Products from Dimethyl Hex-2-en-1-yne-1,6-dioate and Dimethyl Penta-2,3-diene-1,5-dioate with Compounds possessing Two Adjacent Nucleophilic Centres

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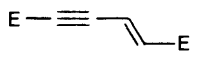
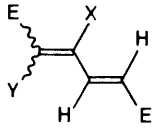
Thioureas and thioamides were found to add *via* sulphur mainly to position 5 of dimethyl hex-2-en-4-yne-1,6-dioate; often this was followed by cyclisation to give γ-lactams. In some cases *cis*-addition was observed as well as *trans*-addition, even in methanol. Imidazoline-2-thione and benzimidazole-2-thione also reacted at position 4 to give fused thiazinone derivatives. 2-Amino-benzothiazole, -thiazole, and -pyridine all added *via* the ring nitrogen to position 4, and subsequent cyclisation gave fused pyrimidones. 1,2-Diaminobenzene and 2-aminobenzenethiol reacted like the thioureas at position 5, but addition to position 4 was followed by a further Michael addition to position 3. These benzene derivatives reacted with dimethyl penta-2,3-diene-1,5-dioate to give cyclic compounds with exocyclic unsaturated ester groups. In contrast, thioureas reacted with the allene to give derivatives of methyl 4-oxothiazin-6-ylacetate. Structures of the new compounds were deduced from their ^1H and ^{13}C n.m.r., u.v., i.r., and mass spectra.

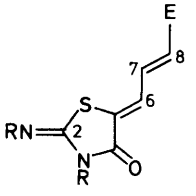
DIMETHYL HEX-2-EN-4-YNE-1,6-DIOATE (DMHD) (1) is readily prepared by dimerisation of methyl propiolate with *N*-methylpiperidine at 0 °C.[1] In principle, nucleophiles could add to either end of the triple bond to give *E*- and *Z*-isomers of either of the adducts (2) and (3), which could be distinguished by their ^1H n.m.r. spectra. Under base-catalysed conditions methoxide ion is reported to add to the 4-position,[2] while secondary amines in diethyl ether add to position 5;[3] in both cases two geometric isomers were formed. However, our preliminary examination of the ^1H n.m.r. spectra of reaction mixtures from diethylamine and DMHD in various solvents showed that nucleophilic addition never occurred exclusively to either position. Thus, while nucleophilic addition was mainly to position 5 in acetonitrile (mainly *cis*-addition) and methanol (mainly *trans*-addition), in dimethyl sulphoxide addition to positions 4 and 5 occurred to similar extents. The reactions of DMHD with a variety of compounds possessing two nucleophilic centres are now reported.



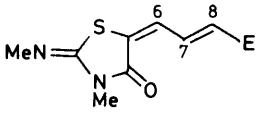
(1)



(2) X = nucleophile, Y = H
(3) X = H, Y = nucleophile



(4) R = Me
(5) R = Ph



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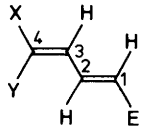
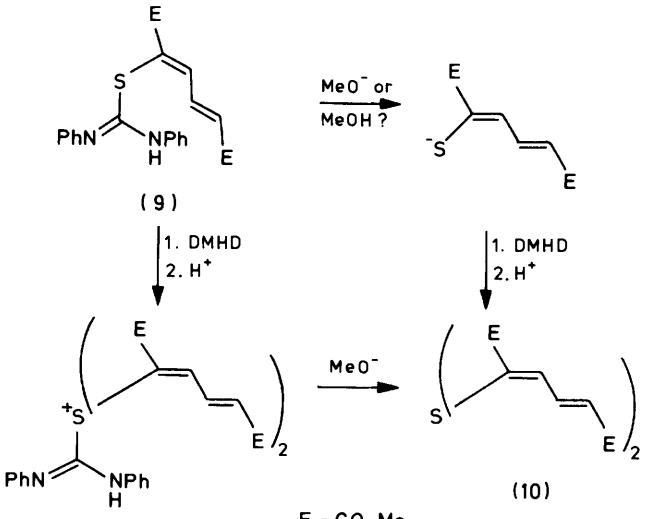


(7) X = CO_2Me, Y = H
(8) X = H, Y = CO_2Me

E = CO_2Me

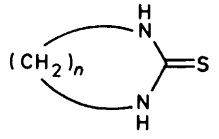
N,N'-Dimethylthiourea with DMHD in methanol gave the cyclic compounds (4) (52%) and (6) (1.6%), which result from the addition of sulphur to position 5 and the condensation of nitrogen with the adjacent ester group. Compound (6) appears to be the first example of the *cis*-addition of a thiourea moiety and the associated proton to an activated acetylene. When the reaction was carried out in dry acetonitrile, a precipitate containing both isomers was obtained, with the *cis*-adduct predominating (86 : 14). The assignment of these two structures is based on the strong similarity of the chemical shifts of the vinyl protons to those in *trans-trans*-(7) and *cis,trans*-dimethyl muconate (8).[4] In particular the central vinyl proton in the *cis*-adduct (6) is deshielded (τ 1.31) by the nearby ester and lactam carbonyls [*cf.* τ 1.60 in compound (8)]. The vinyl protons of the *trans*-isomer (4) have similar chemical shifts, giving a complex spectrum even at 300 MHz.

N,N'-Diphenylthiourea with DMHD in methanol gave the analogous *trans*-addition product (5) and the sulphide (10). The latter product was identified from its 300 MHz ^1H n.m.r. spectrum and a strong $(M + 1)^+$ peak (80%) in its chemical ionisation mass spectrum. Possible mechanisms for its formation are suggested in Scheme 1. Methyl propiolate formed a mixture of similar diacrylates with thioacetamide.[5] *trans*-Addition to the cyclic thioureas (11) and (12) in methanol gave the bicyclic compounds (14) and (15). The formation of the sulphide (10) in the reaction with diphenylthiourea may be related to a slow rate of cyclisation of the 1 : 1 adduct (9) resulting from steric hindrance by the phenyl groups in the transition state. In contrast, the imidazoline-2-thione (13) added to DMHD in methanol by both *cis*- and *trans*-modes, giving compounds (18) and (19) as well and the adduct (17), which is formed by attack of sulphur at position 4. Only the *trans*-addition product (19) could be isolated by chromatography. The adduct (18) was the sole product obtained at room temperature in dry

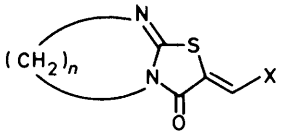


SCHEME 1

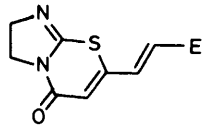
acetonitrile, and was recovered unchanged after refluxing for 1 h in dry methanol. Its formation in methanol thus occurs directly *via* the zwitterion (21) and is not a result of isomerisation. The addition of imidazoline-2-thione to dimethyl acetylenedicarboxylate (DMAD) in dry acetonitrile gave only the *trans*-addition product. No *cis*-additions of thioureas to DMAD have been observed, probably because in such a structure [*e.g.* (20)] there would be an end-to-end interaction between the lactam and ester carbonyl groups. In the DMHD *cis*-addition



(11) n = 3
(12) n = 4
(13) n = 2



(14) n = 3, X = (*E*)-CH=CHE
(15) n = 4, X = (*E*)-CH=CHE
(16) n = 4, X = CO_2Me



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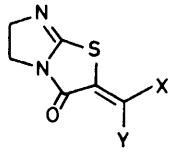
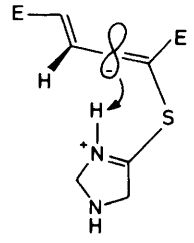


(18) X = H, Y = (*E*)-CH=CHE
(19) X = (*E*)-CH=CHE, Y = H
(20) X = H, Y = CO_2Me

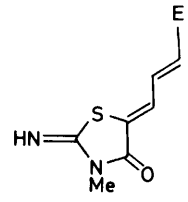
E = CO_2Me

products this is replaced by a lactam–olefinic proton interaction which is sterically and electronically more favourable.

