Some Reactions of Enaminones with Isothiocyanates

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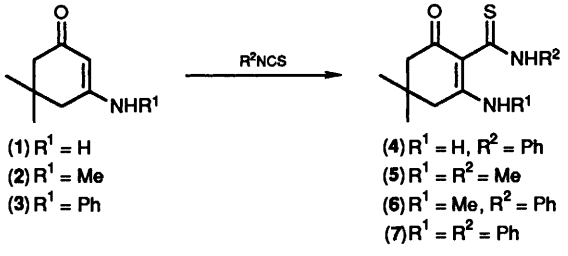
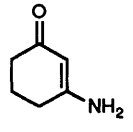
Two primary and two secondary enaminones derived from cyclohexane-1,3-dione have been shown to react with methyl isothiocyanate and phenyl isothiocyanate. The dimedone derivatives (**1**) and (**2**) only reacted at high temperature to give products of C-2 substitution, (**4**)–(**6**). The primary enaminones (**1**) and (**10**) were deprotonated with strong bases to give products of *N*-substitution, (**8**), (**9**), (**11**), and (**12**). 3-Aminocyclohex-2-enone (**10**) reacted with methyl isothiocyanate in the presence of sodium hydride to give an unexpected new spirodihydrotriazine (**15**) the structure of which was established by an X-ray crystal structure determination of its diethyl acetal (**16**). The reaction of 5,5-dimethyl-3-methylaminocyclohex-2-enone (**2**) with sodium hydride and phenyl isothiocyanate in tetrahydrofuran gave the same mixture of four products as the reaction of 3-anilino-5,5-dimethylcyclohex-2-enone (**3**) with methyl isothiocyanate under the same conditions.

We are currently investigating the use of isothiocyanate derivatives of enaminones as intermediates for the preparation of certain new heterocyclic ring systems. Although the derivatives we report here would appear to have considerable potential in this respect, we have been unable to find any similar reactions in the literature. Our preliminary work sought to establish the conditions under which enaminones derived from cyclohexane-1,3-diones would react with two simple isothiocyanates.

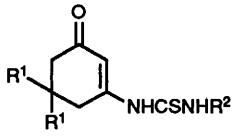


(1) R^1 = H
(2) R^1 = Me
(3) R^1 = Ph

(4) R^1 = H, R^2 = Ph
(5) R^1 = R^2 = Me
(6) R^1 = Me, R^2 = Ph
(7) R^1 = R^2 = Ph



(10)



(8) R^1 = R^2 = Me
(9) R^1 = Me, R^2 = Ph,
(11) R^1 = H, R^2 = Ph,
(12) R^1 = H, R^2 = Me

First attempts to achieve reaction between the enaminones (**1**) and (**2**) and methyl or phenyl isothiocyanate were unsuccessful. The reagents were heated under reflux in various solvents [tetrahydrofuran (THF), acetonitrile, or toluene] for various periods, but only starting materials were recovered. Only when reactions were performed in acetonitrile in the presence of triethylamine at 120 °C in a steel pressure reaction vessel were the 2-substituted derivatives (**4**), (**5**), and (**6**) obtained. The structures of these products were readily established by their mass spectra and the absence of vinyl proton signals in the NMR spectra.

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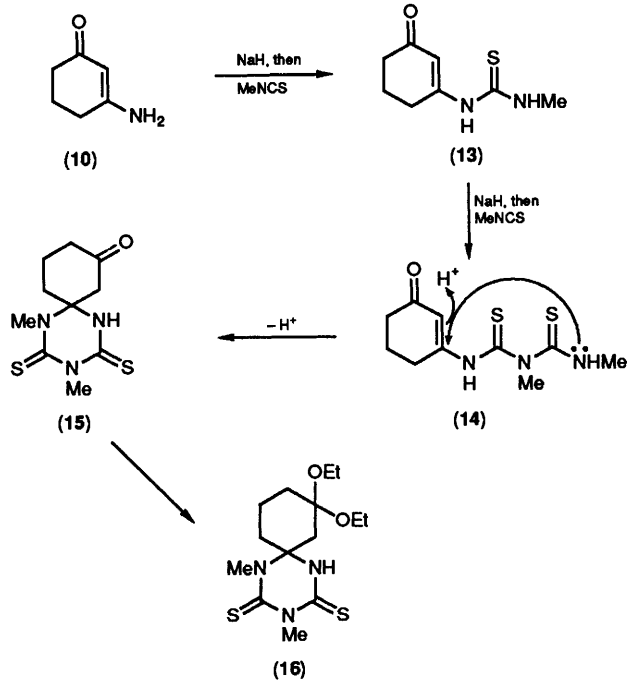
In attempts to obtain thioureas by substitution on the enaminone nitrogen atom, the enaminone (**1**) was first deprotonated with sodium hydride in THF. Subsequent treatment with isothiocyanates gave the thioureas (**8**) and (**9**). The mass spectra and the presence of vinyl proton signals in the NMR spectra provided the crucial evidence for these structures. When this procedure was applied to the secondary enaminone (**3**) it reacted with phenyl isothiocyanate in THF or toluene to give the 2-substituted derivative (**7**). Other combinations of enaminone and isothiocyanate gave mixtures of products. These reactions are discussed below. The reaction of 3-aminocyclohex-2-enone (**10**) similarly with sodium hydride



Scheme 1.

in THF followed by phenyl isothiocyanate gave the thiourea (**11**), but to get the thiourea (**12**) from methyl isothiocyanate it was necessary to work with sodamide in liquid ammonia.

