalent carbons in the dithiane ring (Scheme 2).

To obtain the information on the pathway of the dithiane formation, thietane 3a-i was irradiated in the presence of 1. As expected, a mixture of dithianes was obtained, and the ¹H-NMR spectrum suggested the presence of four isomers (7a-d) on the basis of a signal due to *N*-CH₃ protons. After column chromatography, two

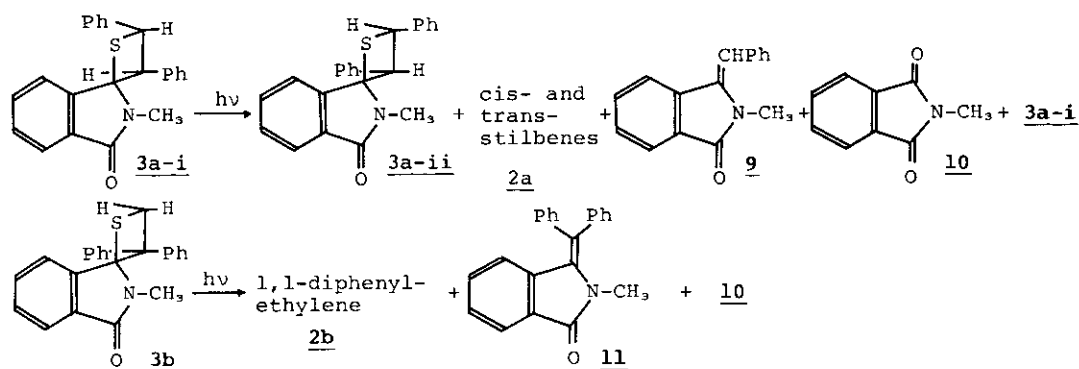
components (7a,b and 7c,d) were separated in 33 and 34% yields accompanied by 3a-i (13%), but further separation of their components was difficult. Similarly, photolysis of the other isomer 3a-ii with 1 also gave an unseparable mixture of dithianes (7e-h) which are different from the mixture (7a-d) on the basis of the $^{13}\text{C-NMR}$ spectrum. On standing the mixture of 7a and 7b in deuteriochloroform containing one drop of conc. hydrochloric acid, equilibrium between 7a and 7b was observed in the $^1\text{H-NMR}$ spectrum. Similarly, each equilibrium between 7c,7e,7g and 7d,7f,7h, was also observed. This equilibrium seems to be due to mobility of benzylic protons of 7 under acidic conditions (Scheme 3).



To see the location of sulfur atoms in the dithiane ring, chemical desulfurization was carried out. Treatment of the mixture (7a and 7b) with Raney nickel gave a simple biphthalimidine 8-i in 42% yield together with the unchanged dithianes (32%). Similarly, from the mixture of 7c and 7d a desulfurized product 8-ii was obtained in 54% yield with unchanged dithiane (11%). The mass spectra of both compounds 8-i and 8-ii showed a similar fragmentation pattern which consisted of two characteristic peaks at m/z 326 (M^+ -phthalimidine) and 291 (M^+ - PhCH_2CHPh). In addition, their elemental analyses and spectral data were in accord with the structure of 8. Thus in the $^1\text{H-NMR}$ spectrum of 8-i, two singlets due to N-CH_3 protons appeared at δ 3.53 and 3.68, and a singlet at δ 5.46 in a lower field region indicated the presence of a methine proton adjacent to both a nitrogen atom and a phenyl ring. Three protons at two benzylic positions appeared at δ 3.6-4.4 as a multiplet. Further, in the off-resonance decoupled $^{13}\text{C-NMR}$ spectrum of 8-i, one triplet and two doublets appeared at δ 36.2, 52.6, and 63.3, indicating the presence of one methylene and two methine groups, respectively. In the higher field region, two quartets appeared at δ 30.3 and 33.1, supporting the presence

of two N-CH₃ groups. Likewise, the ¹H- and ¹³C-NMR spectra of isomer 8-ii were analogous to those of 8-i. Although the stereochemistry of 8-i and 8-ii was unknown, it was deduced from these results that 8-i is a diastereoisomer of 8-ii, and the original mixtures (7a-d) consist of the 1,2-dithianes, since 1,3- and 1,4-dithianes should lead to different desulfurized products (Scheme 3). A possibility of the other 1,2-dithiane (7-iii in Scheme 7) is excluded in view of the structure of the desulfurized product 8. However, the stereochemistry of 1,2-dithiane (7) has been left unsolved.

