Stereochemical Studies. Part 86.[1] Saturated Heterocycles. Part 81.[1] Preparation of New Thiouracils *via* Retrodiene Decomposition of Methylene-bridged Quinazolone Thiones

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endo- and *exo*-Norbornene (**1**) and (**3**) and norbornane (**2**) and (**4**) amino acids and isothiocyanates give methylene-bridged 2-thioxohexahydro- (**10**) and (**11**) and octahydro- (**12**) and (**13**)-quinazolin-4-ones. Compounds (**10**) and (**11**) decompose in a retro-Diels–Alder reaction when heated to melting, to give new 3-substituted thiouracils (**14a—e**); no convenient general suitable method was previously known for the preparation of these compounds.

Besides the theoretical, primarily stereochemical, interest in compounds with a norbornane skeleton, they are also used as pharmaceuticals.[2,3] We therefore previously prepared a number of 1,3-oxazine derivatives with norbornane and norbornene skeletons.[4] These compounds and their derivatives with a fused azetidinone ring were systematically studied through ^{1}H and ^{13}C n.m.r. spectroscopy.[5]

In the present work we report on the synthesis of methylene-bridged saturated and partially saturated thioxoquinazolones; the retrodiene reactions of these compounds occur under mild conditions and afford a very convenient route to new thiouracil derivatives, as shown in the Scheme.

Results and Discussion

Ammonolysis of the Diels–Alder adduct of cyclopentadiene and maleic anhydride, followed by Hofmann degradation with sodium hypochlorite, gave 3-*endo*-aminobicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylic acid (**1**).[4a] Catalytic hydrogenation of the ester salt of (**1**) furnished the corresponding saturated bicyclic *endo* amino acid (**2**).[4b] The stereoisomeric unsaturated *exo* analogue (**3**)[6] and the saturated *exo* isomer (**4**)[4a] were prepared from the cycloadducts of the norbornadiene or norbornene and chlorosulphonyl isocyanate, as reported previously. The amino acids with norbornene (**1**) and (**3**) and norbornane (**2**) and (**4**) skeletons were allowed to react with isothiocyanates (**5**) to give the thioureas (**6**)—(**9**); these were cyclized by acid catalysis to yield 3-substituted 2-thioxo-2,3,*r*-4a,*t*-5,*t*-8,*c*-8a-hexahydro-5,8-methanoquinazolin-4(1*H*)-ones (**10**), -2,3,*r*-4a,*c*-5,*c*-8,*c*-8a-hexahydro-5,8-methanoquinazolin-4(1*H*)-ones (**11**), -2,3,*r*-4a,-*t*-5,6,7,*t*-8,*c*-8a-octahydro-5,8-methanoquinazolin-4(1*H*)-ones (**12**), and -2,3,*r*-4a,*c*-5,6,7,*c*-8,*c*-8a-octahydro-5,8-methanoquinazolin-4(1*H*)-ones (**13**).

