Photocycloaddition Reactions of Thioimides with Alkynes *

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Photochemical reaction between *N*-methyl(thiophthalimide) and diphenylethyne or hex-3-yne involves selective cycloaddition at the C=S bond, and yields a spiro-thiete product. A related spiro-1,2-dithiole isolated from the reaction mixture may be formed during the work-up procedure. With bis-(alkythio)ethynes, both *N*-methyl(thiophthalimide) and *N*-methyl(dithiophthalimide) form α-alkythio α,β-unsaturated dithioesters; such 1:1 adducts are most readily explained on the basis of initial spiro-thiete formation.

N-Substituted phthalimides,[1] unlike related amides, undergo quite efficient and high-yielding photoreactions, often to give products that are not those expected on the basis of similar reactions with other carbonyl compounds such as ketones. For example, intramolecular hydrogen abstraction and cyclization in appropriately substituted phthalimides can yield macrocyclic products,[2] and with alkenes 2-benzazepine -1,5-diones (1) are formed (rather than oxetanes).[3] However, evidence of photochemical reaction between imides and alkynes is, surprisingly, unavailable, in contrast to the well studied reactions of imides with alkenes.


(1)

(2) 66 %
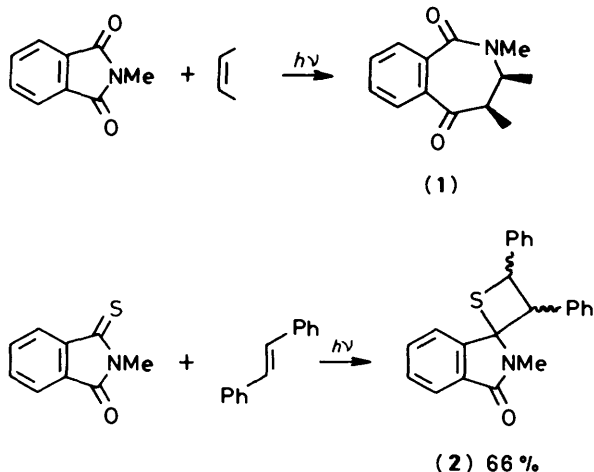
The photochemistry of thioketones is well documented,[4,5] and these compounds behave like ketones in many respects. In particular, they give thietanes or thietes by cycloaddition with alkenes or alkynes respectively. Other thiocarbonyl compounds such as thiophosgene,[6] *O*-alkyl thiocarboxylates,[7] thioparabanates,[8] and thiouracils,[9] also give thietanes on irradiation with alkenes. Photochemical cyclisation of thioimides *via* intramolecular hydrogen abstraction can occur,[10,11] though the isolated products are often not those formed after the initial ring-closure,[12,13] We recently reported[14] that with alkenes thioimides give spiro-thietanes (2), and an independent report of similar reactions has

appeared.[15] Our studies also included photocycloaddition of thioimides with diphenylketene and a ketenimine.[16] We now present the results[17] of a study of the photochemical reactions between *N*-methyl(thiophthalimide) or *N*-methyl-(dithiophthalimide) and diaryl-, dialkyl- or bis(alkylthio)-ethynes, which yield spiro-thietes or compounds derived from them.

Results and Discussion

Photochemical reaction of thioketones with alkynes yields as the major product a thiete (3),[8] or a benzothiapyran (4) derived by attack on an adjacent aromatic ring of the proposed intermediate biradical.[18]