The chemical shifts and coupling constants between the vinyl protons in the adduct (18), measured from a 300 MHz spectrum, are in close agreement with those from the *cis,trans*-muconate (8). An n.O.e. experiment suggests that the butadiene residue in compound (18) is co-planar. Irradiation of the 6-H signal enhanced that from 8-H but not that from 7-H, and irradiation of the 8-H signal enhanced that from 6-H. Had the double bonds been orthogonal the 7-H signal should have been affected at least as much as 8-H. The ^{13}C n.m.r. spectrum of the adduct (15) was similar to that of the corresponding DMAD adduct (16) [6] except that C-5 was less deshielded (δ 134.2, *cf.* δ 149.3) because of the weaker electron-withdrawing effect of the vinyl group compared with that of the ester group. *N*-Methylthiourea reacted with DMHD in methanol to give compound (22) and a little of the corresponding *cis*-adduct. The alternative structure (23) is excluded since C-2 is not strongly



(21)



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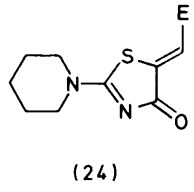

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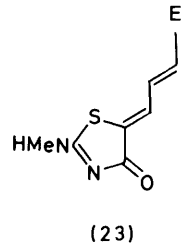


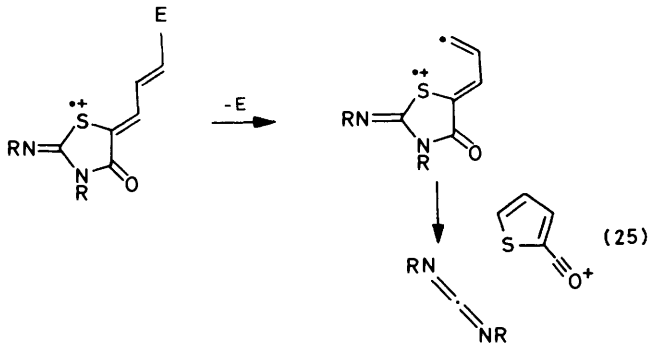
(23)

E = CO_2Me

deshielded in the ^{13}C n.m.r. spectrum [*cf.* C-2 in (24) [6,7] δ 175.9) and is more in agreement with that of structure (15). The possibility of an exocyclic methylimino-group is clearly excluded by the chemical shift of the *N*-methyl carbon which is 10 p.p.m. upfield of the expected position (δ 39.0).[6] The highly insoluble precipitate from thiourea and DMHD in methanol was identified by ^1H n.m.r. spectroscopy as being a mixture of *cis*- and *trans*-addition products in the ratio 1 : 2. The mass spectra of the analogous adducts (4), (13), (14), (15), and (17) all show molecular ions, with the loss of an ester group as one possible fragmentation. All these compounds have strong peaks at *m/e* 111 in their spectra which are possibly due to the aromatic ion (25) (Scheme 2). The diphenyl derivative (5) has a base peak corresponding to *N,N'*-diphenylcarbodi-imide which is consistent with this proposal.

Benzimidazole-2-thione reacted with DMHD in methanol to give the cyclic compound (26), derived by initial attack at position 4 on DMHD, and the 1 : 1-molar adduct (28) derived by attack at position 5. The

spectra of compound (26) showed a deshielded aromatic proton (τ 1.54—1.64) and a high lactam carbonyl stretching frequency (1 708 cm^{-1}), similar to those of compound (27) [6] (τ 1.43—1.60; 1 703 cm^{-1}). The 300 MHz spectrum of the other adduct (28) was consistent



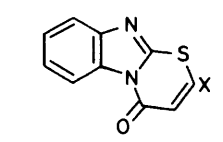
SCHEME 2

with *trans*-addition, but all the vinyl protons were deshielded relative to the *trans*-thiourea adducts and the equivalent muconate. Refluxing this adduct in dry acetonitrile overnight did not affect ring closure to compound (29), in contrast to the reaction of benzimidazole-2-thione with DMAD which, under these conditions, gives product (30).[6] DMHD in methanol with 2-thiohydantoin and tetramethylthiourea gave a tar and a trace of compound (10), respectively.

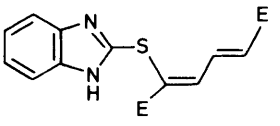
Ethanethioamide and DMHD in methanol gave compound (31), whose ^{13}C n.m.r. spectrum showed a quaternary carbon at δ 97.0 and a strong similarity to that of the corresponding adduct (32) from DMAD.[6] The reaction in acetonitrile gave a precipitate which tarred on isolation. 2-Aminobenzenethioamide and DMHD gave compound (33) which showed typical signals from primary amine bonds in its i.r. spectrum, and an absorption at 478 nm in the u.v. spectrum as observed for the DMAD adduct (34).[6] The mass spectrum of compound (33) showed the molecular ion; the loss of an ester group was followed by a fragmentation similar to that shown in Scheme 2, leading to 2-aminobenzonitrile and the thiole (25).

Pyridine-2-thione and indoline-2-thione with DMHD in methanol gave compounds (35) and (36), respectively identified from their spectra. The adduct (36), in contrast to the corresponding DMAD adduct (37) which gave a thiazino[3,2-*b*]benzimidazole, did not cyclise in refluxing acetic acid to yield the tricyclic derivative (38).

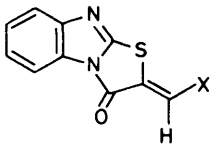
2-Aminobenzothiazole reacted with DMHD to give the cyclic compound (39), in which the heterocyclic nitrogen has attacked position 4 of DMHD. The lactam carbonyl stretching frequency (1 650 cm^{-1}) and the longest wavelength u.v. maximum (302 nm) are in closer agreement with the data for compound (40) (1 640 cm^{-1}; 301 nm) [8] than with those of its isomer (42) (1 675 cm^{-1}; 339 nm),[8] thus supporting the structural assignment. Furthermore, the ^1H n.m.r. spectrum does not show the deshielded aromatic proton expected for structure (43).



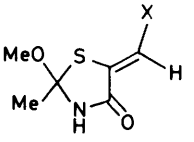
(26) X = (*E*)-CH=CHE
(27) X = E



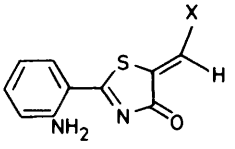
(28)



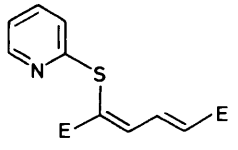
(29) X = (*E*)-CH=CHE
(30) X = E



(31) X = (*E*)-CH=CHE
(32) X = E



(33) X = (*E*)-CH=CHE
(34) X = E



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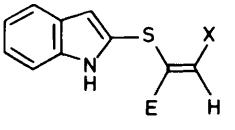
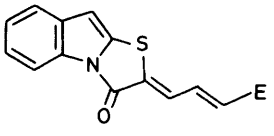


(36) X = (*E*)-CH=CHE
(37) X = E



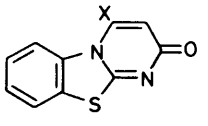
(38)

E = CO_2Me

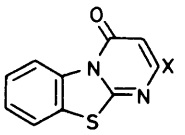
2-Aminothiazole gave the analogous adduct (44), but 2-aminothiazoline only gave a tar. In their mass spectra compounds (39) and (44) show molecular ions which fragment, losing either an ester or carbon monoxide moiety. In a similar manner 2-aminopyridine gave the pyrimidine derivative (45) which was identified primarily by the lack of a strongly deshielded aromatic proton which would be expected in the 6-position of the alternative pyrido[1,2-*a*]pyrimidin-4-one structure.[9]

1,2-Diaminobenzene gave compounds (46) and (47) with DMHD in methanol. For the amide (46), the *E*-arrangement of the enaminic double bond is proposed since the central vinyl proton is strongly deshielded by the adjacent lactam carbonyl. The ester-carbonyl stretching frequency is very low (1 688 cm^{-1}) suggesting strong delocalisation of electrons from the enaminic nitrogen through the diene system into the ester group. In the mass spectrum compound (46) showed a molecular ion which successively lost ' CO_2Me ' and then ' H_2O ' to give an ion which could have the aromatic structure (48). The isolation of this *cis*-addition product from a reaction in methanol suggests that isomerism to the *trans*-

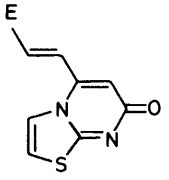
addition product is much more difficult than for the equivalent DMAD adduct, since it is unlikely that the adduct (46) is the thermodynamically more stable isomer. Such isomerisations probably proceed *via* an imine intermediate,[10] but for DMHD adducts this would



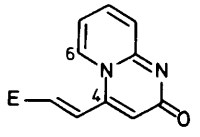
(39) X = (*E*)-CH=CHE
(40) X = H
(41) X = E



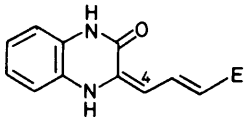
(42) X = H
(43) X = (*E*)-CH=CHE



(44)



(45)



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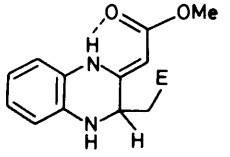
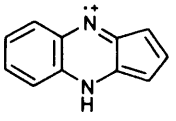


(47)

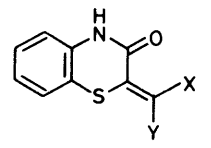


(48)

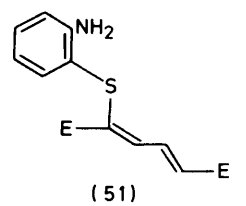
E = CO_2Me

involve the loss of a conjugated butadiene system. The ^1H n.m.r. spectrum of the ester (47) shows an NH resonance (τ 4.02) coupled to a single proton (τ 5.87, J 2.8 Hz), which is itself coupled (J 6.8 Hz) to a pair of protons. The couplings were confirmed by double-resonance experiments. The other NH resonance (τ −0.07) is not exchanged on shaking with D_2O, suggesting the presence of a hydrogen bond to the adjacent ester carbonyl which has a very low stretching frequency (1 654 cm^{-1}).