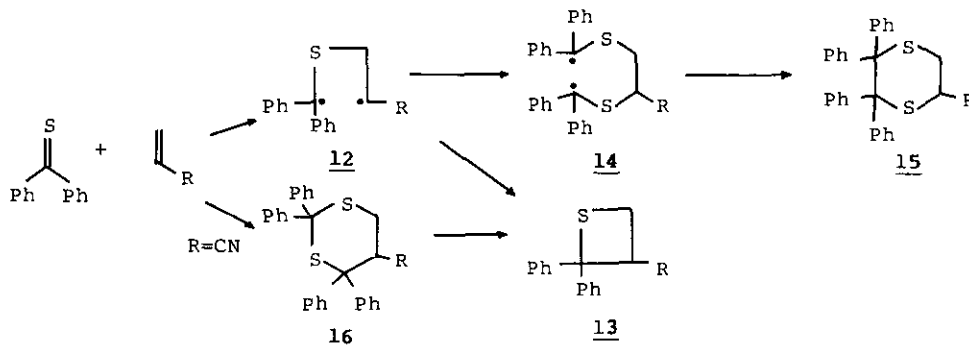
Next, to see the photochemical properties of the thietane itself, an acetonitrile solution of 3a-i was irradiated in the absence of 1 for 30 h. The products were the stereoisomer 3a-ii (10%), *cis*- and *trans*-stilbenes 2a (16%), enamide 9 (14%) and N-methylphthalimide 10 (21%) together with unchanged 3a-i (30%). Similarly, upon photolysis for 35 h, the isomeric thietane 3b^{1a} gave a major product 11 (71%) accompanied by 1,1-diphenylethylene 2b (6%) and 10 (9%). The structures of the enamides 9 and 11³ were determined on the basis of elemental analysis and spectral data. Thus, the thietanes with aromatic substituents 3, initially formed from 1 and the phenyl derivatives of styrene, suffer from secondary photolysis by prolonged irradiation and may be converted to enamides (9 and 11) and/or undergo *retro*-Paterno-Büchi reaction to regenerate 1, which was further oxidized to 10 in analogy with the oxidation of thiones⁴ (Scheme 4).