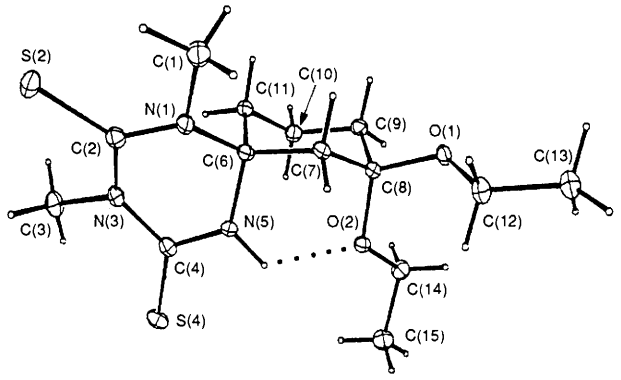


Figure. Perspective view and atom labelling of the crystal structure of (**16**). Hydrogen bond shown as dotted line.

Attempted reaction of the enaminone (**10**) with methyl isothiocyanate in THF gave much polymer and a trace of a product with M_r 257. A better yield was obtained in dioxane. The new compound had an IR band at 1 720 cm^{-1} (nonconjugated ketone group). It did not show typical enaminone IR absorption, but there were strong bands between 1 400 and 1 500 cm^{-1}. On refluxing in ethanol containing a trace of hydrogen chloride it was converted to the acetal (*m/z* 331; no carbonyl IR band, accurate mass determination gave the molecular formula $C_{14}H_{25}N_3O_2S_2$). An X-ray crystal structure determination of the acetal showed it to be the spirodihydrotriazine (**16**), so the ketone had the structure (**15**). The NMR data and elemental analyses (see Experimental section) were consistent with these structures. Our proposed mechanism for this reaction is shown in Scheme 1. It is reasonable to assume that initial reaction at nitrogen would given the thiourea (**13**), which reacted further under the influence of the base to give the dithiobiuret (**14**). This presumably cyclised *via* an internal Michael addition to give the product (**15**).

The Figure shows a perspective view and atom labelling of the crystal structure of the acetal (**16**). Final atom co-ordinates are listed in Table 1, and non-hydrogen bond lengths and angles in Table 2. The dihydrotriazine ring exists in a form intermediate between boat and sofa conformations, wherein C(6) and N(3) lie 0.597(3) and 0.212(3) Å respectively above the mean plane described by the other four ring atoms. Further to minimise steric interactions the two sulphur atoms lie below the mean plane [0.158(2) and 0.370(2) Å respectively for S(2) and S(4)]. Similar geometries and conformations exist in previously reported related structures.[1–4] The cyclohexane ring exists in a chair conformation with N(5) and O(2) in axial orientations. In the solid state this conformation is maintained by an intramolecular hydrogen bond between O(2) and N(5)–H(5), with N(5) and O(2) separated by only 2.717(3) Å. No unusually short intermolecular contacts exist.

Next, the secondary enaminone (**2**) was heated under reflux in THF with sodium hydride for 15 min then with phenyl isothiocyanate for 2 h. This resulted in an unusual mixture. First isolated by recrystallisation was a 32.5% yield of the aniline derivative (**3**). The structure was established by comparison with an authentic sample[5] (IR, TLC, and mixed m.p.). After column chromatography of the residues we were able to separate and characterise compounds (**7**) (14.3%), (**17**) (5.6%), and (**18**) (12.2%) (Scheme 2). Reasonable mechanisms to explain these results are shown in Scheme 2, although it must be emphasised that other routes could be envisaged. Finally, the reverse reaction was carried out. The enaminone (**3**) was treated with methyl isothiocyanate under the conditions just described. TLC (silica plates with dichloromethane or 5% methanol in dichloromethane as eluant) of the mixture of products from the two reactions gave exactly the same pattern of spots. From column chromatography were isolated compounds (**7**) (14.3%), (**17**) (3.7%), and (**18**) (8.7%) and recovered starting material (23.3%). The presence of the 1,3-dimethylquinazoline (**17**) shows that the spiro intermediate (**19**) is capable of opening in either direction and when the enaminone (**3**) was the starting material produced a small amount of enaminone (**2**).