(3) 91%
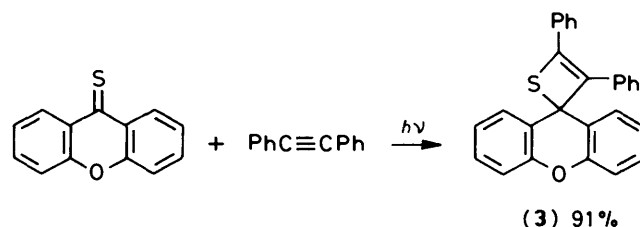
Irradiation of *N*-methyl(thiophthalimide) with diphenylethyne produced a spiro-thiete in good yield (5). Support for the product structure comes from elemental microanalysis, which indicates a 1:1 adduct of the substrates, whilst the ^{13}C n.m.r. spectrum reveals an amide carbonyl (168 p.p.m.) but no signal
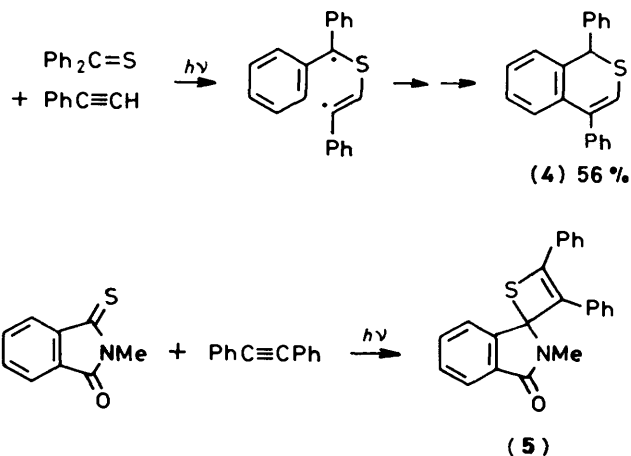

(4) 56 %

(5)

for a thiocarbonyl carbon (190—230 p.p.m.); instead there is a signal for a highly deshielded quaternary aliphatic carbon (78 p.p.m.). The i.r. spectrum shows an amide carbonyl stretching band(1 715 cm^{-1}). The spiro-thiete is quite stable thermally, though it decomposes slowly on heating above its melting temperature and also on heating under reflux in ethanol with added benzenesulphonic acid; in neither case is a single product formed cleanly.

It is noteworthy that reaction occurs at the thiocarbonyl, rather than the carbonyl, group; this is proving a general feature in most thioimide photochemistry, and it has already been noted in cycloadditions with alkenes[14,15] or ketene derivatives,[16] and in processes that might proceed by way of intramolecular hydrogen transfer.[10–13] Explanation may be attributed either to: (a) localisation of excitation energy in the C=S rather than the C=O bond, or (b) unfavourable energetics of reaction from a low-lying excited state (E_T is estimated to be ca. 210 kJ mol^{-1}) in which the much stronger C=O bond is disrupted.

After photolysis, the N-methyl region of the ^{1}H n.m.r. spectrum indicates an initial very high yield of spiro-thiete; also present are unchanged substrates and N-methylphthalimide (formed by oxidation of the thioimide). Furthermore there is no evidence for a product, analogous to that found for thiobenzophenone and alkynes (4), in which cyclisation to one of the aromatic rings has taken place. The reason for this may be that an intermediate biradical (6) in the thioimide reaction has a much greater degree of rigidity than the corresponding intermediate from the thioketone, imposed by the incorporation of the thiocarbonyl group in a five-membered ring fused to the aromatic ring.


(6)   (7)
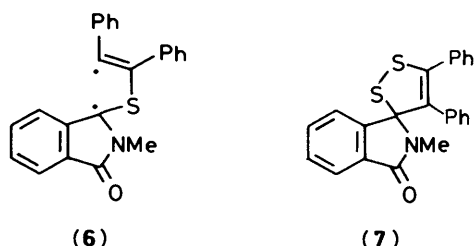
The spiro-1,2-dithiole (7) (1%) isolated from the mother liquors of the recrystallisation of the spiro-thiete, was identified as being related to the thiete (5) in which an extra sulphur atom has been incorporated into the molecule. Its i.r. and ^{1}H n.m.r. spectra are similar to those of the major product, and the mass spectrum (supported by elemental microanalysis results) demonstrates the presence of two sulphur atoms. In the original mixture after photolysis spiro-1,2-dithiole (7) is not present above the limit of n.m.r. detection (2%); thus we suspect it may be formed from the thiete during recrystallisation. This is in keeping with the observation[19] that a small amount of a spiro-1,2-dithiolane is produced when the photocycloadduct between N-methyl(thiophthalimide) and stilbene is heated under reflux in ethanol. A similar spiro-dithiole product has been found[8,20] in the reaction of a thioparabanate with diphenylethyne (8).