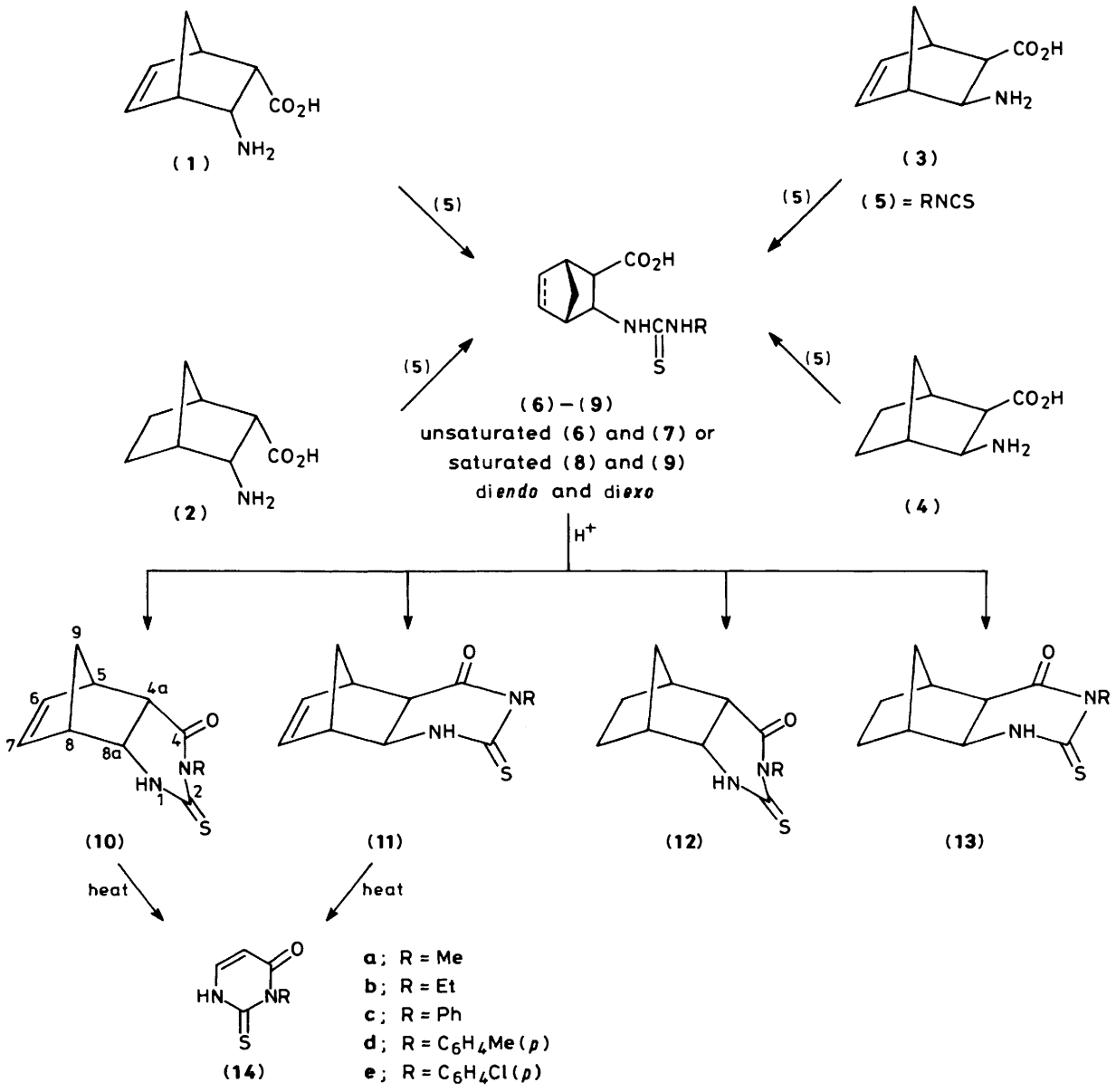
In a similar manner to the related tricyclic 1,3-oxazin-4-ones we investigated earlier,[6,7] compounds (**10**) and (**11**) readily undergo decomposition when heated to their melting points; cyclopentadiene is split off, and the monocyclic 2,3-dihydro-2-thioxopyrimidin-4(1*H*)ones (**14a—e**) are formed. Compounds (**14a—e**) can be isolated from the reaction products in 54—85% yield by elution from a silica gel column. The importance of this procedure is that in this way 3-substituted 2-thiouracil derivatives of type (**14**) can be synthesized. While several pathways have been reported for the synthesis of 1-substituted thiouracils,[8] the 3-substituted derivatives cannot be prepared in an analogous way or by alkylation, for in the latter case the pyrimidines containing a thiocarbonyl group will be alkylated first on the sulphur atom.[9]

Warrener and Cain[10] described the synthesis of 3-alkyl-2-thiouracils by the ammonolysis of *N*-alkyl- (ethyl, methyl)-1,3-thiazines. They regarded this thiazine-into-pyrimidinone conversion as chemical evidence of the structures of the 3-ethyl and 3-methyl derivatives prepared. Further, in the proof of the structure of the 3-substituted 2-thiouracils they relied upon the u.v. absorption data of Shugar and Fox,[11] published in 1952, who studied 3-ethyl-2-thiouracil, but without giving any experimental preparative data. Another investigation[12] dealt with an ESCA study of 3-methyl-2-thiouracil, but the paper[13] referred to in this publication does not describe the synthesis of this compound. The melting point of 3-methyl-2-thiouracil is given in the literature[10] as 207 °C. In our experiments, this compound, with its structure confirmed by i.r. and ^{1}H and ^{13}C n.m.r. spectroscopy, had m.p. 292—294 °C. This significant difference in m.p. leads us to assume that the compound prepared by Warrener and Cain[10] was not 3-methyl-2-

Table 1. Characteristic i.r. frequencies of compounds (**10**)—(**14**) in KBr (cm^{-1})