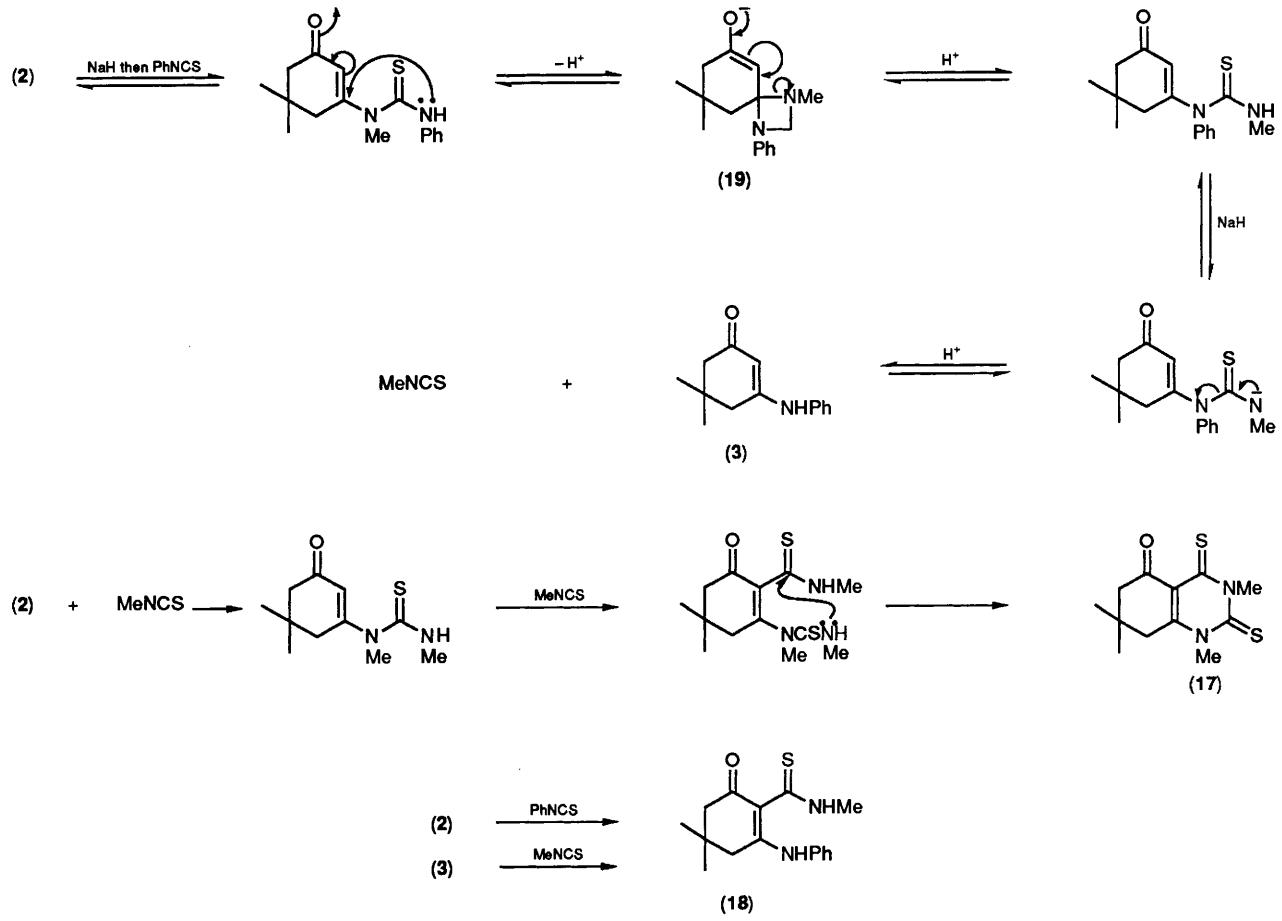
The samples of compound (**7**) isolated from these two reactions were identified by comparison (IR, TLC, and mixed m.p.) with the sample prepared from 3-anilino-5,5-dimethylcyclohex-2-enone and phenyl isothiocyanate described above. The samples of (**17**) isolated from the two reactions were

Table 1. Fractional atom co-ordinates ($\times 10^4$) for the crystal structure of (**16**)

Atom	*x/a*	*y/b*	*z/c*
N(1)	2 891(2)	2 580(2)	4 157(2)
C(1)	1 690(3)	2 432(3)	3 563(2)
C(2)	3 788(3)	3 572(2)	3 430(2)
S(2)	3 612(1)	4 717(1)	1 869(1)
N(3)	4 967(2)	3 563(2)	4 084(2)
C(3)	5 819(3)	4 741(3)	3 413(2)
C(4)	5 533(3)	2 364(2)	5 222(2)
S(4)	7 383(1)	1 944(1)	5 757(1)
N(5)	4 486(2)	1 518(2)	5 882(2)
C(6)	2 723(3)	2 040(2)	5 593(2)
C(7)	2 023(3)	690(2)	6 299(2)
C(8)	1 701(3)	207(2)	7 789(2)
C(9)	598(3)	1 541(2)	8 178(2)
C(10)	1 358(3)	2 847(2)	7 497(2)
C(11)	1 560(3)	3 345(2)	6 025(2)
O(1)	763(2)	−836(2)	8 400(1)
C(12)	1 447(3)	−2 170(3)	8 106(2)
C(13)	559(3)	−3 287(3)	9 122(2)
O(2)	3 393(2)	−471(2)	8 188(1)
C(14)	3 478(3)	−1 115(3)	9 572(2)
C(15)	5 360(3)	−1 781(3)	9 764(2)

Table 2. Bond lengths (Å) and angles (°) for (**16**).