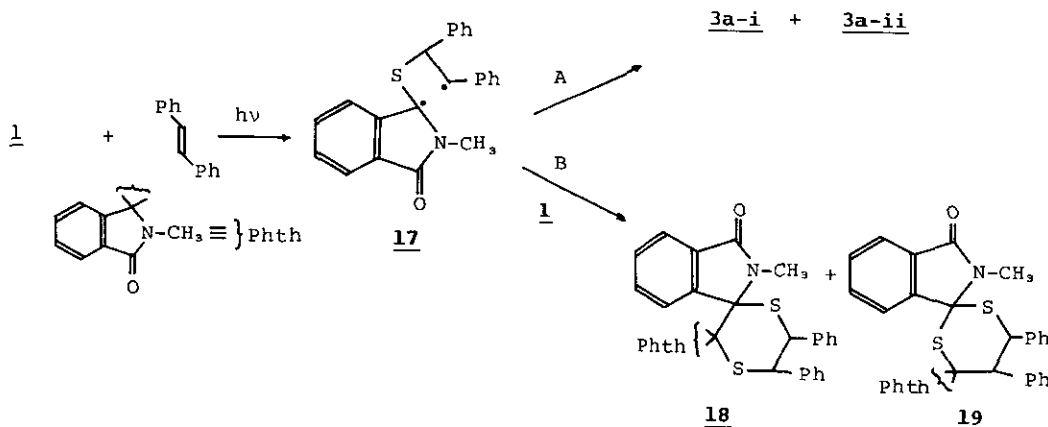
Scheme 4

In the photoreactions of thiones with olefins having electron-releasing substituents, the formation of 1,4-dithianes (15) from two molecules of a thione and one molecule of an olefin was established by the studies of Tsuchihashi and Ohno et al.^{5,6} de Mayo et al.⁷ have also reported that such reaction gives

1,4-dithianes (15) and unstable 1,3-dithianes (16), the latter of which undergoes thermal decomposition to form thietanes (13) (Scheme 5). Whether the dithiane (15) or thietane (13) is formed depends both on the specific olefin and the concentration of thione, and the formation is believed to be a consequence of the efficient radical-trapping abilities of thiobenzophenone. The high reactivity of thiobenzophenone to biradical 12, highly stabilized by two phenyl group and a sulfur atom, results in the formation of biradical 14 leading to 1,4-dithiane (15).

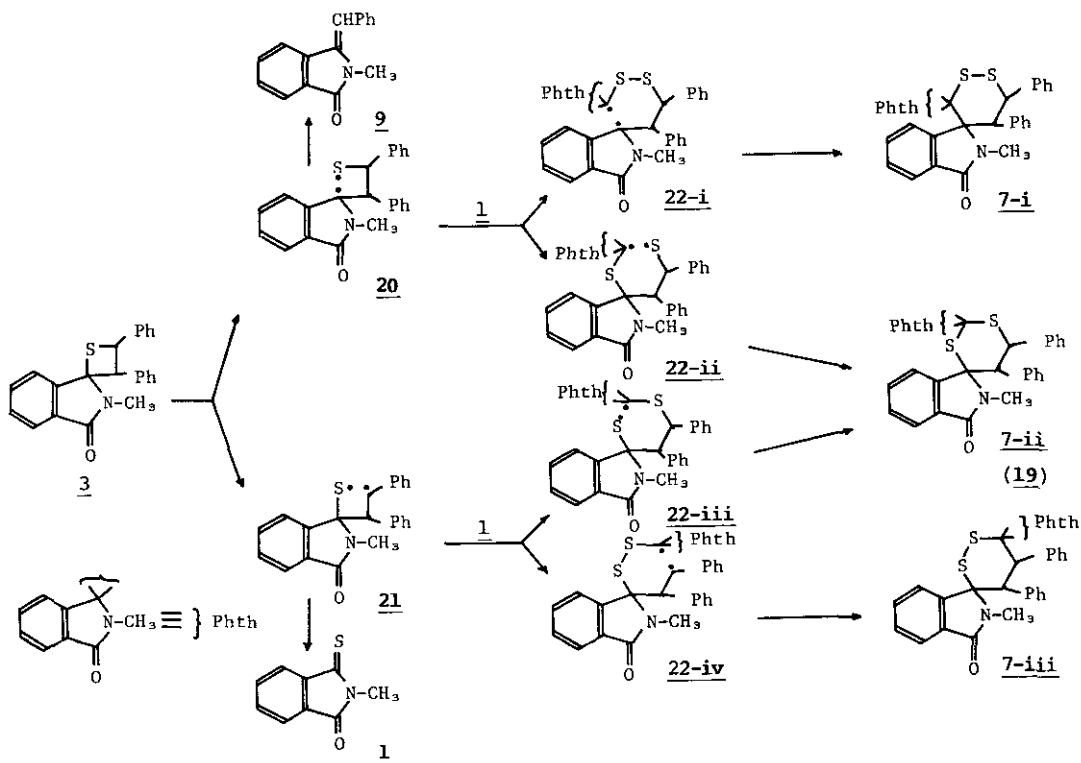


In the present study photoexcited 1 initially attacks the styrene derivatives to generate a biradical 17 in analogy with photochemical behavior of simple thiones (Scheme 6).⁵⁻⁷ Subsequently, the biradical 17 immediately collapses leading to thietane 3 via a pathway A in competition with a pathway B in which the 17 traps another molecule of 1 to form dithianes 18 and/or 19. In contrast to the case of thiobenzophenone (Scheme 5) preference of the thietane formation with the monothio-phthalimide was supported by monitoring fast appearance of products (3) using