	ν_{NH}[a]	$\nu_{C=O}$	$\nu_{C=S}$	δ_{NH}[b]
(**10a**)	3 267	1 661	1 371	1 550
(**10b**)	3 308	1 668	1 366	1 556
(**10c**)	3 292	1 676	1 367	1 545
(**10d**)	3 292	1 676	1 364	1 551
(**10e**)	3 179	1 703	1 362	1 589
(**11a**)	3 296	1 666	1 366	1 555
(**11c**)	3 182	1 705	1 362	1 574
(**11d**)	3 192	1 701	1 352	1 576
(**11e**)	3 175	1 707	1 358	1 574
(**12a**)	3 323	1 676	1 366	1 551
(**12c**)	3 304	1 682	1 362	1 553
(**12d**)	3 173	1 703	1 364	1 582
(**12e**)	3 180	1 703	1 364	1 587
(**13a**)	3 323	1 676	1 366	1 551
(**13c**)	3 190	1 707	1 362	1 580
(**13d**)	3 204	1 701	1 369	1 574
(**13e**)	3 206	1 709	1 371	1 574
(**14a**)	3 107	1 645	1 281	1 537
(**14b**)	3 300—2 750	1 645	1 230[c]	1 510
			1 259[c]	1 539
(**14c**)	3 115	1 711	1 244[c]	
(**14d**)	3 285	1 680	1 231[c]	1 506
(**14e**)	3 206	1 668	1 231	1 522

[a] Centre of a broad absorption. [b] Broadened maximum of the in-plane deformation vibration. [c] Split maxima.



Scheme.

thiouracil. As concerns the 3-ethyl derivative, the m.p. of our compound (189—190 °C) did not differ so much from that given in the literature,[10] *i.e.* 177 (165) °C. In view of the above data, our syntheses are the first of the 3-methyl- and aryl-substituted 2-thiouracil derivatives.

I.r. and ^{1}H *and* ^{13}C *N.m.r. Spectra.*—The principles of the spectroscopic determination of the structures of norbornane and norbornene derivatives have been described in detail earlier.[5a] The main evidence for the presence of the –NH–CS–NR–CO– functional group is given by the ν_{CO}, ν_{NH}, δ_{NH}, and thioamide group vibration bands of $\nu_{C=S}$ character in the range 1 350—1 370 cm^{-1} in the i.r. spectra[14a] (Table 1), and also by the NH signals in the proton spectra (Table 2) and the ^{13}C n.m.r. signals of the amide and thioamide carbon atoms at 166.9—169.3 p.p.m. and 180.0—181.6 p.p.m. respectively.

Unsaturation of the alicyclic ring in compounds (**10a—e**) and (**11a, c—e**) is shown in the ^{1}H n.m.r. spectra of these compounds by the two doublets of doublets between δ_H 6.15 and 6.40, appearing in the range characteristic of olefins, assignable to 6- and 7-H (Table 2), and also by the signals of the olefin carbons at δ_C 136.5—140.5 p.p.m. (Table 3). For compounds (**12a, c—e**) and (**13a, c—e**), instead of these signals the proton spectra have methylene signals of 4 H-intensity (δ_H 1.1—1.8), and the carbon resonance lines due to the two methylene groups are also present in the range characteristic of saturated compounds (δ_C 21—30 p.p.m.). To establish the annelation of the hetero ring, the coupling constant J(8-H, 8a-H), deduced from the ^{1}H n.m.r. spectra, is of primary importance; this gives a splitting of the 8a-H signal of about 3 Hz in the di*endo* compounds (**10a—e**) and (**12a, c—e**). In the di*exo* analogues, in agreement with the C(8)–H(8), C(8a)–H(8a) dihedral angle of about 90°,[15] this coupling does not give rise to a significant splitting (*cf.* footnotes *d* and *k* in Table 2).