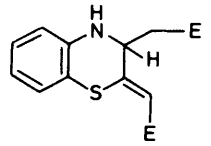
2-Aminobenzenethiol reacted with DMHD in methanol at room temperature to give compound (51) by *trans*-addition; this compound showed absorption frequencies in its i.r. spectrum characteristic of a primary aromatic amine. On heating it cyclised to the benzothiazine (49), which precipitated from a refluxing mixture of the reactants in methanol. It did not show a low-field proton in its n.m.r. spectrum, so structure (50) is excluded. Chromatography of the filtrate also yielded



(49) X = H, Y = (*E*)-CH=CHE
(50) X = (*E*)-CH=CHE, Y = H



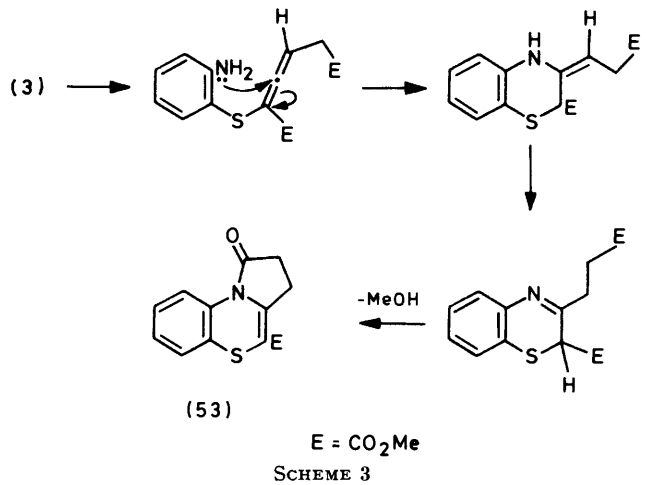
(51)



(52)

E = CO_2Me

the diester (52) and some tricyclic compound (53). The ^1H n.m.r. spectrum of the thiazine (52) showed an uncoupled vinylic proton (τ 4.23), an eight-line system (τ 7.49) corresponding to a diastereotopic methylene group coupled to a methine proton (τ 5.57), and an uncoupled (possibly due to rapid exchange) NH proton. Compound (53) may be formed by tautomerism of the initial 1 : 1 adduct to give an allene, followed by cyclisation (shown in Scheme 3). In the ^1H n.m.r. spectrum, the CH_2CH_2



(53)

E = CO_2Me

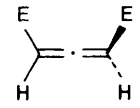
SCHEME 3

resonances form an A_2B_2 system and the 9-proton (τ 1.60—1.90) is deshielded by the lactam carbonyl. This last-named group shows a high stretching frequency (1 719 cm^{-1}) in its i.r. spectrum, and in the mass spectrum the molecular ion (100%) loses fragments of *m/e* 28 or 59.

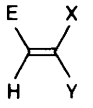
Dimethyl penta-2,3-diene-1,5-dioate (54), available [11] from dimethyl 3-oxopentane-1,5-dioate, reacts with nucleophiles at position 3.[12] Although *cis*- and *trans*-additions cannot be distinguished, two geometric isomers (55) and (56) can be produced; thus diethylamine and methanol both gave adducts like (55), while cyclohexylamine gave the other type, like (56), which in this case contains an intramolecular hydrogen bond [shown in (57)].[12]

Several compounds containing two adjacent nucleo-

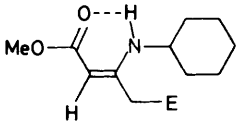
philic centres have now been found to give cyclic compounds of structural type (58) or (59). The former structure is preferred for the adduct (60), obtained from 1,2-diaminobenzene, since the resonance of the β-enaminic proton (τ 5.32) is very similar to that of compound (47), but is quite different from that of the tricyclic



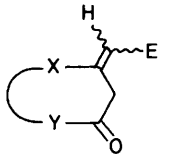
(54)



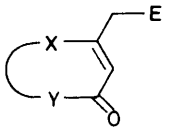
(55) X = CH_2E, Y = nucleophile
(56) X = nucleophile, Y = CH_2E



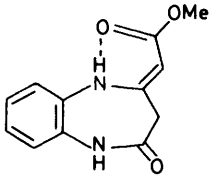
(57)



(58)



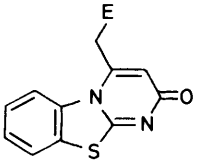
(59)



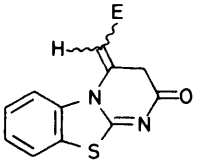
(60)

E = CO_2Me

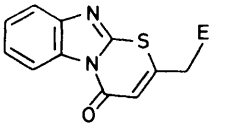
compound (41). There appears to be a hydrogen bond between the 5-proton and the ester carbonyl since in the ^1H n.m.r. spectrum one of the NH signals cannot be exchanged with D_2O and the ester carbonyl stretching frequency is low (1 695 cm^{-1}). The mass spectrum showed one major fragmentation path involving successive losses of masses 32 and 42 (possibly CH_2=C=O) from the molecular ion (83%) to give a base peak at *m/z* 158. In contrast the adduct (61), obtained from 2-aminobenzothiazole, is assigned a structure of the same type as (59) since the β-enaminic proton signal (τ 3.72) is too low for the alternative structure (62). The lactam stretch at 1 642 cm^{-1} is similar to that observed for compounds (39) and (40), supporting the postulated addition of the heterocyclic nitrogen to the allene system. The adduct from benzimidazole-2-thione has been identified as having structure (63) rather than (64) since the ^{13}C n.m.r. spectrum of the ring system strongly resembles that of the thiazine (27);[6] in particular the C-3 resonances are closely comparable (δ 120.0 and 121.3 p.p.m. respectively) while an exocyclic vinyl carbon would be expected to appear at higher field as for compound (30) (δ 112.9 p.p.m.).[6] Furthermore the ester carbonyl carbon resonance (δ 169.0 p.p.m.) is too low for an unsaturated ester [*cf.* for (30), δ 165.7 p.p.m.] and its stretching frequency in the i.r. spectrum (1 740 cm^{-1}) is too high. *N,N'*-Dimethylthiourea gave a similar adduct (65) which showed an olefinic carbon resonance at δ 118.5 p.p.m. and a low ester carbonyl carbon resonance (δ 169.4 p.p.m.). The carbon at the centre of the thiourea moiety resonates at δ 146.5 p.p.m. in a similar position to that of the DMHD adduct (14) (δ 147.4 p.p.m.). The i.r. spectrum again shows a high ester carbonyl stretching frequency (1 742 cm^{-1}) and an amide stretching signal at 1 663 cm^{-1}.



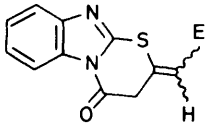
(61)



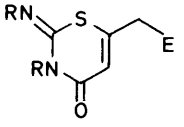
(62)



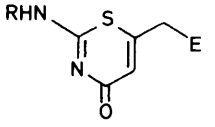
(63)



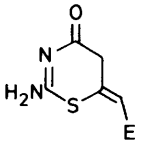
(64)



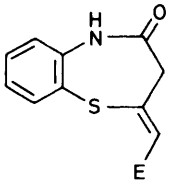
(65) R = Me
(66) R = Ph



(67) R = Me
(68) R = H



(69)



(70)

E = CO_2Me

N,N'-Diphenylthiourea gave an analogous adduct (66), though the amide stretch was at higher frequency (1 697 cm^{-1}). In contrast methylthiourea gave the 2-methylaminothiazinone (67) which was identified by the two strongly deshielded carbons (C-2, δ 163.1 and C-4, δ 168.2 p.p.m.) which are similar to those observed for the DMAD adduct (24). Thiourea gave the corresponding adduct (68) (deduced from the similarity of the ^{13}C n.m.r. spectra), but the i.r. spectrum (Nujol mull) of this compound showed a low ester stretching frequency (1 710 cm^{-1}) suggesting that in the solid phase it might have structure (69). Both the solid and solution phase spectra of the previous adduct (67) suggest a saturated ester. 2-Aminobenzenethiol reacted with the allenic diester to give the benzothiazepinone (70) whose i.r. spectrum shows an unsaturated ester carbonyl stretch.

EXPERIMENTAL

Most instruments and chromatographic procedures have been described previously.[6] Unless specified otherwise, i.r. spectra were measured in Nujol and u.v. spectra in dry methanol (M) or dry methanol acidified with one drop of 72% perchloric acid (A). 300 MHz N.m.r. spectra were measured on a Bruker WH 300 spectrometer. Methanol was dried with magnesium and distilled. Acetonitrile was dried with calcium hydride. Dimethyl hex-2-en-4-yne-1,6-dioate (DMHD) (1) was prepared by treating methyl propiolate [13] with *N*-methylpiperidine, and purified by sublimation on a 10-g scale (overall yield 82%) which gave a white solid, m.p. 53—54 °C (lit.,[1] 53—54 °C, 88%). Alternatively, the acetylene was purified by crystallisation from hexane. Dimethyl penta-2,3-diene-1,5-dioate (54) was prepared from dimethyl 3-oxopentane-1,5-dioate [11] (25%), b.p. 79—80 °C at 0.12 mmHg (lit.,[11] 80 °C at 0.1 mmHg; 26%).

