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Synthesis of Hindered Hydrazones and Their Reaction with Thionyl Chloride

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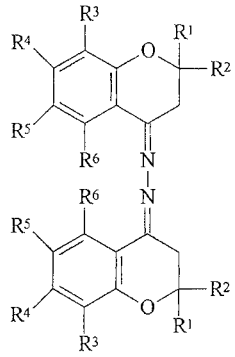
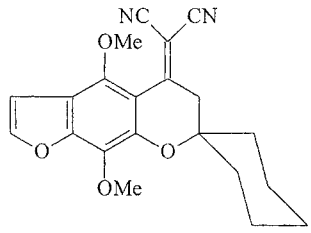
ABSTRACT: *Hydrazones* **12a–c** *and ketazines* **13a–c** *were prepared by the reaction of ketones* **11a–c** *with hydrazine hydrate depending on the temperature and the reaction time. Some ketone (aryl)hydrazone derivatives* **14a,c,e** *reacted with thionyl chloride to afford the chlorothiadiazoline derivatives* **15a–c**. *Surprisingly, the chlorine atom in the latter compounds was found to undergo smooth nucleophilic substitution, and by boiling these compounds in absolute ethanol gave the corresponding ethoxythiadiazoline derivatives* **16a–c**. *The structure of the ethoxythiadiazoline* **16b** *was confirmed by single crystal X-ray determination.* © 2003 Wiley Periodicals, Inc. Heteroatom Chem 14:223–228, 2003; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10125

INTRODUCTION

Harradence et al. [1] have reported that when an ethanolic solution of 4-chromanone was refluxed with an aqueous solution of hydrazine sulfate and sodium acetate, the ketazine **1a** was formed. In a similar reaction of the corresponding 4-chromanone derivatives with hydrazine hydrate, the ketazine derivatives **1b–d** were obtained as hydrates, which were converted into the anhydrous ketazines on boiling with acetic acid [2]. Recently, El-Desoky [3] reported that the ketazine **1e** could not be formed directly from the reaction of the corresponding 4-chromanone derivative with hydrazine hydrate, but could be formed from the reaction of ylidene malononitrile **2** with hydrazine hydrate.



1a-e



2

a, $R^1 = R^2 = R^3 = R^4 = R^5 = R^6 = H$

b, $R^1 = CH_3$, $R^2 = R^3 = R^5 = R^6 = H$, $R^4 = OCH_3$

c, $R^1 = CH_3$, $R^2 = H$, $R^4R^5 = -CH_2CH_2O-$, $R^3 = R^6 = OCH_3$

d, $R^1 = CH_3$, $R^2 = H$, $R^4R^5 = -CH{=}CHO-$, $R^3 = R^6 = OCH_3$

e, $R^1 - R^2 = (CH_2)_5$, $R^4R^5 = -CH{=}CHO-$, $R^3 = R^6 = OCH_3$

Also, it has been reported [4–7] that the reactions of thionyl chloride with some types of ketone (aryl)hydrazones **3–6** gave the 1,2,3-thiadiazol-*S*-oxides **7, 8** or the 1,2,3-thiadiazole derivatives **9, 10**, respectively (Scheme 1).

These results prompted us to study such reactions with some hindered [8] ketones, namely 3-ethyl-1,2,3,4-tetrahydro-3-methylnaphthalen-1-one

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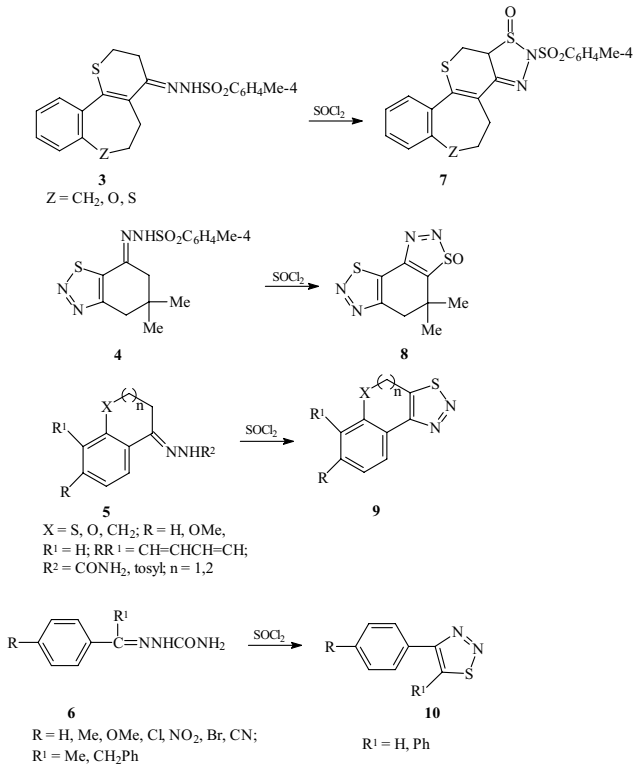
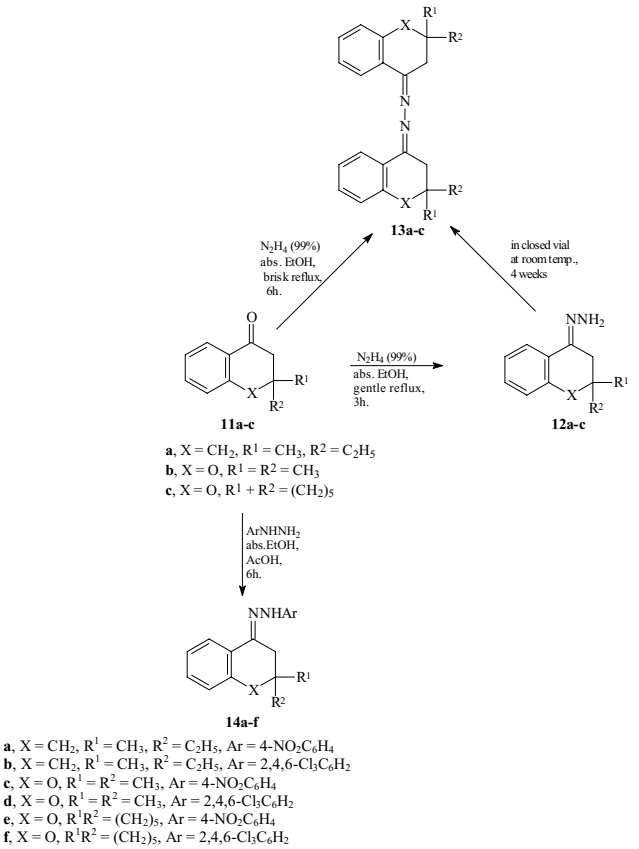