The presence of the substituent R is indicated by the proton and carbon signals of the *N*- and *C*-methyl groups or, in series (**c**) by AA′BB′C in series (**d**) and (**e**) by AA′BB′ multiplets, of 5 H- or 4 H-intensity, assigned to aromatic

Table 2. ^{1}H n.m.r. data for compounds (**10**)—(**14**)[a]

Compd.	Chemical shifts δ_H									
	1-H (NH) s (1 H)[b]	4a-H[c] d[d] or dd[e] (1 H)	5-H s (1 H)[f,g]	6-H	7-H	9-H	8-H s (1 H)[f]	8a-H d[d] or dt[k] (1 H)	Ch in 3-R s (3 H)	3-C_6H_4X 2 or 3 ms (5 H) for (**c**), AA′BB′ multiplet (4 H) for (**d**) and (**e**)
(**10a**)	9.75	~3.33	3.25	6.17[l]		1.40[l]	~3.33	4.00	3.33[c]	—
(**10b**)	~8.1	~3.33[l]		6.25[l]		1.37, 1.55	3.55	4.00	1.19[m]	—
(**10c**)	9.90	~3.38	3.25	6.29	6.36	1.40, 1.45	~3.35	4.05	—	~6.9 (1 H)[n], ~7.05 (1 H)[n], 7.25—7.40 (3 H)
(**10d**)	9.85	~3.40	3.28	6.30	6.36	1.40, 1.50	~3.36	4.08	2.32	~6.8 (1 H)[n], ~6.9 (1 H)[n], 7.16 (2 H)
(**10e**)	10.00	~3.42	3.26	6.29	6.36	1.40, 1.48	~3.38	4.08	—	~6.95 (1 H)[n], ~7.15 (1 H)[n], 7.42 (2 H)
(**11a**)	9.90	2.46	3.04	6.15	6.38	1.29, 1.38	3.18	3.30	3.43	—
(**11c**)	10.05	2.75	3.12	6.20	6.40	1.45, 1.56	3.21	3.43	—	~7.1 (2 H)[n], 7.3—7.4 (3 H)
(**11d**)	10.05	2.74	3.11	6.20	6.39	1.45, 1.55	3.20	3.41	2.32	~7.15 (2 H)[n], 7.16 (2 H)
(**11e**)	10.15	2.75	3.12	6.20	6.39	1.44, 1.56	3.21	3.41	—	~7.15 (2 H)[o], 7.45 (2 H)
(**12a**)	7.55	3.05	2.54	~1.54 ~s (4 H), 1.30, 1.65			2.83	3.80	3.61	—
(**12c**)	~8.3	3.16[p]	2.60	~1.55 m (5 H), 1.80 d (1 H)			2.90	3.90	—	~7.2 (2 H)[o], 7.4—7.5 (3 H)
(**12d**)	8.05	3.16[p]	2.58	1.5—1.6 m (5 H), 1.80 d (1 H)			2.87	3.88	2.39	~7.05 (2 H)[o], 7.26 (2 H)
(**12e**)	9.90	3.16	2.50[q]	1.3—1.5 m (6 H)			2.60	3.82	—	~7.10 (1 H)[o], ~7.15 (1 H)[o], 7.44 (2 H)
(**13a**)	9.64	2.80	2.40	1.1—1.6 m (6 H)			2.58	3.50	3.41	—
(**13c**)	8.70	2.90	2.45	1.1—1.8 m (6 H)			2.85	3.90	—	7.18 (2 H)[o], 7.4—7.5 (3 H)
(**13d**)	9.82	2.88	2.43	1.1—1.6 m (6 H)			2.57	3.55	2.31	6.93 (2 H)[o], 7.15 (2 H)
(**13e**)	8.10	2.89	2.46	1.2—1.8 m (6 H)			2.85	3.63	—	7.08 (2 H)[o], 7.40 (2 H)
(**14a**)	?	—	5.95	7.45	—	—	—	—	3.52	—
(**14b**)	~12.5	—	5.95	7.44	—	—	—	—	1.19[m]	—
(**14c**)	~12.6	—	6.04	7.52	—	—	—	—	—	7.17 (2 H), 7.3—7.5 (3 H)
(**14d**)	~12.6	—	6.02	7.50	—	—	—	—	2.34	7.04 (2 H), 7.25 (2 H)
(**14e**)	~12.7	—	6.05	7.53	—	—	—	—	—	7.25 (2 H), 7.51 (2 H)