Irradiation of N-methyl(dithiophthalimide) (9) with diphenylethyne under similar conditions led to recovery of almost all the dithioimide; small quantities of other material separated by column chromatography were comparatively polar and appeared to arise via oxidation (C=O stretching bands in the i.r. spectrum). The triplet energy of the dithioimide (<185 kJ mol^{-1}) is lower than that of the thioimide (ca. 210 kJ mol^{-1}), and it could be that photocycloaddition is thermodynamically unfavourable for the substrate with the lower excited state energy. However, the energy difference is not large, and certain

42-57%   (8) 22%

(9)
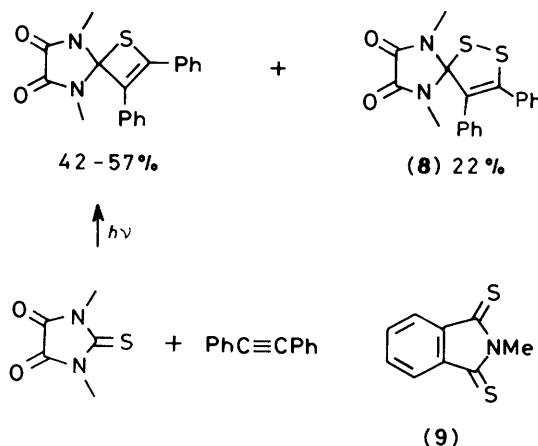
alkynes (see below) do react with the dithioimide in a manner analogous to that of the thioimide. It therefore seems more likely the much lower quantum efficiency reflects instead a shorter lifetime of the reactive excited state for the dithioimide.

Products (10) from the photochemical reaction of N-methyl-(thiophthalimide) with an aliphatic alkyne (hex-3-yne) parallel those formed from the aryl-substituted ethyne. The yield of spiro-1,2-dithiole (10b) is higher (10%) in this system, but we are not able to say with certainty whether it is a direct product of the photochemical reaction or is formed subsequently from spiro-thiete (10a). The ^{1}H n.m.r. spectrum of (10b) shows that

(10a)   (10b)
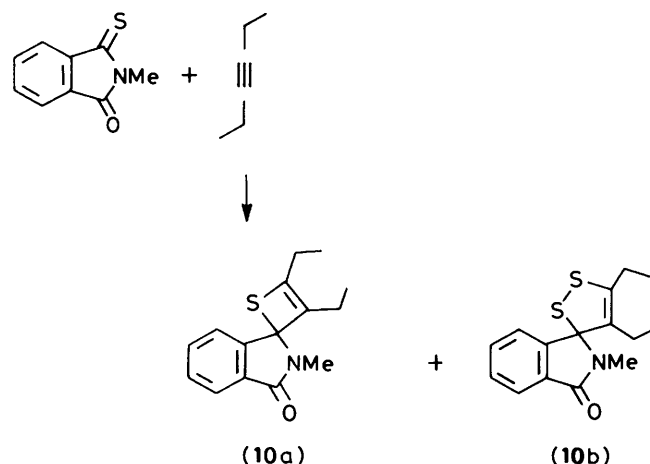
the ethyl groups are in different environments, which is in accord with the 1,2-dithiole structure rather than an alternative, symmetrical 1,3-dithiole isomer.

In the reaction of thioparabanates with dimethyl acetylenedicarboxylate[8,20] the major product can be rationalised as arising by initial formation of a spiro-thiete, ring opening to give an unsaturated thioketone, and (4 + 2) cycloaddition of a second molecule of alkyne to yield the enethione (11). Products of the unsaturated thiocarbonyl type are formed readily when thioketones react photochemically with bis(alkylthio)alkynes.[21] Thus we irradiated N-methyl(thiophthalimide) with bis-(methylthio)ethyne.