thin layer chromatography.

From above results coupled with general information on photodecomposition of thietanes,^{8,9,10} possible pathways of the phthalimide-dithiane formation may be illustrated as follows (Scheme 7). At first, the key intermediate is the initially formed thietane 3. Secondary photolysis of the thietane ring will generate two possible biradical intermediates 20 and 21, presumably both involving a thiyl radical due to homolysis of a sulfur-carbon bond, as affected by a substitution mode on the thietane ring. A biradical (20) either undergoes addition with 1 to lead to dithiane 7-i and/or 7-ii via an intermediate 22, or leads to the enamide 9 by elimination of a thiocarbonyl fragment. The other one (21) also forms the adducts with 1 to give 7-ii and/or 7-iii, or undergoes retro-Paterno-Büchi reaction to give 1. Thus, the two biradical intermediates 20 and 21 are likely to undergo efficient addition with another molecule of the thioimide. Generally bond dissociation energies of C-S bond are relatively low.⁸ Although a formation of 1,3-dithiane (7-ii) was suggested on the basis of the competitive generation of biradicals 20 and 21, the 7-ii was not isolated even in



Scheme 7

the presence of an excess thioimide 1, but 1,2-dithiane 7-i was predominantly obtained probably via an intermediate 22-i. However, the formation of 1,3-dithiane 7-ii may not be excluded because on photolysis of 1 and α -methylstyrene, an unstable adduct¹¹ was obtained, which was easily converted to the thietane derivative and 1 at room temperature in analogy with the behavior of thiones⁷.

As for the dithiane formation there is a marked difference in the behavior of the thiones and thioimides: 1,3- and 1,4-dithianes from the former and 1,2-dithianes from the latter. This difference is reasonably explained by the proposed assumption: in the thione photoreactions the major pathway is the reaction of the biradical 12 with the second molecule of the thione (due to its high reactivity) leading to the 1,4-dithianes 15 in preference to the thietane 13, while in the thioimides the major pathway is formation of the thietane 3 which subsequently produces 1,2-dithianes 7-i (7a-d). In conclusion, the photoreactions of N-methylmonothiophthalimide 1 with styrenes provide a first example of the 1,2-dithiane formation in the photochemistry of the thiocarbonyl systems.

EXPERIMENTAL

All melting points were determined on a Yamato melting point apparatus (model MP-21) and are uncorrected. IR spectra were recorded on a JASCO-A-102 spectrometer. NMR spectra were taken on a Hitachi R-40, a JEOL FX-60, and a JEOL JNM-FX-90Q spectrometers. Chemical shifts are reported in ppm (δ) relative to TMS (0.0 ppm) as an internal standard. The abbreviations used are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Mass spectra (MS) were obtained on a JEOL JMS-QH-100 mass spectrometer. Preparative irradiations were conducted by using a 500 W high-pressure mercury lamp (Eikosha PIH-500) through Pyrex glass at room temperature unless otherwise noted. Stirring of the reaction mixture was effected by the introduction of a stream of nitrogen at the bottom of outer jacket. Column chromatography was conducted using silica gel (Merck, Kieselgel 60, 70-230 mesh).

Preparation of compounds 1 and 3a,b.

Preparation of compounds 1 and 3a,b was described in a previous paper.^{1a}

Irradiation of N-methylmonothiophthalimide 1 in the presence of thietane 4.

