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The acyl thioacetanilide **3** condensed with 2-bromotetralone to give the spiroketone **5**. A similar reaction of the tetralone with the acyl-*N*-ethylthioacetamide **4** afforded small amounts of the unsaturated spiroketone **6** with the isomeric dihydrobenz[*g*]indole **7** as the major product. Compound **7** was aromatized to the benz[*g*]indole **8** in high yield.

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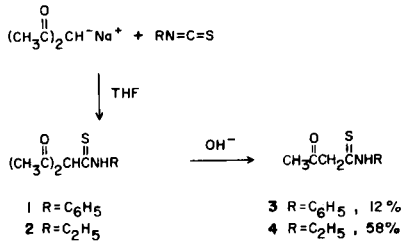
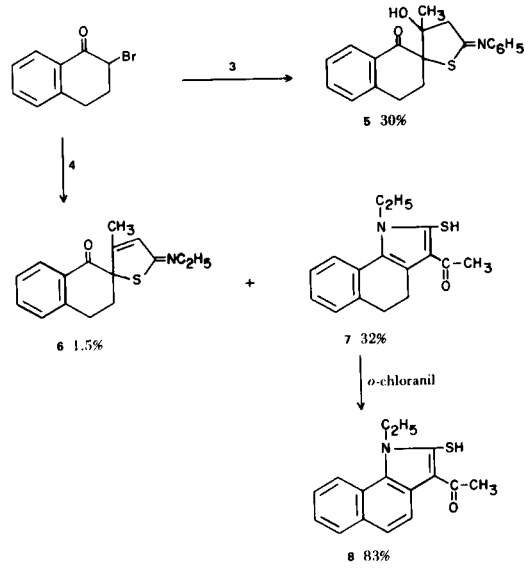
Synthesis and modification of a class of active methylene compounds, acyl thioacetanilides, in our experiments have led to fuctionalized heterocycles with unusual structures. The original preparation of 2-acetylthioacetanilide (**3**), described by Worrall (**1**), was altered and extended to the aliphatic analog, 2-acetyl-*N*-ethylthioacetamide (**4**), as shown below. The diacetyl precursors, **1** and **2**, were easily hydrolyzed to the desired monoacetyl products.



Condensations of **3** and **4** with 2-bromo-3,4-dihydro-1(2*H*)naphthalenone (2-bromotetralone) in the presence of sodium methylate afforded the heterocyclic products shown below. Compound **7** was further aromatized with *o*-chloranil to the indole **8**.



Thiolane **5** and thiolene **6** showed normal bands in the ir at 1675 cm^{-1} for ketone carbonyl groups. Indoles **7** and **8** had carbonyl peaks for the conjugated, exocyclic acetyl groups shifted to 1593 cm^{-1} and 1600 cm^{-1}, respectively. Proton nmr spectra for the acetyl thioamides exhibited signals for enolized keto-methylene protons at 5.3-5.5 δ, as well as acetyl methyl peaks at 1.9-2.0 δ for the enolized forms. Thiolane **5** and thiolene **6** both displayed multiplets at 2.2-3.2 δ for vicinal methylene protons on the tetralone ring. Additionally, compound **5** showed 1-proton doublets for non-equivalent gem protons on the 5-membered ring at 3.08 δ and 4.08 δ. Compound **6** showed a vinyl proton at 6.25 δ. Dihydrobenzindole **7** and benzindole **8** both had exchangeable S-H protons at 8.8-9.0 δ and acetyl methyl groups at 2.2-2.4 δ. Mass spectral patterns were consistent with the structures, and ^{13}C nmr with off-resonance decoupling characterized the molecules completely. Detailed assignments are included in the Experimental Section.

Formation of the spiro compounds **5** and **6** proceeds through nucleophilic attack of the sulfur of the thioamides **3** and **4** on the reactive 2-position of the tetralone. Subsequent ring closure on the same 2-carbon atom completes the spiro structure. In contrast, the dihydrobenz[*g*]indole **7** requires reaction of the active methylene anion from **4** with the 2-position of 2-bromotetralone, followed by carbon-nitrogen ring closure.

Reaction of 2-bromocyclohexanone with compound **4** was much less facile than 2-bromotetralone. A complex mixture of products resulted, none of which corresponded to **5**, **6** or **7**.

EXPERIMENTAL

The melting points were determined with a Thomas Hoover capillary melting point apparatus and are corrected. The ir spectra were recorded on a Perkin Elmer 457, mass spectra on an AEI MS902, proton nmr on a Varian XL100 FFT or Varian A-60D, and ^{13}C nmr on a Varian XL100 FFT with off-resonance decoupling.