N(1)–C(1)	1.470(4)	N(1)–C(2)	1.354(3)
N(1)–C(6)	1.476(3)	C(2)–S(2)	1.662(2)
C(2)–N(3)	1.412(4)	N(3)–C(3)	1.469(4)
N(3)–C(4)	1.383(2)	C(4)–S(4)	1.676(3)
C(4)–N(5)	1.335(3)	N(5)–C(6)	1.458(3)
C(6)–C(7)	1.533(3)	C(6)–C(11)	1.534(3)
C(7)–C(8)	1.536(3)	C(8)–C(9)	1.521(3)
C(8)–O(1)	1.412(3)	C(8)–O(2)	1.433(3)
C(9)–C(10)	1.527(4)	C(10)–C(11)	1.518(3)
O(1)–C(12)	1.438(3)	C(12)–C(13)	1.504(3)
O(2)–C(14)	1.439(3)	C(14)–C(15)	1.508(3)
C(1)–N(1)–C(2)	120.1(2)	C(1)–N(1)–C(6)	119.4(2)
C(2)–N(1)–C(6)	117.7(2)	N(1)–C(2)–S(2)	124.7(2)
N(1)–C(2)–N(3)	115.2(2)	S(2)–C(2)–N(3)	120.1(2)
C(2)–N(3)–C(3)	118.1(2)	C(2)–N(3)–C(4)	121.9(2)
C(3)–N(3)–C(4)	119.2(2)	N(3)–C(4)–S(4)	124.4(2)
N(3)–C(4)–N(5)	114.4(2)	S(4)–C(4)–N(5)	121.2(1)
C(4)–N(5)–C(6)	121.5(2)	N(1)–C(6)–N(5)	104.4(2)
N(1)–C(6)–C(7)	112.3(2)	N(5)–C(6)–C(7)	108.0(2)
N(1)–C(6)–C(11)	109.8(2)	N(5)–C(6)–C(11)	111.9(2)
C(7)–C(6)–C(11)	110.3(2)	C(6)–C(7)–C(8)	112.6(2)
C(7)–C(8)–C(9)	111.8(2)	C(7)–C(8)–O(1)	111.8(2)
C(9)–C(8)–O(1)	104.7(2)	C(7)–C(8)–O(2)	104.5(2)
C(9)–C(8)–O(2)	113.3(2)	O(1)–C(8)–O(2)	111.0(1)
C(8)–C(9)–C(10)	111.6(2)	C(9)–C(10)–C(11)	110.1(3)
C(6)–C(11)–C(10)	111.8(2)	C(8)–O(1)–C(12)	116.7(2)
O(1)–C(12)–C(13)	106.9(2)	C(8)–O(2)–C(14)	116.4(2)
O(2)–C(14)–C(15)	107.3(2)		



Scheme 2.

identical (IR, NMR, and mixed m.p.). The structure of compound (**17**) followed from the mass spectrum where the parent peak was the base peak at *m/z* 268. The IR spectrum showed only two bands between 1 500 and 2 000 cm^{-1}. That at 1 690 cm^{-1} was assigned to the C=O stretch and a very strong, broad band at 1 550 cm^{-1} was assigned to a combination of the two C=S stretches. The ^1H NMR spectrum had a 6-proton singlet at δ 1.15 for the *gem*-dimethyl group, two 2-proton singlets at δ 2.47 and 2.73 for the methylene groups, and two 3-proton singlets at δ 3.89 and 4.23 for the *N*-methyl groups. Finally, the ^{13}C NMR spectrum had quaternary carbon signals at δ 192.65, 182.38, and 175.28 for the carbonyl carbon and two thiocarbonyl carbons respectively. The *N*-methyl signals were at δ 40.54 and 44.08 and the other signals were as expected for the structure drawn; (see Experimental section). The two samples of the remaining compound were identical (mp., mixed m.p., IR, and TLC) with each other. From the mass spectrum and NMR data (see Experimental section) the structure could have been either (**6**) or (**18**). The compound was different (IR, TLC, and m.p.) from compound (**6**) so must have the structure (**18**). The production of (**18**) from enaminone (**3**) and methyl isothiocyanate is reasonable. Its formation from enaminone (**2**) is explained by the observed ready conversion of (**2**) into (**3**) in the presence of phenyl isothiocyanate with the release of methyl isothiocyanate.

So far we have only been able to obtain the required thioureas from primary enaminones, but the products are now available in reasonable yields and high purity. We are currently investigating their further reactions. As a result of attack at carbon instead of nitrogen, we have four thioamides available which we also intend to investigate as possible intermediates for synthesis of heterocyclic systems. The several unexpected products isolated during the course of this work emphasise the need for caution in interpreting the structures of any compounds arising from reactions between enaminones and isothiocyanates.

Experimental

UV spectra were determined with a Pye–Unicam SP 800 spectrophotometer, IR spectra with a Perkin-Elmer 297 spectrophotometer, and mass spectra on an AEI 902 spectrometer. NMR spectra were determined on a Perkin-Elmer R 12 spectrometer at 60 MHz, but where ^{13}C spectra are reported both proton and carbon (broad-band decoupled and DEPT 135) spectra were determined on a JEOL GX 270 FT spectrometer at 270 and 67.8 MHz respectively.

2-Amino-4,4-dimethyl-6-oxo-N-phenylcyclohex-1-enecarbothioamide (**4**).—A solution of 3-amino-5,5-dimethylcyclohex-2-enone (**1**) (1.4 g, 10 mmol), phenyl isothiocyanate (1.2 ml, 10 mmol), and triethylamine (2 ml) in acetonitrile (70 ml) was kept at 120 °C in a steel pressure reaction vessel overnight. The solvent was evaporated off, and the residue dissolved in dichloromethane (70 ml) and washed with dilute hydrochloric acid (2 × 50 ml). The organic phase was separated, dried ($MgSO_4$), and evaporated to give the *thioamide* (**4**) (1.2 g, 77%), m.p. 218 °C (from ethanol) (Found: C, 65.7; H, 6.6; N, 10.1; S, 11.6. $C_{15}H_{18}N_2OS$ requires C, 65.7; H, 6.6; N, 10.2; S,

11.7%); *m/z* 274; λ_{max}(EtOH) 276 nm (ε 11 500); λ_{max}(H_2O) 275 nm (ε 10 500); λ_{max}(0.1M HCl) 274 nm (ε 10 000); λ_{max}(0.1M NaOH) 293 nm (ε 7 500); δ_H($CDCl_3$) 1.05 (6 H, s, Me), 2.41 (2 H, s, CH_2), 2.45 (2 H, s, CH_2), 6.50 (3 H, s, NH), and 7.1–7.5 (5 H, m, Ph).