[a] At 250 MHz, in $(CD_3)_2SO$: (**10a,c—e**), (**11a,c—e**), (**12e**), (**13a**, and **d**), and (**14a—e**); or $CDCl_3$: (**10b**), (**12a,c** and **d**), and (**13c**, and **e**); δ $SiMe_4$ = 0 p.p.m. coupling constants in Hz. [b] Broad signal. [c] In (**10a,c—e**), partially or fully masked by the overlapping maximum of water in the $(CD_3)_2SO$ solvent. [d] In (**11a,c—e**) and (**13a,c—e**), J(4a,8a) 9.0—9.1 Hz, J(4a,5) ≈ J(8,8a) < 0.5 Hz. [e] J(4a,8a), 12.6 (**12a**), 12.2 (**12c** and **d**), and 12.3 Hz (**12e**); J(4a,5) 4.3 (**12a**), 5.0 (**12c**), 4.9 (**12d**), and 4.8 Hz (**12e**). [f] Singlet-like signal, due to very close overlapping lines (**10a,c—e**)—(**13a,c—e**). In (**14a—e**) d[g]. [g] A or B part (d) of the AB spectrum of 5- and 6-H, J(5,6) 7.5 (**14a** and **e**), 7.6 (**14b** and **d**), and 7.7 Hz (**14c**). [h] In (**10c—e**) and (**11a,c—e**), J(6,7) 5.6—5.7 Hz, J(5,6) ≈ J(7,8) 2.6—3.0 Hz. [i] Overlapping multiplets of the methylene groups (positions 6, 7, and 9) or 6 H intensity, (**12a,c—e**) and (**13a,c—e**). In (**12a**) both, and in (**12c** and **d**) one, of the doublets of 9-H can be recognized separately. [j] In (**10a—e**) and (**11a,c—e**), AB multiplet, J(A,B) ≈ 9 Hz. For (**12a,c—e**) and (**13a,c—e**), see footnote *i*. [k] In (**10a—e**) and (**12a,c—e**), J(8,8a) ≈ J(8a,9$_{exo}$) 2.8—3.0 Hz, J(4a,8a) 9.7 (**10a—e**). For (**12a,c—e**), see footnote *e*. [l] Singlet-like signal of 2 H intensity. [m] Ethyl group t, J 7 Hz, CH_2, q 4.25 (**10b**) and 4.32 p.p.m. (**14b**). [n] The 2′ and 6′-H signal(s) of the *ortho*-protons (2 × 1 H or 1 × 2 H), broadened due to hindered rotation of the aromatic ring, sharpened into dd (J ~9 and ~2 Hz) at higher (~423 K) temperatures. [o] Barely significant broadening. [p] Further splitting to ddd by long-range interaction, probably with the 9-H$_{exo}$ atom, J(4a,9$_{exo}$) 1.2 Hz. Barely significant triplet splitting can be observed for the AB lines of the 9-methylene protons, *e.g.* in (**11a**). [q] Masked by the light isotope content of the solvent.

protons; the spectra of compounds in series (**c—e**) each contain four lines due to the carbon atoms of the benzene ring. The broadening and chemical non-equivalence of the aromatic *ortho*-proton signals, indicative of hindered rotation, can be taken as indirect evidence of the degree of saturation of the skeleton, the di*exo* or di*endo* annelation, and the presence of the CO–NR–CS functional group; this effect is greatest in compounds (**10c—e**), less pronounced in series (**11c—e**) and (**12c—e**), and hardly observable in the spectra of compounds (**13c—e**). Our assumption relating to the cause of the effect is substantiated by ^{1}H n.m.r. measurements at higher temperatures (about 140 °C), when the splitting and broadening of the signals disappeared. Weak conjugation in compounds (**10c** and **d**) and (**12c**) due to the non-coplanar conformation of the carbonyl group and the aromatic π-systems (hindered rotation) is also shown by the barely increasing $\nu_{C=O}$ and δ_{NH} i.r. frequencies as compared with those of the *N*-methyl derivatives. *N*-Aryl substitution in the other compounds, (**11c—e**), (**12d** and **e**), and (**13c—e**), gives rise to the usual increase of frequency,[14b] as expected from the $-I$ effect of the substituent. Accordingly, the $\nu_{C=O}$ and δ_{NH} bands at 1 660—1 676 and 1 550—1 555 cm^{-1} in the spectra of the methyl-substituted compounds are shifted to 1 700—1 707 and 1 574—1 589 cm^{-1}, respectively. The corresponding values for compounds (**10c** and **d**) and (**12c**) are 1 676, 1 676, 1 682 (CO) and 1 545, 1 551, 1 553 cm^{-1} (NH), respectively.

The gradually decreasing extent of hindered rotation in the series (**10**)—(**13**) follows from the above considerations and is in agreement with the stereostructures of the compounds.