2-Acetylthioacetanilide (**3**).

Sodium pellets (11.5 g., 0.5 mole) were dissolved in 300 ml. of dry methanol, and the solvent was removed at reduced pressure. The white solid was slurried with 100 ml. of dry tetrahydrofuran, and to this stirred mixture was added a solution of 50.06 g. (0.5 mole) of 2,4-pentanedione in 50 ml. of tetrahydrofuran. The sodium methylate dissolved, leaving a pale yellow, slightly murky suspension. To this was added 67.6 g. (0.5 mole) of phenyl isothiocyanate with rapid stirring at room temperature. A yellow solution formed immediately, then turned orange. After 45 minutes, tlc on silica gel in benzene or benzene/chloroform (1/1)

showed no more phenyl isothiocyanate at high R_f and a new, yellow spot at the origin. The tetrahydrofuran was evaporated and the residual yellow resin was treated with dilute hydrochloric acid, giving a copious, yellow precipitate. This was filtered, washed with water, and the moist solid was dissolved in 500 ml. of ethyl acetate. The aqueous layer was decanted, and the ethyl acetate solution was treated with Nuchar, dried over anhydrous magnesium sulfate and evaporated to 250 ml. Hexane (300 ml.) was added, and the resulting yellow solid was filtered, dried and weighed 68.1 g. Tlc of this material on silica gel in butyl acetate/toluene/chloroform (1/2/4) gave 2 spots at R_f 0.6 and R_f 0.7.

This product mixture was dissolved in 50 ml. of methanol, and 200 ml. of 1*N* sodium hydroxide solution was added. After gentle heating on the steam bath, the orange-brown solid was filtered and dried and weighed 28.4 g. A second crop separated for a total yield of 37.3 g. (0.13 mole, 52%) of bis (phenylthiocarbamyl)methane, $(C_6H_5NHCS)_2CH_2$, m.p. 156-157° (lit. m.p. 149°) (2); ir (potassium bromide): 3220 (N-H), 1120 (C=S) cm^{-1}; H^1 nmr (DMSO-d_6): δ (ppm) 4.53 (s, 1, CH_2), 7.15-8.05 (mult. 5, ArH) 13.4 (broad s, 1, NH).

Anal. Calcd. for $C_{15}H_{14}N_2S_2$: C, 62.9; H, 4.9; N, 9.8; S, 22.4. Found: C, 63.1; H, 5.1; N, 9.5; S, 22.5.

From the mother liquors, a total of 11.7 g. (0.06 mole, 12.2%) of acetylthioacetanilide separated and was filtered and dried, m.p. 73-75° (lit. m.p. 63.5-65°) (1); ir (potassium bromide): 3320 (N-H), 1635 (C=O), and major peaks at 1540, 1410, 1330, 1230, 1220, 793, 770, 710, 600 cm^{-1}; ^1H nmr (deuteriochloroform): δ (ppm) 2.0 (s, $CH_3C(OH)=O$ enol form), 2.4 (s, $CH_3C=O$ keto form) (combined enol and keto integral = 3; ratio enol/keto = 1/2); 4.1 (s, $C(=O)CH_2C=S$ keto form); 5.5 (s, $C(OH)=CHC=S$ enol form) (combined keto and enol integral = 2; ratio keto/enol = 2/1), 7.2-7.3 (mult, 5, ArH); 14.4 (s,1,NH); ms: m/e 286 P^+.

Anal. Calcd. for $C_{10}H_{11}NOS$: C, 62.1; H, 5.7; N, 7.2; S, 16.6. Found: C, 62.2; H, 5.9; N, 7.4; S, 16.4.

2,2-Diacetyl-*N*-ethylthioacetamide (**2**).