Reactions of DMHD (1).—(*a*) *With* N,N'-*dimethylthiourea*. DMHD (5.65 g) was added to a stirred solution of *N,N'*-dimethylthiourea (3.50 g) in methanol (100 ml), the thiourea having been previously dried *in vacuo*. After being stirred at room temperature for 6 h, the mixture was filtered to give *methyl* (2E,4Z)-4-(3-*methyl*-2-*methylimino*-4-*oxo*-1,3-*thiazolin*-5-*ylidene*)*but*-2-*en*-1-*oate* (4) (3.21 g, 39.8%), as white microneedles (from chloroform–methanol), m.p. 188—190 °C (Found: C, 49.6; H, 5.0; N, 11.7. $C_{10}H_{12}N_2O_3S$ requires C, 50.0; H, 5.0; N, 11.7%); $\nu_{max.}$ 1 720s, 1 660s, 1 620m, and 1 593m cm^{-1}; $\lambda_{max.}$ (M) 232 (ε 12 500) and 349 nm (23 900); $\lambda_{max.}$ (A) 242 (ε 8 900), 284infl. (10 600) and 327 nm (26 700); *m/e* 240 (M^+, 38), 181 (55), 114 (29), 111 (M − 119$^+$, 100), 99 (15), 83 (10), 71 (20), and 69 (17%); *M** 157.0 (209 ⟶ 181), 136.5 (240 ⟶ 181), and 62.0 (111 ⟶ 83). Further product (4) was precipitated overnight giving an overall yield of 52.0%. The reaction residue was chromatographed and a yellow band eluted with chloroform. The evaporated fraction was triturated with diethyl ether to give methyl (2E,4E)-4-(3-*methyl*-2-*methylimino*-4-*oxo*-1,3-*thiazolidin*-5-*ylidene*)*but*-2-*en*-1-*oate* (6) (0.13 g, 1.6%), as white feathers (from chloroform–diethyl ether), m.p. 134—136 °C (Found: C, 49.8; H, 4.8; N, 11.8. $C_{10}H_{12}NO_3S$ requires C, 50.0; H, 5.0; N, 11.7%); $\nu_{max.}$ 1 721s, 1 663s, 1 621m, and 1 590m cm^{-1}. When this reaction was carried out in refluxing acetonitrile (30 min) a precipitate (18%) was produced which contained products (4) and (6) in the ratio 3 : 22 (by ^1H n.m.r.).

(*b*) *With* N,N'-*diphenylthiourea*. DMHD (4.00 g) was added to a stirred solution of *N,N'*-diphenylthiourea (5.43 g) in warm, dry methanol and the mixture stirred for 9 h. Filtration gave *bis*[1Z,3E)-1,4-*dimethoxycarbonylbuta*-1,3-*dien*-1-*yl*]*sulphide* (10) (0.89 g, 20.2%), as pale salmon microneedles (from chloroform–methanol), m.p. 167—168.5 °C (Found: C, 52.0; H, 4.6%. $C_{16}H_{18}O_8S$ requires C, 51.9; H, 4.9%); $\nu_{max.}$ 1 700s, 1 621w, and 1 568w cm^{-1}; *m/e* (CI; CH_4) 399 (M + 29$^+$, 66), 371 (M + 1$^+$, 80), 340 (M − 30$^+$, 95), 339 (M − 31$^+$, 100), and 307 (100%). On standing at room temperature for 7 d, the filtrate deposited *methyl* (2E,4Z)-4-(3-*phenyl*-2-*phenylimino*-4-*oxo*-1,3-*thiazolidin*-5-*ylidene*)*but*-2-*en*-1-*oate* (5) (1.68 g, 19.4%), as yellow needles (from chloroform–methanol), m.p. 157—160 °C (Found: C, 65.7; H, 4.3; N, 7.6. $C_{20}H_{16}N_2O_3S$ requires C, 65.9; H, 4.4; N, 7.7%); $\nu_{max.}$ 1 704s, 1 700s, 1 660infl., 1 637s, 1 612s, and 1 588s cm^{-1}; $\lambda_{max.}$ (M) 233.5infl. (ε 10 400) and 342.5 nm (11 400); *m/e* 364 (M^+, 55), 305 (16), 195 (25), 194 (M − 170$^+$, 100), 169 (77), 111 (57), 97 (25), 95 (28), 85 (21), 83 (26), 77 (25), 69 (31), and 67 (21%); *m** 255.5 (364 ⟶ 305). The filtrate was evaporated and the residue triturated with methanol to give *N,N'*-diphenylthiourea (1.19 g). The remaining reaction residue was chromatographed and a yellow band eluted with toluene. The ^1H n.m.r. spectrum indicated a mixture of compound (10) and its (1*E*,3*E'*)-isomer, the presence of the latter being inferred from a double doublet at δ 1.34 (*J* 11.9 and 15.7 Hz).

(*c*) *With perhydropyrimidine*-2-*thione* (11). DMHD (6.00 g) was added to a solution of the thiourea (11) (4.14 g) in methanol (100 ml) and the mixture stirred at room temperature for 16 h. The solvent was removed and the residue chromatographed. A pale yellow band, eluted with chloroform, yielded *methyl* (2E,4Z)-4-(2,3,6,7-*tetrahydro*-3-*oxo*-5H-*thiazolo*[3,2-a]*pyrimidin*-2-*ylidene*)*but*-2-*en*-1-*oate* (14) (2.18 g, 24.4%), as pale orange plates (from methanol), m.p. 132—134 °C (Found: C, 52.4; H, 4.8; N, 11.1. $C_{11}H_{12}N_2O_3S$ requires C, 52.3; H, 4.8; N, 11.1%); $\nu_{max.}$ 1 694s, 1 630s, 1 615s, and 1 593s cm^{-1}; *m/e* 252 (M^+, 29), 193 (M − 59$^+$, 100), 165 (36), 114 (15), 111 (25), 99 (11), 83 (17), and 82 (11%); *m** 184.2 (237 ⟶ 209), 168.5 (221 ⟶ 193), 148.1 (252 ⟶ 193), 141.1 (193 ⟶ 165), 86.0 (114 ⟶ 99), and 62.0 (111 ⟶ 83).

(*d*) *With perhydro*-1H-1,3-*diazepine*-2-*thione* (12). DMHD (6.50 g) was added to solution of the thiourea (12) (5.00 g) in warm methanol (100 ml) and stirred at room temperature for 24 h. The solvent was removed and the residue chromatographed. A yellow band, eluted with chloroform, gave *methyl* (2E,4Z)-4-(2,3,5,6,7,8-*hexahydro*-3-*oxothiazolo*[3,2-a]-[1,3]*diazepin*-2-*ylidene*)*but*-2-*en*-1-*oate* (15) (2.69 g, 28.9%), as cream needles (from methanol), m.p. 118—120 °C (Found: C, 54.2; H, 5.4; N, 10.4. $C_{12}H_{14}N_2O_3S$ requires C, 54.1; H, 5.3; N, 10.5%); $\nu_{max.}$ 1 720s, 1 661s, 1 620s, and 1 594s cm^{-1}; $\lambda_{max.}$ (M) 233.5 (ε 10 600), 260.5 (6 600), and 351 nm (21 900); $\lambda_{max.}$ (A) 243.5 (ε 7 400), 259.5 (7 500), 332 (24 900), and 341infl. nm (23 600); *m/e* 266 (M^+, 58), 208 (13), 207 (M − 59$^+$, 100), 179 (32), 114 (13), 111 (45), 99 (11), 98 (17), 83 (14), and 68 (22%); *m** 161.1 (266 ⟶ 207).

(*e*) *With methylthiourea*. Methylthiourea (2.76 g) and DMHD (5.04 g) were stirred together in methanol (80 ml) for 8 h. A cream precipitate was formed which contained a mixture of compounds (22) and (23). Recrystallisation from methanol yielded *methyl* (2E,4Z)-4-(2-*imino*-3-*methyl*-4-*oxo*-1,3-*thiazolidin*-5-*ylidene*)*but*-2-*en*-1-*oate* (22) (2.83 g, 40.8%), as white microneedles (from methanol), m.p. 179—180 °C (Found: C, 47.6; H, 4.4; N, 12.2%. $C_9H_{10}N_2O_3S$ requires C, 47.8; H, 4.5; N, 12.4%); $\nu_{max.}$ ($CHCl_3$) 3 325w, 1 710s, 1 632infl., 1 620s, and 1 597m cm^{-1}; *m/e* 226 (M^+, 29), 167 (M − 59$^+$, 100), 114 (42), 111 (70). 99 (27). 83 (17). and 39 (47%).