4,4-*Dimethyl*-2-*methylamino*-6-*oxo*-N-*methylcyclohex*-1-*enecarbothioamide* (**5**).—By the above procedure, using compound (**2**) and methyl isothiocyanate, the *thioamide* (**5**) was obtained, (0.8 g, 35%), m.p. 158–159 °C (from ethanol) (Found: C, 58.3; H, 8.2; N, 12.4. $C_{11}H_{18}N_2OS$ requires C, 58.4; H, 8.0; N, 12.4%); *m/z* 226; λ_{max}(EtOH) 271 nm (ε 24 500); λ_{max}(H_2O) 269 nm (ε 19 000); λ_{max}(0.1M HCl) 268 nm (ε 22 000); λ_{max}(0.1M NaOH) 269 nm (ε 19 000); ν_{max}(KBr) 3 420, 2 750, 1 620, 1 580, and 1 500 cm^{-1}; δ_H($CDCl_3$) 1.04 (6 H, s, Me), 2.30 (2 H, s, CH_2), 2.41 (2 H, s, CH_2), 3.00 (3 H, d, Me), and 3.10 (3 H, d, Me).

4,4-*Dimethyl*-2-*methylamino*-6-*oxo*-N-*phenylcyclohex*-1-*enecarbothioamide* (**6**).—By the above procedure using compound (**2**) and phenyl isothiocyanate, the *thioamide* (**6**) was obtained (1.05 g, 37%), m.p. 182 °C (from ethanol) (Found: C. 66.7; H, 7.0; N, 9.4; S, 11.1. $C_{16}H_{20}N_2OS$ requires C, 66.7; H, 6.9; N, 9.7; S, 11.1%); *m/z* 288; λ_{max}(EtOH) 280 nm (ε 20 500); λ_{max}(H_2O) 280 nm (ε 16 000); λ_{max}(0.1M HCl) 280 nm (ε 15 500); λ_{max}(0.1M NaOH) 311 nm (ε 13 500); ν_{max}(KBr) 1 620s, 1 600vs, 1 500vs, and 1 470vs cm^{-1}; δ_H($CDCl_3$) 1.02 (6 H, s, Me), 2.32 (2 H, s, CH_2), 2.40 (2 H, s, CH_2), 2.90 (3 H, d, HN*Me*), and 7.1–7.5 (5 H, m, Ph).

2-*Anilino*-4,4-*dimethyl*-6-*oxo*-N-*phenylcyclohex*-1-*enecarbothioamide* (**7**).—A mixture of 3-anilino-5,5-dimethylcyclohex-2-enone (**3**) (2.15 g, 10 mmol) and sodium hydride (0.48 g, 20 mmol) in tetrahydrofuran (THF) (80 ml) was heated under reflux for 15 min and allowed to cool. Phenyl isothiocyanate (1.2 ml, 10 mmol) was added and refluxing continued for a further 2 h. Most of the solvent was evaporated off and the residue dissolved in dichloromethane (100 ml) and washed with dilute hydrochloric acid (2 × 50 ml). The organic phase was dried ($MgSO_4$) and the solvent evaporated off to give the *thioamide* (**7**) (2.3 g, 57%), m.p. 168–169 °C (from toluene) (Found: C, 72.0; H, 6.4; N, 8.0; S, 9.2. $C_{21}H_{22}N_2OS$ requires C, 72.0; H, 6.3; N, 8.0; S, 9.1%); *m/z* 350; λ_{max}(EtOH) 281 nm (ε 25 000); λ_{max}(H_2O) 310 nm (ε 12 500); λ_{max}(0.1M HCl) 305 nm (ε 11 000); λ_{max}(0.1M NaOH) 325 nm (ε 19 000); ν_{max}(KBr) 3 450, 2 550, 1 620, 1 570, 1 500, 1 480, and 1 440 cm^{-1}; δ_H($CDCl_3$) 1.05 (6 H, s, Me), 2.48 (2 H, s, CH_2), 2.51 (2 H, s, CH_2), 7.1–7.5 (5 H, m, Ph), 14.69 (1 H, s, NH), and 16.01 (1 H, s, NH); δ_C($CDCl_3$) 27.81 (2 × CH_3), 30.31 (C), 42.98 (CH_2), 52.29 (CH_2), 104.64 (C), 126.15 (CH), 126.23 (CH), 126.50 (CH), 127.70 (CH), 128.71 (CH), 129.63 (CH), 136.90 (C), 139.17 (C), 170.69 (C), 189.74 (C), and 196.21 (C) (C = quaternary carbon).