To a slurry of 27 g. (0.5 mole) of sodium methylate in 150 ml. of dry tetrahydrofuran was added a solution of 50 g. (0.5 mole) of 2,4-pentanedione in 50 ml. of tetrahydrofuran. The mixture was allowed to stir for 2 hours, then the solvent was removed, and the white solid was dried under vacuum. This was again slurried with 100 ml. of tetrahydrofuran, and 43.5 g. (0.5 mole) of ethyl isothiocyanate was added with stirring. After stirring overnight, a moist yellow-orange solid remained. This was filtered, washed with ethyl acetate and dried, affording 87.8 g. (0.47 mole, 93.7%) of the desired crude product. No distinct melting point could be obtained, since the rather unstable solid decomposed over a broad, variable range. Attempts to purify this material for elemental analysis led either to hydrolysis product **4** or back to the starting material, 2,4-pentanedione. The following analytical data were obtained on the crude sample: ir (potassium bromide): 3450 (enol O-H), 3210 (N-H), 3000, 2950, 2900 (C-H), 1620 (C=O), and major peaks at 1480-1380, 1350, 1290, 1230, 1150, 1045, 1025, 1000, 960, 910, 880, 820, 780, 680 cm^{-1}; ^1H nmr (pyridine-d_5): δ (ppm) 1.30 (t, CH_3CH_2 keto form), 1.62 (t, CH_3CH_2 enol form) (combined keto and enol integral = 3), 1.90 (s, $CH_3C(OH)$ enol form), 2.36 (s, $CH_3C=O$, keto form) (combined enol and keto integral = 3; (ratio enol/keto~1/2), 3.62 (q. CH_2CH_3 keto form), 4.0 (q, CH_2CH_3 enol form) (combined keto and enol integral = 2), 5.30 (s, 1, CHC=S exchangeable), 10.8 (broad s, 1, NH exchangeable); mass spectrum m/e: 187 P^+. The ms fragmentation pattern was similar to that for the deacetylated product 4.

2-Acetyl-*N*-ethylthioacetamide (**4**).

A 94.8 g. (0.52 mole) sample of 2,2-diacetyl-*N*-ethylthioacetamide was stirred into 200 ml. of water at room temperature, and the resulting syrupy mixture was stirred overnight. The aqueous layer had *p*H 8 and was neutralized to *p*H 7 with concentrated hydrochloric acid. The aqueous mixture was extracted twice with ethyl acetate, and the ethyl acetate layer was treated with Nuchar, dried over anhydrous magnesium sulfate and evaporated. A 44 g. (0.31 mole, 58%) yield of amber-colored oil remained; ir (flim): 3300 (N-H), 3050, 2970, 2930, 2870 (C-H), 1730 (C=O), and major peaks at 1540, 1450-1400, 1360, 1330, 1225, 1180, 1165, 1095, 795 cm^{-1}; ^1H nmr (deuteriochloroform): δ (ppm) 1.20, 1.26, (two overlapping t, 3, CH_3CH_2 keto and enol forms), 1.90 (s, $CH_3C(OH)$ enol form), 2.26 (s, $CH_3C=O$ keto form) (combined enol and keto integral = 3; ratio enol/keto = 1/8), 3.55 3.60 (two overlapping q, 2, CH_2CH_3 keto and enol forms), 3.91 (s, $C(=O)CH_2C=S$ keto form), 5.36 (s, $C(OH)=CHC=S$ enol form) (combined keto and enol integral = 2), 9.0 (broad s, 1, NH), 14.3 (s, 1, OH); mass spectrum m/e 145 P^+, and high intensities for 102 P-CH_3CO, 62 C_4H_6N, 44 C_2H_5NH, 43 CH_3CO.

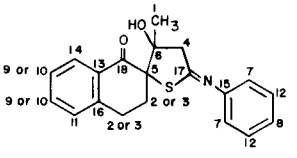
This material was of suitable quality to use in the subsequent condensation reactions. Samples for elemental analysis were distilled at 103°/0.05 mm, but distilled material was unnecessary for the remaining conversions.

Anal. Calcd. for $C_6H_{11}NOS$: C, 49.6; H, 7.6; N, 9.6. Found: C, 49.9; H, 8.1; N, 9.5.

Spiro[3,4-dihydro-1-(2*H*)naphthalenone-2,2′-(3′-hydroxy-3′-methyl-5′-phenyliminothiolane)] (**5**).

To a solution of 3.95 g. (2 x 10^{-2} mole) of 2-acetylthioacetanilide and 1.04 g. (2 x 10^{-2} mole) of sodium methylate in 30 ml. of dry methanol was added 4.52 g. (2 x 10^{-2} mole) of 2-bromo-3,4-dihydro-1(2*H*)naphthalenone. (3) The solution was heated to boiling on the steambath for 20 minutes and then cooled to room temperature. A precipitate settled, was filtered, washed with 30 ml. of methanol and dried, affording 4.56 g. of crude product. Tlc on silica gel in benzene/chloroform (1/1) or butyl acetate/toluene/chloroform (1/2/4) showed a spot at high R_f for residual 2-acetylthioacetanilide, a minor spot at lower R_f and the product spot at low R_f. The filtrate was evaporated and left only water-soluble residue.