As correction of the literature data seems necessary, the spectral evidence relating to the structures of the 3-substituted 2-thiouracils must be discussed in detail. The presence of the NH group in compounds (**14a—e**) is unequivocally shown by the ν_{NH} and δ_{NH} bands in the i.r. spectra (Table 1). The frequencies of the bands are essentially unaltered as compared with those for compounds (**10**)—(**13**). The carbonyl frequency in the conjugated hetero ring is more sensitive to substitution, and the vibration frequencies of the thiocarbonyl group are fundamentally different from those for compounds (**10**)—(**13**). However, the presence of the carbonyl and thiocarbonyl functions are certain, on the basis of the ^{13}C signals at δ_C 162 and 179 p.p.m.

The presence of unsaturation is shown by olefin proton signals (δ_H 5.95—6.05 and 7.45—7.53) and carbon signals (δ_C 105.4—106.5 and 142—143 p.p.m.). The large shift differences of these signals are characteristic of α,β-unsaturated ketones (enones) and can be explained by the mesomerism C=C–C=O ⟷ $^+$C–C=C–O$^-$.[16a] The $J_{5\text{-H},6\text{-H}}$ coupling constant of 7.5—7.7 Hz (footnote *g* in Table 2) is characteristic of six-membered cyclic olefins.[16b] The ^{1}H and ^{13}C n.m.r. signals of the substituents R do not differ significantly from those found for compounds (**10**)—(**13**).

Table 3. ^{13}C N.m.r. data for compounds (10)—(14)[a]

Compd.	Chemical shifts δ_C/p.p.m. C-2	C-4	C-4a	C-5[b]	C-6[c]	C-7[c]	C-8[b]	C-8a	C-9	CH_3 in 3-R	C-1′	C-2′-6′	C-3′-5′	C-4′
(10a)	180.6	169.0	47.2	50.8	137.7	136.9	50.4	54.6	43.4	33.7	—	—	—	—
(10b)[d]	180.4	166.8	46.3	49.6[e]	135.1	136.8	50.1[b]	53.8	42.8	13.1[e]	—	—	—	—
(10c)	180.4	169.1	47.7	50.9	137.8	137.1	50.6	55.3	43.5	—	141.0	130.9	129.7	128.9
(10d)	180.6	169.1	47.5	50.9	137.8	137.1	50.6	55.3	43.5	22.3	138.4[f]	130.6[g]	130.2[g]	138.2[f]
(10e)[h]	180.2	169.1	47.5	50.9	137.8	137.1	50.6	55.4	43.5	—	139.8	132.8[i]	129.7	133.7
(11a)	180.4	168.6	45.2	50.5	136.6	140.2	52.6	54.7	43.0	34.2	—	—	—	—
(11c)	180.3	168.7	45.3	50.7	136.8	140.3	52.7	55.5	43.1	—	141.3	131.1	129.8	129.1
(11d)	180.4	168.7	45.3	50.8	136.8	140.3	52.7	55.5	43.2	22.3	138.4[j]	130.4[k]	130.4[k]	138.4[j]
(11e)	180.0	168.7	45.3	50.7	136.8	140.4	52.7	55.6	43.2	—	139.9	133.0	129.9	133.9
(12a)[d,h]	181.6	167.7	44.1[b]	42.9	25.0	21.1	42.3	54.1	36.7	33.2	—	—	—	—
(12c)[d]	181.3	167.6	44.0	43.0	25.1	21.2	42.1	54.7	36.9	—	139.0	129.2	128.9	128.5
(12d)	181.1	169.3	44.8	43.8	26.2	22.2	42.7	55.4	37.5	22.2	138.3[f]	130.7[g]	130.3[g]	138.4[f]
(12e)[l]	180.5	169.3	44.7	43.7	26.2	22.3	42.6	55.5	37.5	—	139.9	132.9	129.9	133.7
(13a)	180.6	168.5	45.0	47.6	30.1	26.1	46.5	58.3	34.0	35.1	—	—	—	—
(13c)[d]	180.5	167.0	44.2	47.0	29.2	24.9	46.0	58.1	34.2	—	138.9	129.3	128.8	128.4
(13d)	180.5	168.6	45.1	47.7	30.0	26.1	46.6	58.9	35.2	22.3	138.3[f]	130.8[g]	130.3[g]	138.4[f]
(13e)[d]	180.6	166.9	44.2	47.0	29.2	24.9	46.2	58.2	34.2		137.3	130.6	129.2	134.6
(14a)	178.5	162.1	—	105.4	142.1	—	—	—	—	34.6	—	—	—	—
(14b)	178.1	161.7	—	106.0	142.0	—	—	—	—	13.1[e]	—	—	—	—
(14c)	179.5	162.3	—	106.5	142.7	—	—	—	—	—	140.8	130.6	130.2	129.7
(14d)	179.6	162.3	—	106.4	142.6	—	—	—	—	22.3	138.2[f]	131.1[g]	129.8[g]	139.0[f]
(14e)	179.5	162.2	—	106.5	142.9	—	—	—	—	—	139.7	132.2	130.8	134.5