N^1-(5,5-*Dimethyl*-3-*oxocyclohex*-1-*enyl*)-N^2-*methylthiourea* (**8**).—A mixture of 3-amino-5,5-dimethylcyclohex-2-enone (**1**) (14 g, 100 mmol) and sodium hydride (2.4 g, 100 mmol) in dry dioxane (400 ml) was heated under reflux for 0.5 h and allowed to cool. Methyl isothiocyanate (7.3 g, 100 mmol) was added and the mixture stirred overnight. Water (20 ml) was added, the solvent evaporated off, and the product extracted with dichloromethane. The organic layer was separated and dried ($MgSO_4$), and the solvent evaporated off to give the *thiourea* (**8**) (10.7 g, 47.5%), m.p. 190 °C (from ethanol) (Found: C, 56.3; H, 7.6; N, 13.1; S, 15.2. $C_{10}H_{16}N_2OS$ requires C, 56.6; H, 7.6; N, 13.2; S, 15.1%); *m/z* 212; λ_{max}(EtOH) 303 nm (ε 18 000); λ_{max}(H_2O) 307 nm (ε 18 500); λ_{max}(0.1M HCl) 307 nm (ε 18 000); λ_{max}(0.1M NaOH) 298 nm (ε 15 000); ν_{max}(KBr) 3 320, 1 600, and 1 500 cm^{-1}; δ_H[$(CD_3)_2SO$] 0.95 (6 H, s, Me), 2.02 (2 H, s, CH_2), 2.28 (2 H, s, CH_2), 2.85 (3 H, d, Me), 6.55 (1 H, s, =CH–), 8.20 (1 H, s, NH), and 9.25 (1 H, s, NH).

N^1-(5,5-*Dimethyl*-3-*oxocyclohex*-1-*enyl*)-N^2-*phenylthiourea* (**9**).—A mixture of 3-amino-5,5-dimethylcyclohex-2-enone (**1**) (1.4 g, 10 mmol) and sodium hydride (0.5 g, 20 mmol) in toluene (80 ml) was heated under reflux for 0.5 h and cooled. Phenyl isothiocyanate (1.2 ml, 10 mmol) was added and refluxing continued for a further 4 h. The solvent was evaporated off and the residue dissolved in dichloromethane (70 ml) and washed with dilute hydrochloric acid (2 × 50 ml). The organic phase was dried ($MgSO_4$) and the solvent evaporated off to give the *thiourea* (**9**) (0.8 g, 30%), m.p. 161 °C (from ethanol) (Found: C, 65.7; H, 6.7; N, 10.2; S, 11.7. $C_{15}H_{18}N_2OS$ requires C, 65.7; H, 6.6; N, 10.2; S, 11.7%); *m/z* 274; λ_{max}(EtOH) 321 nm (ε 23 500); λ_{max}(H_2O) 311 nm (ε 22 000); λ_{max}(0.1M HCl) 322 nm (ε 20 000); λ_{max}(0.1M NaOH) 312 nm (ε 20 000); ν_{max}(KBr) 3 350, 3 250, 3 200, 3 150, 1 620, 1 595, 1 580, and 1 540 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.02 (6 H, s, Me), 2.13 (2 H, s, CH_2), 2.44 (2 H, s, CH_2), 6.76 (1 H, s, =CH–), 7.19 (1 H, t, Ph), 7.37 (2 H, t, Ph), 7.48 (2 H, d, Ph), 9.66 (1 H, s, NH), and 10.32 (1 H, s, NH); δ_C[$(CD_3)_2SO$] 27.67 (2 × CH_3), 32.33 (C), 42.14 (CH_2), 50.00 (CH_2), 108.50 (CH), 123.55 (CH), 125.18 (CH), 128.49 (CH), 138.55 (C), 155.33 (C), 178.68 (C), and 197.82 (C).

N^1-(3-*Oxocyclohex*-1-*enyl*)-N^2-*phenylthiourea* (**11**).—A solution of 3-aminocyclohex-2-enone (**10**) (3.3 g, 30 mmol) and sodium hydride (1.44 g, 60 mmol) in dry THF (100 ml) was heated under reflux for 0.5 h and cooled. Phenyl isothiocyanate (3.6 ml, 30 mmol) was added and refluxing continued for a further 2 h. After cooling, water (10 ml) was added and the solvent was evaporated off. The residue was recrystallised to give the *thiourea* (**11**) (2.5 g, 34%), m.p. 181 °C (from methanol) (Found: C, 63.4; H, 5.8; N, 11.4; S, 13.4. $C_{13}H_{14}N_2OS$ requires C, 63.4; H, 5.8; N, 11.4; S, 13.0%); λ_{max}(EtOH) 308 nm (ε 23 500); λ_{max}(H_2O) 308 nm (ε 24 000), λ_{max}(0.1M HCl) 308 nm (ε 18 000); λ_{max}(0.1M NaOH) 310 nm (ε 20 000); ν_{max}(KBr) 3 340, 3 250, 3 200, 3 210, 3 050, 1 600, 1 580, and 1 520vs cm^{-1}; δ_H[$(CD_3)_2SO$] 1.90 (2 H, m, CH_2), 2.10 (2 H, m, CH_2), 2.50 (2 H, m, CH_2), 6.70 (1 H, s, =CH–), 7.30 (5 H, m, Ph), 9.65 (1 H, s, NH), and 10.20 (1 H, s, NH).