(*f*) *With imidazoline*-2-*thione* (13). (i) In methanol. DMHD (6.50 g) was added to a solution of the thiourea (13) (3.48 g) in warm methanol (100 ml) and the mixture stirred at room temperature for 6 h. A white precipitate was filtered off and shown by ^1H n.m.r. spectroscopy to be a mixture of at least three compounds. This mixture was chromatographed using chloroform as eluant and the first band (which showed blue fluorescence on irradiation at 350 nm) gave *methyl* (2E,4Z)-4-(2,3,5,6-*tetrahydro*-3-*oxo*-*imidazo*[2,1-b]*thiazol*-2-*ylidene*)*but*-2-*en*-1-*oate* (19) (1.05 g 12.6%) as yellow feathers (from chloroform–methanol), m.p. 179—184.5 °C (Found: C, 50.5; H, 4.3; N, 11.8. $C_{10}H_{10}N_2O_3S$ requires C, 50.4; H, 4.2; N, 11.8%); $\nu_{max.}$ ($CHCl_3$ 1 710s, 1 630s, and 1 590w cm^{-1}; *m/e* 238 (M^+, 26), 179 (M − 59$^+$, 100), 114 (23), 111 (73), 99 (13), 85 (19), 83 (29),

74 (21), 71 (18), and 69 (13%); *m** 134.8 (238 → 179), 86.0 (114 → 99), and 62.0 (111 → 83). Later bands eluted with chloroform gave mixtures of compounds (17) and (18) (^{1}H n.m.r. spectrum).

(ii) *In acetonitrile.* DMHD (2.16 g) was added to a suspension of compound (13) (1.16 g) in warm acetonitrile and stirred overnight. The fawn-coloured precipitate formed was chromatographed and a brown band eluted with chloroform to give *methyl* (2E,4E)-4-(2,3,5,6-*tetrahydro*-3-*oxoimidazo*[2,1-b]*thiazol*-2-*ylidene*)*but*-2-*en*-1-*oate* (18) (0.38 g, 14.0%) as cream needles (from chloroform), m.p. 204—206 °C (Found: C, 50.7; H, 4.4; N, 11.9. $C_{10}H_{10}N_2O_3S$ requires C, 50.4; H, 4.2; N, 11.8%); $\nu_{max.}$ ($CHCl_3$) 1 720infl., 1 705s, and 1 623s cm^{-1}; *m/e* 238 (M^+, 22), 180 (12), 179 ($M - 59^+$, 100), 111 (12), 83 (17), 68 (17), and 39 (25%).

(*g*) *With benzimidazole*-2(3H)-*thione.* The thione (1.00 g) and DMHD (1.12 g) were refluxed in methanol (25 ml) for 20 min to give a yellow feathery precipitate of *methyl* (E)-3-(4-*oxo*-4H-[1,3]*thiazino*[3,2-b]*benzimidazol*-2-*yl*)*prop*-2-*en*-1-*oate* (26) (0.69 g, 36.2%) as yellow microneedles (from DMF), m.p. 255—257 °C (Found: C, 58.7; H, 3.6; N, 9.6. $C_{14}H_{11}N_2O_3S$ requires C, 58.5; H, 3.9; N, 9.8%); $\nu_{max.}$ 1 710s, 1 692s, 1 653w, 1 630m, 1 603w, and 1 564w cm^{-1}; *m/e* 286 (M^+, 100) and 227 (58%); *m** 180.4 (286 → 227). After 2 h at room temperature, more crystals had been deposited from the filtrate. These were filtered off to give *dimethyl* (2Z,4E)-2-(1H-*benzimidazol*-2-*ylthio*)*hexa*-2,4-*diene*-1,6-*dioate* (28) (0.44 g, 20.8%) as yellow microplates (from methanol), m.p. 175—177 °C (Found: C, 56.5; H, 4.3; N, 8.9. $C_{15}H_{14}N_2O_4S$ requires C, 56.6; H, 4.4; N, 8.8%); $\nu_{max.}$ 1 718s, 1 708s, 1 625w, and 1 572w cm^{-1}; *m/e* (CI, NH_3) 319 ($M + 1^+$, 39), 318 (M^+, 18), 289 (49), 288 (38), 287 (71), 286 (56), 259 (30), 256 (21), 245 (27), 228 (60), 227 ($M - 91^+$, 100), 169 (28), 150 (25), 111 (30), 91 (39), and 78 (23%).

(*h*) *With ethanethioamide.* Ethanethioamide (2.00 g) and DMHD (4.50 g) were refluxed together in methanol (65 ml) for 20 h. The volume of solvent was reduced to 10 ml and diethyl ether (30 ml) added to give a precipitate of *methyl* (2E,4Z)-4-(2-*methoxy*-2-*methyl*-4-*oxo*-1,3-*thiazolidin*-5-*ylidene*)*but*-2-*en*-1-*oate* (31) (0.98 g, 15.1%) as cream-coloured plates (from methanol), m.p. 141—152 °C (Found: C, 49.5; H, 5.5; N, 5.5. $C_{10}H_{13}NO_4S$ requires C, 49.4; H, 5.4; N, 5.8%); $\nu_{max.}$ ($CHCl_3$) 3 400w, 1 701s, 1 622w, 1 590w, 1 460s, and 1 436m cm^{-1}.

(*i*) *With 2-aminobenzenethioamide.* DMHD (4.00 g) was added to a solution of the thioamide (3.62 g) in methanol (80 ml) and the mixture stirred at room temperature for 8 h. It was then filtered to give *methyl* (2E,4Z)-4-(2-*aminophenyl*)-4,5-*dihydro*-4-*oxothiazol*-5-*ylidene*]*but*-2-*en*-1-*oate* (33) (1.82 g, 24.0%) as deep-red crystals (from chloroform), m.p. 198—200 °C (Found: C, 58.5; H, 4.2; N, 9.5. $C_{14}H_{12}N_2O_3S$ requires C, 58.3; H, 4.2; N, 9.7%); $\nu_{max.}$ 3 384m, 3 260m, 1 721s, 1 687s, 1 622s, 1 584w, 1 549m, 1 538w, and 1 511s cm^{-1}; $\lambda_{max.}$ (M) (220 (ε 21 700), 251infl. (7 600), 318 (12 100), 372 (5 500), and 478 nm (8 700); $\lambda_{max.}$ (A) 232infl. (ε 6 900). 261infl. (2 900), 310 (8 200), 387infl. (900), and 483 nm (1 400); *m/e* 288 (M^+, 66), 229 ($M - 59^+$, 54), 170 (15), 142 (22), 118 (71), 114 (81), 111 (M − 177$^+$, 100), 99 (31), 91 (13), and 83 (19%); *m** 182.0 (288 → 229), 86.0 (114 → 99), 70.0 (118 → 91), and 62.0 (111 → 83). A further crop of the product (33) was obtained after 7 d at room temperature (overall yield 38.7%).

(*j*) *With pyridine*-2(3H)-*thione.* The thione (3.57 g) and DMHD (4.50 g) were stirred together in methanol (80 ml) for 17 h. The solvent was evaporated under reduced pressure to 30 ml and then cooled to −14 °C to give *dimethyl*-(2Z,4E)-2-(*pyridin*-2-*ylthio*)*hexa*-2,4-*diene*-1,6-*dioate* (35) (4.08 g, 46.4%) as pale yellow crystals (from methanol), m.p. 112—114 °C (Found: C, 56.0; H, 4.8; N, 5.0. $C_{13}H_{13}NO_4S$ requires C, 55.9; H, 4.7; N, 5.0%); $\nu_{max.}$ 3 075m, 3 050m, 1 717s, 1 676w, and 1 630m cm^{-1}.

(*k*) *With indoline*-2-*thione.* The thione (1.10 g) and DMHD (1.24 g) were refluxed together in methanol (25 ml) for 8 h and then cooled overnight give to a precipitate of *dimethyl* (2Z,4E)-2-(*indol*-2-*ylthio*)*hexa*-2,4-*diene*-1,6-*dioate* (36) (1.22 g, 51.1%) as yellow feathers (from methanol), m.p. 163—165 °C (Found: C, 60.6; H, 4.9; N, 4.6. $C_{10}H_{15}NO_4S$ requires C, 60.5; H, 4.8; N, 4.4%); $\nu_{max.}$ 3 342m, 1 730s, 1 710s, and 1 620m cm^{-1}.

(*l*) *With 2-aminobenzothiazole.* 2-Aminobenzothiazole (3.84 g) and DMHD (4.30 g) were refluxed together in methanol (70 ml) for 44 h, and then left at −14 °C overnight to give pale brown precipitate of *methyl* (2E)-3-(2-*oxo*-2H-*pyramido*[2,1-b]*benzothiazol*-4-*yl*)*prop*-2-*enoate* (39) (4.27 g, 59.7%) as white microneedles (from chloroform–ether), m.p. 224—226 °C (Found: C, 58.9; H, 3.6; N, 9.4. $C_{14}H_{10}N_2O_3S$ requires C, 58.7; H, 3.5; N, 9.8%); $\lambda_{max.}$ 1 714s, 1 650s, 1 618m, 1 582m, and 1 513s cm^{-1}; $\lambda_{max.}$ (M) 228 (ε 40 900), 262 (19 200), and 302 (11 500); $\lambda_{max.}$ (A) 261 (ε 20 100) and 307 nm (19 600); *m/e* 286 (M^+, 100), 259 (11), 258 (61), 228 (11), 227 (60), 200 (17), 199 (27), 198 (18), 176 (53), 148 (15), and 146 (12%); *m** 232.8 (286 → 258), 180.2 (286 → 227), 154.0 (258 → 199), 149.0 (199 → 172), and 124.5 (176 → 148). Chromatography of the reaction residue yielded no further compounds.