A mixture of E- and Z-α,β-unsaturated dithioesters (12; X = O), was obtained in high yield (ca. 100% by n.m.r. analysis with an internal standard). Unlike spiro-thietes these compounds give thiocarbonyl signals in the ^{13}C n.m.r. spectrum (228 p.p.m.), and the spectral information is consistent with the

(11) 68%

(Y = CO₂Me)
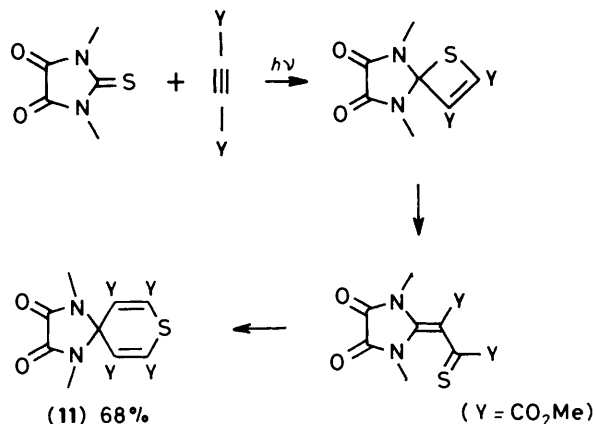
proposed structures. The n.m.r. spectra of the mixture in solution can be interpreted in terms of a 1:2 mixture of E and Z isomers. The signal for the N-methyl group of the E isomer is at a higher chemical shift value (3.76 p.p.m.) than that for the Z isomer (3.29 p.p.m.), which is in keeping with the closer proximity of the strongly deshielding sulphur atom of the thiocarbonyl group to the methyl group in the former isomer. Correspondingly, the signal for one of the aromatic ring protons is at much higher chemical shift value (8.85 p.p.m.) for the Z isomer, in which the thiocarbonyl group is much closer to this ring. It is likely that the two isomers are in equilibrium in solution, and that the thiete provides a ready route for the isomerisation (13). Crystallisation yields red crystals, which appear to be a single compound (sharp melting temperature), in amounts greater than can be attributed to one isomer in a 1:2 mixture; on dissolving these crystals however, the 1:2 mixture is formed immediately.

Reaction of N-methyl(dithiophthalimide) with bis(methylthio)ethyne followed a parallel course, giving a mixture of E

(X = O,S)

E **Z (12)**

(13)
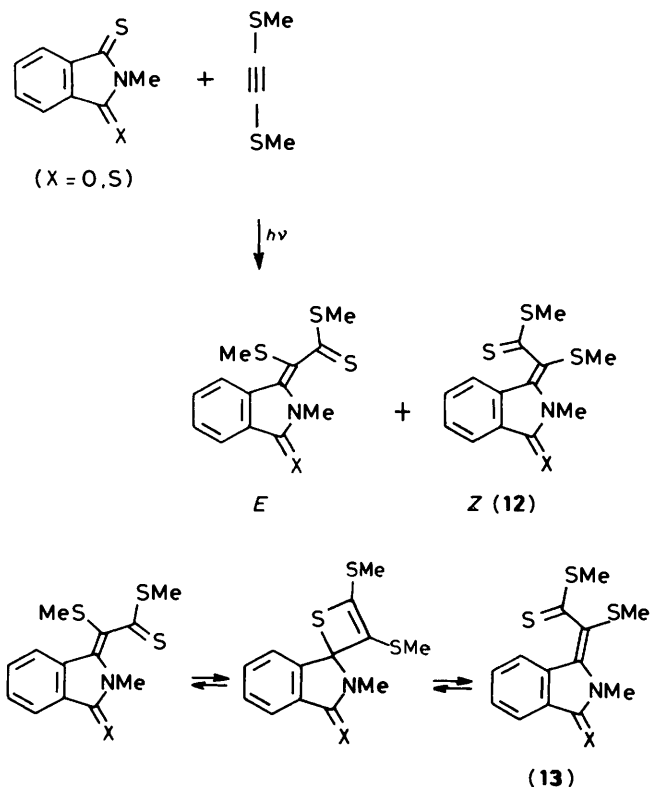
and Z isomers (12; X = S) whose spectra show similar characteristic features (δ_H = 4.22 and <8.2 p.p.m. for NMe and ArH in the E isomer, 3.70 and 8.85 p.p.m. for the Z isomer). N-Methyl(thiophthalimide) reacted with bis(t-butylthio)ethyne in a slightly different way: the yield of crude product was very high, though sacrificial recrystallisation was necessary to remove small amounts of N-methylphthalimide formed as an oxidation product in spite of continuous bubbling with nitrogen. Both the crude and purified product appear to contain only the Z-isomer (δ_H = 3.42 and 9.10 p.p.m. for NMe and ArH). This is reasonable in view of the severe steric interactions between the aromatic ring and the t-butyl group that occur in the E isomer.