A solution of 1 (1 g, 5.6 mmol) and 4 (2.1 g, 28 mmol) in 500 ml of benzene was irradiated with a 1 kW high-pressure mercury lamp (Eikosha EHB-W-1000) for 2 h and worked up as described in the previous paper.^{1a} 1,2-Dithiane (5) and 1,3-dithiane (6) were obtained in 22 and 12% yields, respectively, together with recovery of 1 (28%).

Compound 5: m p 69–71°C. IR (nujol): 1690 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3): δ 2.1–2.6 (4H, m, $-(\text{CH}_2)_2-$), 3.1–3.4 (2H, m, SCH_2), 3.50 (3H, s, N-Me), 7.2–7.9 (4H, m, Ar H). $^{13}\text{C-NMR}$ (CDCl_3): δ 24.8 (q), 31.6 (t), 35.3 (t), 41.6 (t), 82.3 (s), 122.4 (d), 122.9 (d), 130.1 (s), 132.1 (s), 150.5 (s), 166.6 (s). MS m/z: 251 (M^+). Found: C, 57.16; H, 5.17; N, 5.52; S, 25.37. Calc for $\text{C}_{12}\text{H}_{13}\text{NOS}_2$: C, 57.34; H, 5.21; N, 5.57; S, 25.51.

Compound 6: m p 88–90°C. IR (nujol): 1690 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3): δ 1.9–2.3 (2H, m, $-\text{CH}_2\text{CH}_2\text{CH}_2-$), 3.20 (4H, t, $J=6$ Hz, $\text{CH}_2\text{S}\times 2$), 3.30 (3H, s, N-Me), 7.2–7.9 (4H, m, Ar H). $^{13}\text{C-NMR}$ (CDCl_3): δ 22.1 (t), 25.7 (q), 27.9 (t), 71.8 (s), 122.4 (d), 123.5 (d), 129.4 (s), 129.4 (d), 132.3 (d), 149.7 (s), 165.7 (s). MS m/z: 251 (M^+). Found: C, 57.16; H, 5.17; N, 5.52; S, 25.37. Calc for $\text{C}_{12}\text{H}_{13}\text{NOS}_2$: C, 57.34; H, 5.21; N, 5.57; S, 25.51.

Irradiation of thietane 3a-i in the presence of thioimide 1.

A solution of 3a-i (1.788 g, 5 mmol) and 1 (1.772 g, 10 mmol) in 500 ml of acetonitrile was irradiated for 15 h. Work up of the reaction mixture gave two components, dithianes (7a,b and 7c,d) in 33 and 34% yields, respectively, accompanied by 3a-i (13%) and unchanged 1 (59% yield, based on the amounts of 1).

Irradiation of thietane 3a-ii in the presence of thioimide 1.

A solution of 3a-ii (1.788 g, 5 mmol) and 1 (1.772 g, 10 mmol) in 500 ml of acetonitrile was irradiated for 10 h. Work up of the reaction mixture gave a mixture of dithianes (7e,f,g,h) in 39% yield accompanied by 3a-ii (11%) and unchanged 1 (64% yield, based on the amounts of 1).

Raney nickel reductive desulfurization of dithiane 7a,b.

A solution of dithiane (7a,b, 535 mg, 1 mmol) in abs. ethanol was added to Raney nickel (W-2, prepared from 10 g of Raney nickel aluminum alloy) in 5 ml of abs. ethanol. The solution was refluxed for 3 h and the residual oil obtained from the filtrate was chromatographed on silica gel to give 42% of 8-i together with unchanged 7a,b (32%).