(*m*) *With 2-aminothiazole.* The procedure in (*l*) using 2-aminothiazole gave *methyl* (E)-3-(7-*oxo*-7H-*thiazolo*[3,2-a]*pyrimidin*-5-*yl*)*prop*-2-*enoate* (44) (1.30 g, 16.2%) as yellow lumps from (chloroform–diethyl ether), m.p. 207—213 °C (Found: C, 50.4; H, 3.6; N, 11.6. $C_{10}H_8N_2O_3S$ requires C, 50.8; H, 3.4; N, 11.9%); $\nu_{max.}$ 3 250w, 1 715s, 1 639s, 1 628s, 1 592m, and 1 560s cm^{-1}; *m/e* 236 (M^+, 14), 208 (24), 177 (24), 150 (7), 126 (36), 85 (9), and 83 (15%); *m** 183.0 (236 → 208), 133.0 (236 → 177), and 108.0 (208 → 150).

(*n*) *With 2-aminopyridine.* The procedure in (*l*) was repeated with 2-aminopyridine. Most of the solvent was evaporated off, and diethyl ether added to give crude methyl (2*E*)-3-(2-oxo-2*H*-pyrido[1,2-*a*]pyrimidin-4-yl)prop-2-enoate (45) (1.20 g, 90.1%). This contained a polymeric impurity, as shown by ^{1}H n.m.r. spectroscopy which was not removable, either by chromatography nor by recrystallisation from methanol–diethyl ether); $\nu_{max.}$ 3 095w, 3 062w, 1 720s, 1 633s, 1 590s, and 1 550s cm^{-1}; *m/e* 230 (M^+, 61), 202 ($M - 28^+$, 100), 171 ($M - 59^+$, 53), 144 (23), 143 (19), and 120 (51%).

(*o*) *With 1,2-diaminobenzene.* 1,2-Diaminobenzene (3.21 g) and DMHD (5.00 g) were refluxed together in methanol (80 ml) for 30 min and then left at −14 °C overnight. The mixture was filtered to give *methyl* (2E,4E)-4-(1,2,3,4-*tetrahydro*-3-*oxo*-*quinoxalin*-2-*ylidene*)*but*-2-*en*-1-*oate* (46) (3.29 g, 45.4%) as bronze crystals (from DMF), m.p. 226—228.5 °C (Found: C, 63.7; H, 5.1; N, 11.6. $C_{13}H_{12}N_2O_3$ requires C, 63.9; H, 5.0; N, 11.5%); $\nu_{max.}$ 3 308m, 3 200m, 3 103w, 3 068w, 1 688s, 1 677s, 1 639w, 1 603s, and 1 510w, cm^{-1}; *m/e* 244 (M^+, 53), 185 ($M - 59^+$, 100), 184 (54), 167 (12), and 156 (27%); *m** 151.0 (185 → 167) and 140.2 (244 → 185). The filtrate was refluxed for 30 min and cooled to give a further 0.82 g of the product (46) (overall

yield 56.7%). This new filtrate was refluxed for 3 h and cooled to give *methyl* 1,2,3,4-*tetrahydro*-3-*methoxycarbonylmethylenequinoxalin*-2-*ylacetate* (47) (1.95 g, 23.8%) as large, pale-orange prisms (from DMF–several drops of water), m.p. 103.5—104.5 °C (Found: C, 60.9; H, 5.9; N, 10.0. $C_{14}H_{16}N_2O_4$ requires C, 60.8; H, 5.8; N, 10.1%); $\nu_{max.}$ 3 360s, 3 283 m, 1 712s, 1 654s, 1 612s, 1 596s, and 1 500 m cm^{-1}; $\lambda_{max.}$ (M) 254 (ε 10 300), 307infl. (8 000), and 333 nm (13 200); $\lambda_{max.}$ (A) 230infl. (ε 6 600), 269 (9 300), and 318 nm (12 800); *m/e* 276 (M^+, 34), 244 (9), 203 (11), 171 ($M - 105^+$, 100), and 143 (8%); *m** 191.5 (244 ⟶ 216), 149.0 (276 ⟶ 203), 144.0 (217 ⟶ 177), and 120.0 (171 ⟶ 143).

(*p*) *With* 2-*aminobenzenethiol*. (i) In refluxing methanol, DMHD (6.72 g) and freshly distilled 2-aminobenzenethiol (5.00 g, 3.05 ml) were refluxed together in methanol (110 ml) for 32 h. Filtration gave *methyl* (2E,4Z)-(3,4-*dihydro*-3-*oxo*-2H-1,4-*benzothiazin*-2-*ylidene*)*but*-2-*en*-1-*oate* (49) (2.85 g, 27.3%) as yellow-orange microneedles (from chloroform), m.p. 240—242 °C (Found: C, 59.4; H, 4.3; N, 5.3%. $C_{13}H_{11}NO_3S$ requires C, 59.8; H, 4.2; N, 5.4%); $\nu_{max.}$ 3 162m, 3 100w, 1 722s, 1 706m, 1 662s, 1 612m, 1 593s, 1 550w, and 1 500w cm^{-1}; *m/e* 261 (M^+, 40), 202 ($M - 59^+$, 100), 174 (7), and 173 (11%); *m** 156.4 (261 ⟶ 202) and 149.5 (202 ⟶ 174). The filtrate was chromatographed and a red band eluted with chloroform to give *methyl* 2,3-*dihydro*-1-*oxo*-1H-*pyrrolo*-[2,1-c][1,4]*benzothiazine*-4-*carboxylate* (53) (0.03 g, 0.3%) as pale, orange needles (from methanol), m.p. 156.5—158.5 °C (Found: C, 59.6; H, 4.2; N, 5.2. $C_{13}H_{11}NO_3S$ requires C, 59.8; H, 4.3; N, 5.4%); $\nu_{max.}$ (CCl_4) 1 743s, 1 719s, 1 633s, 1 480s, 1 448m, 1 435m, and 1 351m cm^{-1}; $\lambda_{max.}$ (M) 237.5infl. (ε 9 700), 247infl. (17 000), 286 (8 900), 252 (19 000), and 336 nm (4 000); *m/e* 261 (M^+, 100), 218 (14), 202 (23), 173 (20), and 147 (66%); *m** 207.6 (261 ⟶ 233), 156.6 (261 ⟶ 202), and 150.0 (202 ⟶ 174). A yellow band, eluted later with chloroform, gave methyl (*Z*)-3,4-dihydro-3-methoxycarbonylmethyl-2*H*-1,4-benzothiazin-2-ylideneacetate (52) (1.03 g, 8.8%) as a yellow liquid which polymerised on distillation under reduced pressure.

(ii) In methanol at room temperature, DMHD (2.00 g) and the freshly distilled thiol (1.49 g) were stirred together at room temperature for 5 h. The solvent was evaporated under reduced pressure and the residue triturated with a few drops of methanol to give *dimethyl* (4E,2Z)-2-(2-*aminophenylthio*)*hexa*-2,4-*diene*-1,6-*dioate* (51) (0.11 g, 2.63%) as orange cubes (from diethyl ether), m.p. 96 °C (Found: C, 57.3; H, 5.2; N, 4.7. $C_{14}H_{15}NO_4S$ requires C, 57.3; H, 5.3; N, 4.8%); $\nu_{max.}$ 3 461m, 3360m, 1 706s, 1 624m, 1 610m, and 1 561w cm^{-1}; *m/e* 293 (M^+, 44), 234 (42), 202 (57), 194 (40), 174 (52), 173 (23), 169 ($M - 124^+$, 100), 162 (22), 124 (21), 80 (37), and 65 (27%); *m** 150.0 (202 ⟶ 174), 128.3 (233 ⟶ 173), and 117.5 (169 ⟶ 141).

Reactions of Dimethyl Penta-2,3-*diene*-1,5-*dioate* (54).—Unless stated otherwise, equimolar quantities of the nucleophilic compound and the diester (54) were refluxed together in methanol (10-fold amount by mass) for 3 h. The products were isolated by filtration of the cold (−14 °C) solution or by precipitation with diethyl ether from the concentrated reaction mixture, followed by cooling.

(*a*) *With* 1,2-*diaminobenzene*. The diamine (0.69 g) gave *methyl* (Z)-2,3,4,5-*tetrahydro*-4-*oxo*-1H-1,5-*benzodiazepin*-2-*ylideneacetate* (60) (0.31 g, 20.9%) as white feathers (from methanol), m.p. 251—254 °C (Found: C, 61.8; H, 5.1; N, 11.9. $C_{12}H_{12}N_2O_3$ requires C, 62.1; H, 5.1; N, 12.1%); $\nu_{max.}$ 3 210m, 3 080w, 1 695s, 1 672w, 1 663w, 1 638s, 1 600m, and 1 509 cm^{-1}.