Thus, overall our studies reveal that N-methyl(thiophthalimides) react photochemically with alkynes in a way that resembles the reactions of thioketones with alkynes; interaction is always at the thiocarbonyl group, unlike many of the photoreactions of phthalimides with unsaturated addends.

Experimental

Separation of product mixtures after photolysis was by silica-gel column chromatography using chloroform–toluene (50:50)→methanol–chloroform (4:96) as eluant.

N-Methyl(thiophthalimide) (5.6 mmol) and diphenylethyne (8.4 mmol) were irradiated for 22 h in benzene (120 cm³) using a 125-W medium-pressure mercury arc and a Pyrex filter. Separation of the reaction mixture gave diphenylethyne (1.34 g), N-methyl(thiophthalimide) (0.79 g), N-methylphthalimide (13 mg, 7%), and 2-*methyl*-3',4'-*diphenyl*-2,3-*dihydro*-1H-*isoindole*-3-*spiro*-2'-*thiet*-1-*one* (5) (300 mg, 71%). The last fraction was recrystallised from ethanol to give pale yellow crystals (220 mg, 52%), m.p. 153—157 °C (Found: C, 77.7; H, 4.8; N, 3.7; S, 9.4. $C_{23}H_{17}NOS$ requires C, 77.7; H, 4.8; N, 3.9; S, 9.0%); $\nu_{max.}$(KBr) 1 715 cm⁻¹; δ_H(CDCl₃) 3.08 (3 H, s) and 6.9—8.35 (14 H, m); δ_C(CDCl₃) 25.3, 78.0, 122.1, 123.9, 125.5, 127.3, 128.0, 128.7, 129.4, 130.2, 131.3, 132.5, 132.8, 143.7, and 168.1; m/z 355 (M^+), 354, 326, 322, 278, 246, 178 (100%), 121, 117, 77, and 76; m/z (M^+) 355.103 ($C_{23}H_{17}NOS$ requires 355.103). A further crop of green crystals from the recrystallisation solution proved to be 2-*methyl*-4',5'-*diphenyl*-2,3-*dihydro*-1H-*isoindole*-3-*spiro*-3'-(1',2'-*dithiol*)-1-*one* (7) (5 mg, 1%), m.p. 193—194 °C (Found: C, 71.6; H, 4.6; N, 3.6; $C_{23}H_{17}NOS_2$ requires C, 71.3; H, 4.4; N, 3.6%); $\nu_{max.}$(KBr) 1 715 cm⁻¹; δ_H(CDCl₃) 3.15 (3 H, s) and 6.7—7.8 (14 H, m); m/z 387 (M^+), 371, 354, 323 (100%), 322, 246, 178, 165, 130, 105, 77, and 76; m/z (M^+) 387.076 ($C_{23}H_{17}NOS_2$ requires 387.075).

Irradiation of N-methyl(dithiophthalimide) with diphenylethyne in benzene under similar conditions led to recovery of substrates and isolation of small amounts of oxidised material ($\nu_{max.}$ 1 710—1 745 cm⁻¹).