N^1-(3-*Oxocyclohex*-1-*enyl*)-N^2-*methylthiourea* (**12**).—3-Aminocyclohex-2-enone (**10**) (1.1 g, 10 mmol) was added to a solution of sodium (0.46 g, 20 mmol) in liquid ammonia (150 ml) and the mixture stirred for 0.5 h. Methyl isothiocyanate (0.73 g, 10 mmol) was added and stirring continued for another 5 h. Ammonium chloride was added and the solvent allowed to evaporate off. The residue was dissolved in dichloromethane (70 ml) and washed with dilute hydrochloric acid (2 × 50 ml). The organic phase was dried ($MgSO_4$) and evaporated to give the *thiourea* (**12**) (1.1 g, 60%), m.p. 195.5 °C (decomp.) (from ethanol) (Found: C, 52.2; H, 6.6; N, 15.3. $C_8H_{12}N_2OS$ requires C, 52.2; H, 6.6; N, 15.2%); λ_{max}(EtOH) 304 nm (ε 19 500); λ_{max}(H_2O) 306 nm (ε 18 000); λ_{max}(0.1M HCl) 306 nm (ε 10 000); λ_{max}(0.1M NaOH) 350 nm (ε 13 000); ν_{max}(KBr) 3 300, 1 610, 1 580, and 1 520 cm^{-1}; δ_H[$(CD_3)_2SO$] 2.10 (6 H, m, CH_2), 2.90 (3 H, d, HN*Me*), 6.60 (1 H, s, =CH–), 8.30 (1 H, s, *H*NCH_3), and 9.32 (1 H, s, NH).

3,5-*Dimethyl*-2,4-*dithioxo*-1,3,5-*triazaspiro*[5.5]*undecan*-8-*one* (**15**).—A mixture of 3-aminocyclohex-2-enone (**10**) (2.2 g, 20 mmol) and sodium hydride (0.5 g, 20 mmol) was heated under reflux in dioxane (120 ml) for 10 min and cooled in an ice bath. Methyl isothiocyanate (1.5 g, 20 mmol) in dioxane (40 ml) was added during 15 min, and the mixture allowed to warm to room temperature and stirred overnight. Water (2 ml)

was added and the solvent evaporated off. The residue was dissolved in water, the solution acidified with dilute hydrochloric acid, and the product extracted with dichloromethane (2 × 100 ml). The organic solution was dried and the solvent evaporated off to give the *spiro-derivative* (**15**) (0.9 g, 35%), m.p. 181–182 °C (decomp.) (from ethyl acetate) (Found: C, 46.9; H, 5.85; N, 16.4. $C_{10}H_{15}N_3OS_2$ requires C, 46.7; H, 5.85; N, 16.3%); ν_{max}(KBr) 3 300, 1 720, 1 510, 1 480, and 1 290 cm^{-1}; δ_H($CDCl_3$) 2.00 (2 H, m, 10-CH_2), 2.17 (2 H, m, 11-CH_2), 2.49 (2 H, m, 9-CH_2), 2.84 (2 H, q, 7-CH_2), 3.49 (3 H, s, Me), 3.87 (3 H, s, Me), and 7.57 (1 H, s, NH); δ_C($CDCl_3$) 19.36 (CH_2), 32.36 (CH_2), 37.08 (CH_3), 40.05 (CH_2), 42.03 (CH_3), 49.64 (CH_2), 73.76 (C), 176.34 (C), 177.41 (C), and 204.40 (C).

8,8-*Diethoxy*-3,5-*dimethyl*-1,3,5-*triazaspiro*[5.5]*undecane*-2,4-*dithione* (**16**).—A solution of compound (**15**) (0.5 g) in ethanol was treated briefly with hydrogen chloride, heated under reflux for 0.5 h, and cooled. The precipitate was collected to give the *ketal* (**16**) (0.5 g, 78%), m.p. 179 °C (from ethanol) (Found: C, 50.7; H, 7.8; N, 12.7. $C_{14}H_{25}N_3O_2S_2$ requires C, 50.8; H, 7.6; N, 12.7%); ν_{max}(KBr) 3 300, 1 500, and 1 270 cm^{-1}; δ_H($CDCl_3$) 1.18 (3 H, t, OCH*Me*), 1.40 (3 H, t, OCH*Me*), 1.50 (6 H, m, CH_2), 2.20 (2 H, m, CH_2), 3.43 (3 H, s, NMe), 3.52 (4 H, m, 2 × OCH_2Me), 3.90 (3 H, s, NMe), and 9.16 (1 H, s, NH); δ_C($CDCl_3$) 15.22 (CH_3), 15.31 (CH_3), 17.48 (CH_2), 31.14 (CH_2), 31.68 (CH_2), 36.08 (NCH_3), 41.21 (CH_2), 41.76 (NCH_3), 55.90 (CH_2), 56.38 (CH_2), 72.13 (C), 100.35 (C), 175.52 (C), and 177.70 (C).

X-Ray Crystal Structure Determination of the Spiro Compound (**16**).—*Crystal data.* $C_{14}H_{25}N_3O_2S_2$, M = 331.5. Triclinic, a = 8.509(2), b = 10.430(3), c = 11.575(3) Å, α = 62.92(2), β = 73.61(2), γ = 66.60(2)°, V = 832.9 $Å^3$ (by least-squares refinement on 25 accurately centred reflections with $2\theta > 25°$, λ = 0.710 69 Å) at −120 °C. Space group $P\bar{1}$, Z = 2, D_c = 1.32 g cm^{-3}. Colourless parallelepiped with dimensions 0.50 × 0.24 × 0.18 mm, μ(Mo-K_α) = 3.14 cm^{-1}.

Data collection.[6] Nicolet R3m four-circle diffractometer, $\omega/2\theta$ scan mode, graphite-monochromated Mo-K_α radiation, −120 °C; 3 103 reflections measured ($1.5 \leqslant \theta \leqslant 25°$ $\pm h, k, +l$) 2 945 unique (merging R = 0.0178), giving 2 313 with $I > 3\sigma(I)$. No absorption correction or crystal decay.