The crude product was recrystallized from methanol/chloroform to give 2.0 g. (5.9 x 10^{-3} mole, 29.6%) of ivory needles, m.p. 183-184°. Tlc on silica gel in butyl acetate/toluene/chloroform (1/2/4) gave 1 spot at R_f 0.3; ir (potassium bromide): 3400-3200 (bonded O-H), 3070, 3025, 2980, 2930, (C-H), 1675 (C=O), and major peaks at 1640, 1593, 1485, 1450, 1400, 1375, 1354, 1300, 1230, 1220, 1207, 1140, 1095, 1075, 1046, 1030, 900, 840, 830, 820, 777, 770, 754, 735, 700, 648 cm^{-1}; ^1H nmr in DMSO-d_6/deuteriochloroform$_3$ (1/1): δ (ppm) 1.60 (s, 3, CH_3), 2.63-3.0 (mult., 4, CH_2CH_2), 3.08 (d, J = 8Hz, 1, thiolane gem CH), 4.02 (d, J = 8Hz, 1, thiolane gem CH), 4.72 (s, 1, OH exchangeable), 6.83-8.10 (mult., 9, ArH); ms: m/e 319 P-H_2O, and high intensities for 286 P-H_2O-HS, 160 $C_{10}H_{10}NO$, 77 C_6H_5; ^{13}C nmr: (off-resonance decoupled with correct multiplicities) showed 18 signals, which are assignable as indicated on the structure diagram.



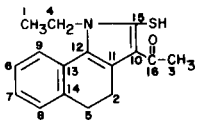
C atom	ppm	C atom	ppm
1	21.92	10	128.73
2	28.13	11	129.77
3	28.58	12	130.04
4	55.38	13	131.53
5	71.34	14	134.80
6	78.46	15	144.00
7	120.58	16	152.44
8	125.22	17	170.93
9	127.96	18	194.83

Anal. Calcd. for $C_{20}H_{19}NO_2S$: C, 71.2; H, 5.7; N, 4.2. Found: C, 71.3; H, 6.2; N, 4.5.

3-Acetyl-1-ethyl-2-mercapto-4,5-dihydrobenz[*g*]indole **7**.

To a solution of 14.5 g. (0.1 mole) of 2-acetyl-*N*-ethylthioacetamide and 5.2 g. (0.1 mole) of sodium methylate in 35 ml. of dry methanol was added 22.5 g. (0.1 mole) of 2-bromo-3,4-dihydro-1(2*H*)-naphthalenone. The dark solution was heated at reflux for 40 minutes. Tlc on silica gel in butyl acetate/toluene/chloroform (1/2/4) or nitromethane showed no more 2-acetyl-*N*-ethylthioacetamide, a spot corresponding to the starting dihydronaphthalenone and a new product spot at lower R_f. Solid product separated from the reaction mixture in several crops. These were filtered, washed with methanol and combined to give 8.88 g. (3.2 x 10^{-2} mole, 32%) of the benzindole product, m.p. 122-123°; ir (potassium bromide) 3070, 3040, 2998, 2978, 2940, 2880, 2840, 2800, (C-H), 1593 (C=O) and major peaks at 1540-1510, 1480, 1450, 1400, 1390, 1372, 1340, 1295, 1270, 1220, 1210, 1140, 1042, 1020, 1000, 960, 900, 820, 780, 770, 740, 696, 654, 638, 625 cm^{-1}; ^1H nmr ($CDCl_3$): δ (ppm) 1.34 (t, 3, CH_3CH_2), 2.38 (s, 3, CH_3CO), 2.60 (t, 2, $ArCH_2CH_2$ 2.82 (t, 2, $ArCH_2CH_2$), 3.29 (two overlapping q, 2, CH_2CH_3 geometric isomers), 7.10 - 7.37 (mult, 4, ArH), 9.0 (broad s, 1, SH exchangeable); mass spectrum m/e 271 P^+ and high intensities for 256 P-CH_3, 239 P-S, 238 P-SH, 228 P-CH_3CO, 43 CH_3CO. ^{13}C nmr (off-resonance decoupled with correct multiplicities) showed 16 signals, which can be assigned as indicated on the structure diagram. Assignments of the non-protonated carbons 11, 12, 13, 14 are based only on chemical shifts and could be interchanged.

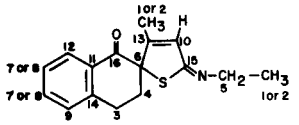
Anal. Calcd. for $C_{16}H_{17}NOS$: C, 70.8; H, 6.3; N, 5.2; S, 11.8. Found: C, 70.7; H, 6.9; N, 5.2; S, 11.9.