N-Methyl(thiophthalimide) (3.9 mmol) and hex-3-yne (8.4 mmol) were irradiated for 6 h in acetonitrile (120 cm³) using a 125-W medium-pressure mercury arc and a Pyrex filter; further additions (9.1 and 5.1 mmol) of hexyne were made after 2 and 4 h. Separation of the reaction mixture gave N-methyl(thiophthalimide) (0.34 g), N-methylphthalimide (81 mg, 25%), and 3',4'-*diethyl*-2-*methyl*-2,3-*dihydro*-1H-*isoindole*-3-*spiro*-2'-*thiet*-1-*one* (10a) (206 mg, 40%) as an oil; $\nu_{max.}$ 1 715 cm⁻¹; δ_H(CDCl₃) 0.78 (3 H, t, J 7 Hz), 1.34 (3 H, t, J 7 Hz), 1.81 (2 H, q, J 7 Hz), 2.65 (2 H, q, J 7 Hz), 2.96 (3 H, s), and 7.1—7.9 (4 H, m); m/z 259 (M^+), 258, 227, 198 (100%), and 76; m/z = 259.1018 ($C_{15}H_{17}NOS$ requires 259.1031).

Also obtained was a small amount (60 mg, 10%) of 4',5'-*diethyl*-2-*methyl*-2,3-*dihydro*-1H-*isoindole*-3-*spiro*-3'-(1',2'-

dithiol)-1-*one* (**10b**) as yellow crystals, m.p. 59—60 °C. (Found: C, 61.5; H, 5.75; N, 4.6; S, 23.8. $C_{15}H_{17}NOS_2$ requires C, 61.9; H, 5.8; N, 4.8; S, 22.0%); $v_{max.}$ 1 705 cm^{-1}; δ_H(CDCl$_3$) 0.70 (3 H, t, J 7 Hz), 1.26 (3 H, t, J 7 Hz), 1.62 (2 H, q J 7 Hz), 2.54 (2 H, q, J 7 Hz), 2.98 (3 H, s), and 7.4—7.9 (4 H, m); δ_C(CDCl$_3$) 14.6, 14.8, 20.6, 24.2, 25.3, 123.6, 125.5, 130.2, and 132.5 (quaternary carbons not seen); $m/z = 291$ (M^+), 258 (100%), 226, 198, and 178.

Irradiation of N-methyl(thiophthalimide) with dimethyl acetylenedicarboxylate, or of N-methyl(dithiophthalimide) with hex-3-yne or with dimethyl acetylenedicarboxylate, under similar conditions led to mxitures from which no component was isolated in a pure state.

N-Methyl(thiophthalimide) (2.8 mmol) and bis(methylthio)ethyne (5.6 mmol) were irradiated for 5.5 h in dichloromethane (105 cm^3) using a 125-W high-pressure mercury arc (Philips HPL-N) and a CuCl$_2$–CaCl$_2$–HCl filter solution. Separation of the mixture gave one major fraction which was recrystallised from ethanol to give 3-[1,2-*bis*(*methylthio*)-2-*thioxoethylidene*]-2-*methyl*-2,3-*dihydro*-1H-*isoindol*-1-*one* (**12**) as red crystals (334 mg, 72%), m.p. 105—109 °C (Found: C, 52.9; H, 4.6; N, 4.7; S, 33.0. $C_{13}H_{13}NOS_3$ requires C, 52.9; H, 4.4; N, 4.7; S, 32.6%); $v_{max.}$(KBr) 1 715 cm^{-1}; δ_H(CDCl$_3$) E-form 2.30 (3 H, s), 2.72 (3 H, s), 3.68 (3 H, s), and 7.15—7.85 (4 H, m); Z-form 2.08 (3 H, s), 2.69 (3 H, s), 3.21 (3 H, s), 7.15—7.85 (3 H, m), and 8.85 (1 H, dd, J 8 and 2 Hz); δ_C(CDCl$_3$) E-form 17.6, 21.0, 31.1, 121.5, 122.0, 123.0, 128.7, 129.0, 131.6, 134.6, 136.4, 167.8, and 228.2; Z-form 17.4, 20.4, 29.7, 123.2, 124.1, 125.8, 129.0, 129.7, 132.3, 136.7, 137.8, 167.7, and 227.8; m/z 295 (M^+), 248, 233, 216 (100%), 201, and 117.