[a] In $(CD_3)_2SO$ at 20.14 MHz; δ ($SiMe_4$) = 0 p.p.m. Primed numbers refer to aryl group. [b,c,f,g] Alternative assignment is also possible. [d] In $CDCl_3$ solution. [e] Ethyl group, CH_2 41.1 (**10b**) and 42.5 p.p.m. (**14b**). [h] On a Bruker WM-250 spectrometer at 62.9 MHz. [i] Broadened, due to hindered rotation of the aromatic ring. [j,k] Two overlapping lines. [l] The orders of the carbons were proved by DEPT measurement, which also allowed identification of the signals masked by the solvent lines.

Table 4. Physical and analytical data for the thioxoquinazolines (10)—(13)[a,b]

Compd.	M.p. (°C)	Yield (%)	Found (%) C	H	N	Formula	Required (%) C	H	N
(10a)	178—180	60	57.4	5.7	13.6	$C_{10}H_{12}N_2OS$	57.67	5.80	13.45
(10b)	170—172	65	59.5	6.4	12.5	$C_{11}H_{14}N_2OS$	59.43	6.35	12.60
(10c)	205—207	75	66.7	5.4	10.1	$C_{15}H_{14}N_2OS$	66.64	5.22	10.36
(10d)	220—221	72	67.4	5.5	9.7	$C_{16}H_{16}N_2OS$	67.58	5.67	9.85
(10e)	214—216	82	59.2	4.3	9.0	$C_{15}H_{13}ClN_2OS$	59.11	4.30	9.19
(11a)	196—198	68	57.8	5.9	13.2	$C_{10}H_{12}N_2OS$	57.67	5.80	13.45
(11c)	198—200	75	66.7	5.4	10.2	$C_{15}H_{14}N_2OS$	66.64	5.22	10.36
(11d)	212—213	78	67.7	5.75	9.7	$C_{16}H_{16}N_2OS$	67.58	5.67	9.85
(11e)	216—218	61	59.0	4.4	9.1	$C_{15}H_{13}ClN_2OS$	59.11	4.30	9.19
(12a)	181—183	55	57.25	6.8	13.4	$C_{10}H_{14}N_2OS$	57.11	6.70	13.32
(12c)	272—274	68	66.3	6.1	10.0	$C_{15}H_{16}N_2OS$	66.14	5.92	10.28
(12d)	297—298	71	67.25	6.4	9.6	$C_{16}H_{18}N_2OS$	67.10	6.33	9.78
(12e)	318—319	67	58.6	5.0	8.9	$C_{15}H_{15}ClN_2OS$	58.72	4.93	9.13
(13a)	201—203	58	57.25	6.8	13.2	$C_{10}H_{14}N_2OS$	57.11	6.70	13.32
(13c)	196—198	60	66.2	5.9	10.4	$C_{15}H_{16}N_2OS$	66.14	5.92	10.28
(13d)	274—276	70	67.2	6.3	10.0	$C_{16}H_{18}N_2OS$	67.10	6.33	9.78
(13e)	281—283	67	58.9	5.0	9.0	$C_{15}H_{15}ClN_2OS$	58.72	4.93	9.13

[a] Crystallized from nitromethane. [b] M.p.s (°C) of compounds (**6**)—(**9**) with satisfactory analyses: (**6c**) 173—175, (**6d**) 183—185, (**7c**) 183—184, (**7d**) 186—188, (**7e**) 207—209, (**8d**) 196—198, (**8e**) 179—181, (**9c**) 183—184, (**9d**) 192—194, (**9e**) 201—203.