Compound 8-i: m p 229–231°C. IR (nujol) 1675 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3): δ 3.53, 3.68 (3H $\times 2$, s $\times 2$, N-Me), 3.6–4.4 (3H, m, $\text{PhCH}_2-\text{PhCH}$), 5.46 (1H, s, NCH), 6.6–7.6 (18H, m, Ar H). $^{13}\text{C-NMR}$ (CDCl_3): δ 30.3 (q), 33.1 (q), 36.2 (t), 52.6 (d), 63.3 (d), 72.7 (s), 122.1 (d), 122.7 (d), 122.8 (d), 123.6 (d), 126.6 (d), 127.0 (d), 127.8 (d), 128.1 (d) $\times 2$, 128.4 (d) $\times 2$, 128.5 (d) $\times 2$, 128.6 (d) $\times 2$, 129.5 (d) $\times 2$, 130.8 (d), 131.8 (d), 132.2 (s), 137.6 (s), 138.4 (s), 142.0 (s), 144.0 (s), 169.7 (s), 171.3 (s). MS m/z: 326 (M^+ -phthalimidine), 291 (M^+ - PhCH_2CHPh). Found: C, 81.34; H, 5.94; N, 5.79. Calc for $\text{C}_{32}\text{H}_{28}\text{N}_2\text{O}_2$: C, 81.33; H, 5.97; N, 5.93.

Raney nickel reductive desulfurization of dithiane 7c,d.

The procedure used for the reduction of dithiane (7c,d) was identical with that used for 7a,b. Separation by column chromatography gave 54% of 8-ii with unchanged 7c,d (11%).

Compound 8-ii: m p 232–233°C. IR (nujol): 1675 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3): δ 2.80, 3.66 (3H $\times 2$, s $\times 2$,

N-Me), 3.8-4.3, 5.5-5.8 (4H, m, PhCH₂-CHPh, NCH), 6.5-7.9 (18H, m, Ar H). ¹³C-NMR (CDCl₃): δ 30.1 (q)x2, 36.0 (t), 52.6 (d), 62.6 (d), 74.5 (s), 121.2 (d), 123.3 (d), 124.1 (d), 124.4 (d), 126.8 (d), 126.9 (d)x2, 127.7 (d)x2, 128.3 (s), 128.6 (d)x4, 129.4 (d)x2, 130.8 (d), 131.2 (d), 131.5 (d), 134.4 (s), 136.8 (s), 138.1 (s), 141.2 (s), 143.7 (s), 168.5 (s), 169.3 (s). MS m/z: 326 (M⁺-phthalimidine), 291 (M⁺-PhCH₂CHPh). Found: C, 80.90; H, 5.96; N, 6.17. Calc for C₃₂H₂₈N₂O₂: C, 81.33; H, 5.97; N, 5.93.

Irradiation of thietane 3a-1.

A solution of 3a-1 (358 mg, 1 mmol) in 10 ml of acetonitrile was irradiated for 30 h. Separation by column chromatography gave the stereoisomer 3a-ii (10%), cis- and trans-stilbenes 2 (16%), enamide 9 (14%) and N-methylphthalimide 11 (21%) together with unchanged 3a-i (30%).

Compound 9: m p 176-178°C. IR (nujol): 1690 cm⁻¹. ¹H-NMR (CDCl₃): δ 3.14 (3H, s, N-Me), 5.42 (1H, br s, PhCH), 7.0-7.8 (9H, m, Ar H). MS m/z: 235 (M⁺).

Irradiation of thietane 3b.

A solution of 3b (72 mg, 0.2 mmol) in 2 ml of benzene was irradiated for 35 h. Separation by column chromatography gave enamide 11 (71%) accompanied by 1,1-diphenylethylene 2b (6%) and 10 (9%).

Compound 11: m p 178-180°C. IR (nujol): 1690 cm⁻¹. ¹H-NMR (CDCl₃): δ 2.83 (3H, s, N-Me), 6.3-6.4 (1H, m, Ar H), 7.0-7.4 (12H, m, Ar H), 7.7-7.8 (1H, m, Ar H). MS m/z: 311 (M⁺). Found: C, 84.92; H, 5.47; N, 4.50. Calc for C₂₂H₁₇NO: C, 84.86; H, 5.50; N, 4.50.

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