N-Methyl(dithiophthalimide) (5.2 mmol) and bis(methylthio)ethyne (5.2 mmol) were irradiated for 29 h in acetonitrile (400 cm^3) using a high-pressure mercury arc and a CuCl$_2$–CaCl$_2$–HCl filter solution. Separation of the reaction mixture gave N-methyl(dithiophthalimide) (0.13 g from ethanol), and 3-[1,2-*bis*(*methylthio*)-2-*thioxoethylidene*]-2-*methyl*-2,3-*dihydro*-1H-*isoindole*-1-*thione* (**12**) (767 mg, 55%), which yielded dark magenta crystals (576 mg) on recrystallisation from ethanol, m.p. 104—106 °C (Found: C, 50.2; H, 4.1; N, 4.5; S, 39.3. $C_{13}H_{13}NS_4$ requires C, 50.2; H, 4.2; N, 4.5; S, 41.2%); δ_H(CDCl$_3$) E-form 2.39 (3 H, s), 2.82 (3 H, s), 4.22 (3 H, s), and 7.15—8.15 (4 H, m); Z-form 2.40 (3 H, s), 2.78 (3 H, s), 3.70 (3 H, s), 7.15—8.15 (3 H, m), and 8.85 (1 H, dd, J 8 and 2 Hz); δ_C(CDCl$_3$) E-form 17.0, 21.2, 36.6, 123.3, 125.1, 126.4, 132.7, 133.2, 134.8, 138.1, 140.0, 192.1, and 226.4; Z-form 17.2, 20.7, 35.4, 125.1, 125.6, 129.1, 129.9, 131.3, 131.9, 136.2, 136.4, 192.1, and 226.4; m/z 311 (M^+), 264, 232 (100%), 217, 185, and 146; m/z (M^+) 310.992 ($C_{13}H_{13}NS_4$ requires 310.993).

N-Methyl(thiophthalimide) (5.6 mmol) and bis(t-butylthio)ethyne (5.9 mmol) were irradiated for 22 h in acetonitrile (440 cm^3) using a high-pressure mercury arc and a CuCl$_2$–CaCl$_2$–HCl filter solution. Separation of the reaction mixture gave N-methyl(thiophthalimide) (0.36 g from ethanol), and 3-[1,2-*bis*(*t-butylthio*)-2-*thioxoethylidene*]-2-*methyl*-2,3-*dihydro*-1H-*isoindol*-1-*one* as red crystals (339 mg, 25%, after two recrystallisations from ethanol), m.p. 93—95 °C (Found: C,

59.95; H, 6.8; N, 3.7; S, 25.3. $C_{19}H_{25}NOS_3$ requires C, 60.2; H, 6.6; N, 3.7; S, 25.3%); $v_{max.}$ 1 715 cm^{-1}; δ_H(CDCl$_3$) 1.50 (9 H, s), 1.67 (9 H s), 3.42 (3 H, s), 7.3—7.9 (3 H, m), and 9.10 (1 H, m); δ_C(CDCl$_3$) 26.4, 28.1, 30.4, 31.2, 51.3, 52.9, 122.0, 123.3, 126.5, 129.9, 132.0, 134.0, 137.9, 168.2, and 234.0; m/z 379 (M^+), 258, 233, 202 (100%), 190, and 117; m/z (M^+) 379.111, ($C_{19}H_{25}NOS_3$ requires 379.110).

Irradiation of either N-methyl(thiophthalimide) or N-methyl(dithiophthalimide) with 1-methylthiopropyne gave mixtures from which no component could be isolated in a pure state. N.m.r. spectra of partially separated fractions were consistent with the presence of two major components in each system, but it was not possible to assign these with certainty to expected product structures.

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