(*b*) *With* 2-*aminobenzothiazole*. This amine (1.00 g) gave *methyl* 2-*oxo*-2H-*pyrimido*[2,1-b]*benzothiazol*-4-*ylacetate* (61) (0.95 g, 52.0%) as yellow cubes (from methanol), m.p. 233—236 °C (decomp.) (Found: C, 56.9; H, 3.8; N, 10.0. $C_{13}H_{10}N_2O_3S$ requires C, 56.9; H, 3.7; N, 10.2%); $\nu_{max.}$ 1 730s, 1 642s, and 1 582s cm^{-1}; *m/e* 274 (M^+, 90), 187 ($M - 87^+$, 100), and 176 (57%).

(*c*) *With benzimidazole*-2-*thione*. The thione (1.44 g) gave *methyl* 4-*oxo*-4H-[1,3]*thiazino*[3,2-a]*benzimidazol*-2-*ylacetate* (63) (1.12 g, 42.6%) as white microneedles (from methanol), m.p. 133—135 °C (Found: C, 56.7; H, 3.6; N, 10.2. $C_{13}H_{10}N_2O_3S$ requires C, 56.9; H, 3.7; N, 10.2%); $\nu_{max.}$ 1 740s, 1 699s, and 1 610s cm^{-1}; *m/e* 274 (M^+, 100), 215 (14), 188 (19), 187 (16), 150 (42), and 85 (17%).

(*d*) *With* N,N′-*dimethylthiourea*. The thiourea (0.87 g) gave *methyl* 3,4-*dihydro*-3-*methyl*-2-*methylimino*-4-*oxo*-2H-1,3-*thiazin*-6-*ylacetate* (65) (1.23 g, 64.5%), as colourless needles (from methanol), m.p. 79—79.5 °C (Found: C, 47.4; H, 5.4; N, 12.1. $C_9H_{12}N_2O_3S$ requires C, 47.4; H, 5.3; N, 12.3%); $\nu_{max.}$ ($CHCl_3$) 1 742s, 1 636s, and 1 600s cm^{-1}; *m/e* 228 (M^+, 100), 158 (24), 155 ($M - 73^+$, 61), 130 ($M - 98^+$, 100), 126 (28), 85 (26), 71 (63), and 69 (40%); *m** 173.6 (228 ⟶ 199), 105.6 (228 ⟶ 155), 99.5 (170 ⟶ 130), and 80.0 (130 ⟶ 102).

(*e*) *With* N,N′-*diphenylthiourea*. The thiourea (1.46 g) gave *methyl* 3,4-*dihydro*-4-*oxo*-3-*phenyl*-2-*phenylimino*-2H-1,3-*thiazin*-6-*ylacetate* (66) (0.76 g, 33.4%) as white microneedles (from methanol), m.p. 156—157 °C (Found: C, 64.5; H, 4.7; N, 7.9. $C_{19}H_{16}N_2O_3S$ requires C, 64.7; H, 4.6; N, 8.0%); $\nu_{max.}$ ($CHCl_3$) 1 742m, 1 697s, 1 638w,

TABLE 1

^{13}C N.m.r. data [a] for the compounds shown

Compd.	δ	δ (CO_2CH_3)	
(15)	147.4 (s, C-2), 165.8 (s, C-4), 134.2 (s, C-5), 124.0 (d, C-6) [b], 137.8 (d, C-7), 127.0 (d, C-8) [b], 48.8 (t, $=NCH_2$), 43.9 (t, $-NCH_2$), and 24.9 and 27.6 (2 t, CH_2CH_2).	51.7	166.1
(22) [c]	151.4 (C-2), 28.3 (3-CH_3), 164.8 (C-4), 133.2 (C-5), 123.8 [b] (C-6), 137.5 (C-7), and 127.8 [b] (8-C).	51.8	165.8
(31)	97.0 (s, C-2), 30.6 (q, 2-CH_3), 50.6 (q, 2-OCH_3), 166.6 (s, C-4), 137.1 (s, C-5), 122.3 (d, C-6) [b], 138.9 (d, C-7), and 125.5 (d, C-8) [b].	51.7	167.0
(63)	145.7 (s, C-2) [b], 42.7 (t, 2-CH_2), 120.0 (d, C-3), 160.5 (s, C-4), 147.6 (s, C-5a),[b] 117.4, 119.1, 125.1, 127.3 (4 d, C-6, -7, -8, -9), 132.3 (s, C-9a), and 143.8 (s, C-10a).	53.3	169.0
(65)	147.9 (s, C-2), 38.5 (q, 2-NCH_3), 31.5 (q, 3-Me), 163.8 (s, C-4), 119.9 (d, C-5), 141.8 (s, C-6), and 42.7 (t, 6-CH_2).	54.2	169.4
(67) [d]	163.1 (s, C-2),[b] 28.4 (q, NMe), 168.2 (s, C-4),[b] 118.4 (d, C-5), 141.3 (s, C-6), and 40.2 (t, 6-CH_2).	52.0	169.6
(68) [d]	164.9 (s, C-2),[b] 168.9 (s, C-4),[b] 118.7 (d, C-5), 141.9 (s, C-6), and 40.0 (t, 6-CH_2).	52.3	170.1

[a] For spectra recorded in $CDCl_3$ at 22.63 MHz; shifts are in p.p.m. downfield from tetramethylsilane; $^{13}C-^1H$ attachments confirmed by off-resonance decoupling techniques. [b] Assignments could be interchanged. [c] Completely decoupled spectrum only. [d] Spectrum recorded in $(CD_3)_2SO$.

TABLE 2

^{1}H N.m.r. data for the compounds shown [a]

Compound	τ	τ (CO_2CH_3)
(1)	3.58 (d, 2-H), 3.17 (d, 3-H) ($J_{2,3}$ 16.3).	6.20 6.22
(4) [b]	6.72 (s, =NMe),[c] 6.78 (s, 3-CH_3),[c] 2.65—2.76 (m, 6-, 7-H), 3.77 (dd, 8-H) ($J_{6,8}$ 2.5, $J_{7,8}$ 11.7).[d]	6.19
(5)	2.58—3.21 (m, 10 ArH, 6-, 8-H), 3.67—4.09 (m, 7-H).	6.31
(6)	6.80 (s, =NMe),[c] 6.85 (s, 3-Me),[c] 3.42 (d, 6-H), 1.31 (dd, 7-H), 4.04 (d, 8-H) ($J_{6,7}$ 12.0, $J_{7,8}$ 16.0).	6.27
(7)[4]	3.85 (1-, 4-H), 2.72 (2, 3-H) ($J_{1,2}$ 15.8, $J_{1,3}$ −0.7, $J_{1,4}$ 0.8, $J_{2,3}$ 11.4).	
(8)[4]	4.05 (1-H), 3.32 (2-H), 1.60 (3-H), 3.88 (4-H) ($J_{1,2}$ 11.6, $J_{1,3}$, 0.9, $J_{1,4}$ 0.7, $J_{2,3}$ 11.6, $J_{2,4}$ 0.7, $J_{3,4}$ 16.0).	
(10) [b]	2.47 (dd, 2-H), 2.06 (dd, 3-H), 3.78 (dd, 4-H): ($J_{2,3}$ 11.6, $J_{2,4}$ 0.8, $J_{3,4}$ 15.4).	6.22 6.27
(14)	2.61—3.06 (m, 3-, 4-H); 3.52—4.09 (m, 8-H), 6.15—6.48 (m, 2 × N-CH_2), 7.90—8.29 (m, CH_2—).	6.24
(15) [b]	2.58—2.76 (m, 3-, 4-H), 3.72 (d, 2-H), 5.95 (t, =NCH_2), 6 06 (t, NCH_2), 7.88 [m $(CH_2)_2$] ($J_{1,2}$ 13.5).[d]	6.13
(17)	2.57 and 2.66 (2 d, CH=CHE, J 15.3,) 3.66 (s, 3-H), 6.04 (s, 6-, 7-H).	6.33
(18) [b]	3.40 (dd, 6-H), 1.37 (dd, 7-H), 3.99 (dd, 8-H) ($J_{6,7}$ 11.7, $J_{6,8}$ 0.8, $J_{7,8}$ 15.6).	6.21
(19)	2.72—3.10 (m, 6-, 7-H), 3.60—4.08 (m, 8-H), 5.47—6.38 (m, N-CH_2).	6.23
(22) [e,f]	6.90 (s, 3-Me), 2.67—3.10 (m, 6-, 7-H), 3.57 (d, 8-H), 0.17 (s, NH) ($J_{7,8}$ 12.5).[d]	6.33
(26) [e,f]	2.24 and 3.32 (d, CH=CHE J 16.4), 2.72 (s, 3-H), 1.54—1.64 (m, 6-H), 2.15—2.61 (m, 3 ArH).	6.21
(28) [e]	2.04 (dd, 2-H), 2.31 (dd, 3-H), 3.25 (dd, 4-H), 2.54—2.57 (m, 2 ArH), 2.84—2.86 (m, 2 ArH) ($J_{2,3}$ 11.2, $J_{2,4}$ 0.8, $J_{3,4}$ 15.3)	6.28 6.34
(31)	8.04 (s, 2-Me), 6.78 (s, 2-OMe), 2.21 (b, 3-H),[g] 2.46—3.06 (m, 6-, 7-H), 3.93 (dd, 8-H) ($J_{2,4}$ 1.3, $J_{3,4}$ 13.1).[d]	6.26
(33) [e]	2.43 (dd, 6-H), 2.71 (dd, 7-H), 3.33 (dd, 8-H), 3.08 (d. 3′-H), 2.60 (dt, 4′-H), 3.33 (t, 5′-H),[h] 2.39 (dd, 6′-H), 1·96 (b, NH_2) ($J_{6,7}$ 11.9, $J_{6,8}$ 0.8, $J_{7,8}$ 15.2, $J_{3',4'}$ 8.0, $J_{4',5'}$ 8.0. $J_{4',6'}$ 1.3, $J_{5',6'}$ 9.2).	6.25
(35) [b]	2.29 (dd, 2-H), 2.14 (dd, 3-H), 3.70 (dd, 4-H), 2.78 (dd, 3′-H), 2.45 (dt, 4′-H), 2.96 (dt, 5′-H), 1.63 (dd, 6′-H) ($J_{2,3}$ 11.3, $J_{2,4}$ 0.5, $J_{3,4}$ 15.2, $J_{3',4'}$ 8.1, $J_{3',5'}$ 1.0, $J_{3',6'}$ 0.9, $J_{4',5'}$ 7.4, $J_{4',6'}$ 1.9, $J_{5',6'}$ 5.0).	6.21 6.27
(36)	2.45—3.10 (m, 4 ArH, 2-H), 2.00 (dd, 3-H), 3.79 (d, 4-H), 3.40 (d, 3′-H) ($J_{2,3}$ 10.9, $J_{3,4}$ 14.7).	6.30 6.60