Experimental

General Methods.—M.p.s are uncorrected. I.r. spectra were run in KBr discs on a Bruker IFS-113v FT spectrophotometer equipped with an Aspect 2000 computer. ^1H and ^{13}C n.m.r. spectra were recorded at room temperature in $CDCl_3$ or $(CD_3)_2SO$ solution in 5- and 10-mm tubes on Bruker WM-250 (^1H) and WP-80 SY (^{13}C) FT spectrometers at 250.13 (^1H) and 20.14 (^{13}C) MHz, respectively, using the deuterium signal of the solvent as the lock and $SiMe_4$ as internal standard. The most important measuring parameters were: sweep width 5 kHz, pulse width 1 (^1H) and 3.5 (^{13}C) μs (~20° and ~30° flip angle), acquisition time 1.64 s, number of scans 16 (^1H) and 1K—4K (^{13}C), computer memory 16K. Complete proton-noise decoupling (~3W) for the ^{13}C spectra, and Lorentzian exponential multiplication for signal-to-noise enhancement were used (line width 0.7 and 1.0 Hz). DEPT experiments were performed by

Table 5. Physical and analytical data for the 2-thiouracils (**14a—e**)[a]

Compd. (formula)	Yield[b] (%)	M.p. (°C)	Found (%) (required) C	H	N
(**14a**)	54	292—294	42.3	4.3	19.8
($C_5H_6N_2OS$)			(42.24)	(4.25)	(19.70)
(**14b**)	83	189—190	46.1	5.1	17.75
($C_6H_8N_2OS$)			(46.14)	(5.16)	(17.93)
(**14c**)	80	247—249	58.8	4.0	13.7
($C_{10}H_8N_2OS$)			(58.81)	(3.95)	(13.71)
(**14d**)	85	231—232	60.4	4.55	13.0
($C_{11}H_{10}N_2OS$)			(60.52)	(4.61)	(12.83)
(**14e**)	85	218—220	50.3	2.9	11.8
($C_{10}H_7ClN_2OS$)			(50.32)	(2.96)	(11.74)

[a] Crystallization solvent EtOH. [b] Yields are given for the purified compounds.

running three spectra with θ-pulses of 45, 90, and 135°, respectively, and editing the subspectra through a linear combination of these. The 90° pulse lengths were 10.8 and 22.5 μs for the ^{13}C and ^{1}H nuclei in the 10 mm probehead. After every scan, a 3 s delay was inserted to allow protons to relax.

Preparation of 3-*Substituted* 2-*Thioxo-hexahydro-* (**10**) *and* (**11**) *and -octahydro-* (**12**) *and* (**13**) -5,8-*methanoquinazolin*-4(1H)-*ones*.—The di*endo*[4a] (**1**) or di*exo*[6] (**3**) 3-aminobicyclo-[2.2.1]hept-5-ene-2-carboxylic acid (1.53 g, 0.01 mol) or the di*endo*[4b] (**2**) or di*exo*[4a] (**4**) 3-aminobicyclo[2.2.1]heptane-2-carboxylic acid (1.55 g. 0.01 mol) was refluxed for 2 h in ethanol (50 ml) with the appropriate isothiocyanate (**5**) (0.01 mol): methyl isothiocyanate (0.75 g), ethyl isothiocyanate (0.87 g), phenyl isothiocyanate (1.35 g), *p*-tolyl isothiocyanate (1.50 g), or *p*-chlorophenyl isothiocyanate (1.70 g). The crude thiourea product obtained on evaporation of the mixture was refluxed for 90 min in ethanol (40 ml) containing 20% hydrogen chloride. The solvent was evaporated off and the solid product was recrystallized from nitromethane. Data on the compounds prepared, (**10**)—(**13**), are shown in Table 4.

Preparation of 3-*Substituted* 2,3-*Dihydro*-2-*thioxo-pyrimidin*-4(1H)-*ones* (**14a—e**).—The 2-thioxo-2,3*r*-4a,*t*-5,*t*-8,*c*-8a-hexahydro-5,8-methanoquinazolin-4(1*H*)-ones (**10a—e**) (1 g) or 2-thioxo-2,3,*r*-4a,*c*-5,*c*-8,*c*-8a-hexahydro-5,8-methanoquinazolin-4(1*H*)-ones (**11a,c—e**) (1 g) were heated in a round-bottomed flask for 10 min at a temperature 10 °C higher than the m.p. of the compound. After the mixture had cooled, the residue was dissolved in ethyl acetate, applied to a silica gel column, and eluted with ethyl acetate. The solvent was evaporated off and the product was crystallized. Data on compounds (**14a—e**) are shown in Table 5.

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