C atom	ppm	C atom	ppm
1	14.89	9	127.94
2	24.38	10	112.59
3	30.50	11	122.56
4	42.42	12	135.64
5	30.79	13	133.61
6	126.16	14	132.79
7	126.31	15	165.43
8	126.65	16	193.59

Spiro[3,4-dihydro-1(2*H*)naphthalenone-2,2′-(5′-ethylimino-3′-methyl-3′-thiolene)] (**6**).

The mother liquors from a repeat of the previous experiment (7.8 x 10^{-2} mole starting materials) were evaporated, dissolved in benzene and chromatographed on Baker silica gel, using cyclohexane-benzene eluents. The benzene fractions yielded 0.33 g. (1.2 x 10^{-3} mole, 1.5%) of ivory solid, m.p. 120-121°, which was characterized as the spiro thiolene, isomeric with the main benzindole product; ir (potassium bromide): 3060, 2975, 2940, 2860 (C-H), 1675 (C=O) and major peaks at 1620, 1595, 1450, 1430, 1375, 1340, 1295, 1225, 1178, 1165, 1155, 1120, 1030, 1020, 903, 860, 850, 830, 780, 765, 740, 650 cm^{-1}; ^1H nmr (deuteriochloroform): δ (ppm) 1.25 (t, 3, CH_3CH_2), 2.02 (d, 3, CH_3C=), 2.28-3.17 (mult., 4, CH_2CH_2), 3.25 (q, 2, CH_2CH_3), 6.25 (q, 1, =CH-), 7.15-7.58 and 7.98-8.17 (mult., 4, ArH); ms: m/e 271 P^+ and high intensities for 256 P-CH_3, 242 P-C_2H_5, 238 P-SH; ^{13}C nmr (off-resonance decoupled with correct multiplicities) showed 16 signals assigned as indicated in the structure diagram.



C atom	ppm	C atom	ppm
1	15.68	9	129.11
2	15.74	10	131.03
3	28.04	11	131.43
4	34.06	12	134.25
5	54.24	13	142.93
6	70.50	14	157.78
7	127.37	15	165.33
8	128.78	16	191.00

Anal. Calcd. for $C_{16}H_{17}NOS$: C, 70.8; H, 6.3; N, 5.2. Found: C, 70.5; H, 6.3; N, 5.3.

3-Acetyl-1-ethyl-2-mercaptobenz[*g*]indole (**8**).

A solution of 2.45 g. (10^{-2} mole) of *o*-chloranil and 2.54 g. (9.37 x 10^{-3} mole) of 3-acetyl-1-ethyl-2-mercapto-4,5-dihydrobenz[*g*]indole in 25 ml. of benzene was heated at reflux for 20 hours. Tlc on silica gel in butyl acetate/toluene/chloroform (1/2/4) showed no more of the starting materials, a new, mobile product spot and residue at the origin. The tetrachlorohydroquinone which had separated was filtered and dried and weighed 1.72 g. (7 x 10^{-3} mole). The filtrate yielded the desired product, contaminated by tetrachlorohydroquinone. Recrystallization from methanol afforded 2.1 g. (7.8 x 10^{-3} mole, 83%) of the mercaptobenzindole, m.p. 119-120°; ir (potassium bromide): 2980, 2930, 2880, (C-H), 1600 (C=O) and major peaks at 1550, 1530, 1475, 1450, 1420, 1390, 1380, 1360, 1300, 1277, 1190, 1170, 1158, 1150, 1020, 895, 807, 788, 758, 700, 673, cm^{-1}; ^1H nmr (deuteriochloroform): 1.34 (t, 3, CH_3CH_2), 2.21 (s, 3, CH_3CO), 3.33 (q, 2, CH_2CH_3), 7.2-8.0 (mult., 6, ArH), 8.8 (broad s, 1, SH exchangeable); ms: m/e 269 P^+ with high intensities for 254 P-CH_3, 252 P-H_2O, 236 P-CH_3CO, 43 CH_3CO.

Anal. Calcd. for $C_{16}H_{15}NOS$: C, 71.3; H, 5.6; N, 5.2; S, 11.9. Found: C, 71.0; H, 5.6; N, 5.3; S, 12.3.

Acknowledgment.

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REFERENCES AND NOTES

(1) D. E. Worrall, *J. Am. Chem. Soc.*, **42**, 1055 (1920).

(2) A. Reissert and A. More, *Ber.*, **39**, 3298 (1906).

(3) 2-Bromotetralone was prepared by a modification of the procedure described in A. L. Wilds and J. A. Johnson, Jr., *J. Am. Chem. Soc.*, **68**, 86 (1946); A. L. Wilds, *ibid.*, **64**, 1421 (1942).