TABLE 2 (*continued*)

Compound	τ	τ (CO_2CH_3)
(39)	2.61 and 3.51 (2 d, CH=CHE) (J 15.3), 3.73 (s. 2-H), 2.31—2·84 (m, 4 ArH).	6.18
(44)	2.71 (d, 2-H), 1.97 (d, 3-H), 2.29 and 3.20 (2 d, CH=CHE, J 16.9), 3.40 (s, 6-H) ($J_{2,3}$ 5.4).	6.25
(45)	3.40 (s, 3-H), 2.28 and 3.42 (2 d, CH=CHE, J 15.7), 2.12 (d, 6-H),[h] 3.15 (t, 7-H),[h] 2.42—2.82 (m, 8-, 9-H) ($J_{6,7}$ 6.9).	6.21
(46) [e]	4.14 (d, 2-H), 1.98 (dd, 3-H), 3.96 (d, 4-H), −1.24 (br, 1′-H), −0.36 (br, 4′-H), 2.75—3.20 (m, 4 ArH) ($J_{2,3}$ 15.9, $J_{3,4}$ 14.1).	
(47)	−0.70 (s, 1-H),[i] 5.41 (s, 2- =CH), 5.59—5.96 (m, 3-H), 7.50 (d, 3-CH_2), 4.02 (d, 4-H),[g] 2.98—3.61 (m, 4 ArH) ($J_{3,4}$ 2.4, J_{3,CH_2} 6.8).	6.45 6.45
(49) [b,e]	2.49—2.63 (m, 2-, 3-H), 3.57 (d, 4-H), −1.13 (br, NH), 2.93 (dd, 5′-H), 2.80 (dt, 6′-H), 2.97 (dt, 7′-H), 2.65 (dd, 8′-H) ($J_{3,4}$ 13.9,[d] $J_{5',6'}$ 8.3, $J_{5',7'}$ 1.0, $J_{6',7'}$ 7.7, $J_{6,8}$ 1.2, $J_{7,8}$ 7.8).	6.21
(51) [b]	2.41 (dd, 2-H), 1.87 (dd, 3-H), 3.61 (dd, 4-H), 5.40 (br, NH_2), 3.18 (dd, 3′-H), 2.76 (dt, 4′-H), 3.22 (dt, 5′-H), 2.61 (dd, 6′-H) ($J_{2,3}$ 11.3, $J_{2,4}$ 0.9, $J_{3,4}$ 15.2, $J_{3',4'}$ 8.0, $J_{3',5'}$ 1.2, $J_{4',5'}$ 7.5, $J_{4',6'}$ 1.5, $J_{5',6'}$ 7.8).	6.07 6.22
(52)	4.20 (s, 2- =CH), 5.57 (q, 3-H), 7.25—7.73 (m, 3-CH_2), 5.12 (br, N—H), 2.86—3.50 (m, 4 ArH) ($J_{3,\alpha\text{-H}}$ 4.0, $J_{3,\beta\text{-H}}$ 7.3).	6.30 6.39
(53)	6.73—8.00 (m, 2-H_2), 8.22—8.53 (m, 3-H_2), 2.78—3.15 (m, 6-, 7-, 8-H), 1.69—1.90 (m, 9-H).	6.25
(54)	4.02 (s, =CH).	6.28
(60) [f]	−0.07 (br, 1-H), 6.96 (s, 3-CH_2), 5.32 (s, 4- =CH), −0.50 (br, 5-H),[i] 3.00 (s, 4 ArH).	6.41
(61)	3.72 (s, 3-H), 5.52 (s, 4-CH_2), 1.94—2.64 (m, 4 ArH).	6.30
(63)	6.33 (s, 2-CH_2). 3.37 (s, 3-H),[h] 1.40—1.58 (m, 6-H), 2.20—2.79 (m, 3 ArH).	6.26
(65) [f]	6.96 (s, =NMe),[c] 6.78 (s, 3-Me),[c] 3.61 (s, 5-H), 6.30 (s, 6-CH_2).	6.36
(66) [f]	2.56—2.92 (m, 10 ArH), 3.63 (s, 5-H), 6.56 (s, 6-CH_2).	6.54
(67) [f]	7.14 (s, NMe), 1.50 (br, N—H), 3.72 (s, 5-H), 6.48 (s, 6-CH_2).	6.38
(68) [f]	1.54 (br, 2-NH_2),[g] 3.65 (s, 5-H), 6.34 (s, 6-CH_2).	6.36
(70)	6.68 (s, 2-CH_2). 4.08 (s, 3-H), 1.78 (br, 5-H), 2.40—3.02 (m, 4 ArH).	6.27

[a] Spectra measured at 60 MHz for solutions in $CDCl_3$. Coupling constants (J) are in Hz. [b] 300 MHz Spectrum. [c] Assignments could be interchanged. [d] Apparent J's in second-order spectrum. [e] Measured in $(CD_3)_2SO$. [f] 90 MHz Spectrum. [g] Disappears on shaking with D_2O. [h] Further splitting. Does not exchange on shaking with D_2O.

1 595w, and 1 492m cm^{-1}; *m/e* 352 (M^+, 100), 351 (44), 243 ($M - 109^+$, 75), 211 (97), 194 (29), and 144 (63%); *m** 290.0 (351 → 319), 183.2 (243 → 211), and 167.8 (352 → 243).

(*f*) *With methylthiourea.* The thiourea (0.58 g) gave *methyl 2-methylamino-4-oxo-4H-1,5-thiazin-6-ylacetate* (67) (0.78 g, 56.6%) as white microplates (from methanol), m.p. 154—155.5 °C (Found: C, 45.1; H, 4.6; N, 12.8. $C_8H_{10}N_2O_3S$ requires C, 44.8; H, 4.7; N, 3.1%); $\nu_{max.}$ ($CHCl_3$) 3 435w, 1 740s, 1 634s, 1 570s, and 1 544s cm^{-1}; *m/e* 214 (M^+, 63), 158 ($M - 56^+$, 83), 130 ($M - 84^+$, 100), 126 (38), and 85 (39%); *m** 107.0 (158 → 130).

(*g*) *With thiourea.* The allene (54) was added to a solution of thiourea (0.48 g) in warm methanol (15 ml). A precipitate was rapidly formed which gave *methyl 2-amino-4-oxo-4H-1,3-thiazin-6-ylacetate* (68) (0.83 g, 65.7%) as white microneedles (from methanol), m.p. 178—179 °C (Found: 42.2; H, 4.0; N, 13.9. $C_7H_8N_2O_3S$ requires C, 42.0; H, 4.0; N, 14.0%); $\nu_{max.}$ 3 355s, 3 300infl., 1 718infl., 1 710s, 1 658infl., 1 650infl., 1 636infl., and 1 625 cm^{-1}; *m/e* 200 (M^+, 29), 158 ($M - 42^+$, 100), 130 (81). 127 (21), 126 (28). and 85 (43%); *m** 124.8 (200 → 158), 107.0 (158 → 130), 101.8 (158 → 127), and 95.2 (169 → 127).

(*h*) *With 2-aminobenzenethiol.* The thiol (0.80 g) gave *methyl 2,3,4,5-tetrahydro-4-oxo-1,5-benzothiazepin-2-ylideneacetate* (70) (0.62 g, 38.9%) as white microneedles (from methanol–diethyl ether). m.p. 226—228 °C (Found: C. 57.7; H, 4.6; N, 5.5. $C_{12}H_{11}NO_3S$ requires C, 57.8; H, 4.5; N, 5.6%); $\nu_{max.}$ 3 190m, 3 110m, 3 060infl., 1 710s, 1 688s, and 1 588s cm^{-1}.

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