Structure solution and refinement. Direct methods gave the positions of all non-hydrogen atoms. Blocked-cascade least-squares refinement used anisotropic thermal parameters for all non-hydrogen atoms, hydrogen atoms in calculated positions with isotropic thermal parameters equal to the isotropic equivalent of their carrier atoms, and the *N*-methyl hydrogens in conformations deduced from a difference map. The function minimised was $\Sigma w(|F_o| - |F_c|)^2$, with $w = [\sigma^2(F_o) + 0.0006F_o^2]^{-1}$. Final R and R_w values are 0.036 and 0.048. Features in the final difference map were all <0.3 e $Å^{-3}$. For programs and computers see ref. 6. Hydrogen atom co-ordinates and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.*

Reaction between 5,5-*Dimethyl*-3-*methylaminocyclohex*-2-*enone* (**2**) *and Phenyl Isothiocyanate.*—A mixture of the enaminone (**2**) (1.53 g, 10 mmol) and sodium hydride (0.48 g, 20 mmol) was heated under reflux in THF (80 ml) for 15 min and cooled. Phenyl isothiocyanate (1.2 ml, 10 mmol) was added and the mixture heated under reflux for 2 h and set aside overnight. The solvent was evaporated off and the residue partitioned between dichloromethane and water. The organic layer was separated and dried ($MgSO_4$), and the solvent evaporated off to give a gummy residue (2.3 g) which was recrystallised from toluene–light petroleum to give 3-anilino-5,5-dimethylcyclohex-2-enone (0.7 g, 32.6%), m.p. 183–185 °C identical (IR, TLC, and mixed m.p.) with an authentic sample.[5] The solvent was removed from the mother liquors and the residue chromatographed on a silica column with dichloromethane followed by 2% methanol in dichloromethane as eluant to give, first, the thioamide (**7**) (0.5 g, 14.3%), m.p. 169 °C, identical (IR, TLC, and mixed m.p.) with the sample prepared in the previous experiment from compound (**3**) and phenyl isothiocyanate. Next was obtained 2-*anilino*-4,4-*dimethyl*-6-*oxo*-N-*methylcyclohex*-1-*enecarbothioamide* (**18**) (0.35 g, 12.2%), m.p. 131–132 °C (from light petroleum, b.p. 80–100 °C) (Found: C, 66.5; H, 6.95; N, 9.6; S, 10.7. $C_{16}H_{20}N_2OS$ requires C, 66.7; H, 6.95; N, 9.6; S, 11.1%); ν_{max}(KBr) 1 600s, 1 580vs, 1 530vs, and 1 480vs cm^{-1}; δ_H($CDCl_3$) 1.00 (6 H, s, Me), 2.40 (2 H, s, CH_2), 2.46 (2 H, s, CH_2), 3.18 (3 H, s, NMe), 7.2–7.5 (5 H, m, Ph), 13.00 (1 H, s, NH), and 15.83 (1 H, s, NH); δ_c($CDCl_3$) 27.76 (2 × CH_3), 30.39 (C), 31.45 (CH_3), 42.76 (CH_2), 52.29 (CH_2), 104.21 (C), 126.20 (CH), 127.49 (CH), 129.56 (CH), 137.08 (C), 169.60 (C), 190.13 (C), and 195.95 (C). Finally, 1,3,7,7-*tetramethyl*-2,4-*dithioxo*-1,2,3,4,7,8-*hexahydroquinazolin*-5(6H)-*one* (**17**) (0.15 g, 5.6%) was obtained, m.p. 186–187 °C (from toluene) (Found: C, 53.9; H, 6.0; N, 10.3. $C_{12}H_{16}N_2OS_2$ requires C, 53.7; H, 6.0; N, 10.5%); *m/z* 268; ν_{max}(KBr) 1 690, 1 550, 1 470, 1 435, 1 420, and 1 100 cm^{-1}; δ_H($CDCl_3$) 1.15 (6 H, s, Me), 2.47 (2 H, s, CH_2), 2.73 (2 H, s, CH_2), 3.89 (3 H, s, NMe), and 4.23 (3 H, s, NMe); δ_C($CDCl_3$) 28.57 (2 × CH_3), 32.25 (C), 40.54 (CH_3), 42.46 (CH_2), 44.08 (CH_3), 51.85 (CH_2), 120.37 (C), 152.31 (C), 175.28 (C), 182.38 (C), and 192.65 (C).

Reaction Between 3-*Anilino*-5,5-*dimethylcyclohex*-2-*enone* (**3**) *and Methyl Isothiocyanate.*—By the procedure described above using compound (**3**) and methyl isothiocyanate was obtained a gummy residue (2.2 g) which was recrystallised from toluene to give the unchanged enaminone (**3**) (0.5 g, 23.3%), m.p. 183–184 °C. Evaporation of the toluene from the mother liquors and column chromatography as in the foregoing experiment gave the following fractions: (i) the thioamide (**7**) (0.5 g, 14.3%), m.p. 169 °C; (ii), the *thioamide* (**18**) (0.25 g, 8.7%), m.p. 132–133 °C; (iii), the *dithione* (**17**) (0.1 g, 3.7%), m.p. 186–187 °C. The products (**7**), (**17**), and (**18**) were identical (IR, TLC, and mixed m.p.) with those described above.

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* For details, see Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1990, issue 1.

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