SCHEME 1



SCHEME 2

(**11a**) [9], 3,3-dimethylchroman-4-one (**11b**) [10], and spirochroman (2,1′)cyclohexane-4-one (**11c**) [11].

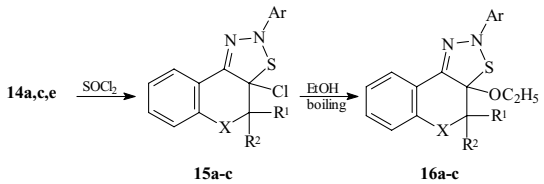
RESULTS AND DISCUSSION

When the ketones **11a–c** were treated with hydrazine hydrate (99%) in absolute ethanol under gentle reflux for 3 h they gave the corresponding hydrazones **12a–c** in moderate yields (Scheme 2). The structures of the hydrazones **12a–c** were confirmed by spectral data and microanalytical data. The IR spectra showed absorption frequencies at 3325–3285 cm^{-1} (ν_{NH2}) and 1605–1595 cm^{-1} ($\nu_{C=N}$), the ^1H NMR spectra showed the signal at δ 5.34–5.37 ppm (br s, 2H, NH_2, exchangeable with D_2O), and the MS spectra showed the molecular ion peak as the base peak (M^+, 100%).

It was noticed that when the hydrazone derivatives **12a–c** were stored in a closed vial for four weeks at room temperature, they were converted into the corresponding ketazines **13a–c**. However, the latter could be obtained in good yields from the reaction of the ketone and hydrazine hydrate in absolute ethanol under brisk reflux for 6 h (Scheme 2). The spectral data and microanalytical data verified the structures of the ketazine derivatives. The MS spectra showed the molecular ion peak as the parent peak.

Five new ketone arylhydrazone derivatives **14a,b,d–f** were prepared by the reaction of the ketones **11a–c** with arylhydrazines in ethanol containing acetic acid. The preparation of the hydrazone **14c** was reported previously by Auwers and Mauss [12]. The ^1H NMR spectra of **14a–f** showed the NH signals at δ 10.01–10.38, which are exchangeable with D_2O.

When compounds **14a,c,e** were treated with thionyl chloride at 20°C, they afforded the corresponding chlorothiadiazolines **15a–c**, respectively (Scheme 3).



SCHEME 3

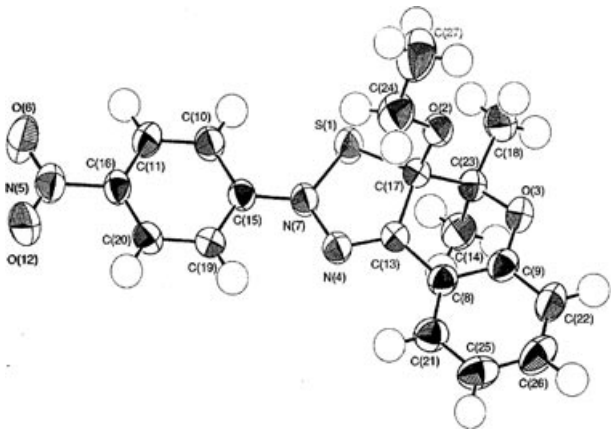


FIGURE 1 Single crystal X-ray structure of **16b**.

The structures of **15a–c** were established by the spectral data as well as the microanalytical data. The ^{1}H NMR spectra indicated the absence of the NH and the methylene protons. The ^{1}H NMR spectrum of compound **15a** showed the presence of the two diasteriomers (see Experimental Section). The MS spectra of **15a–c** showed the ion $M^+ - Cl$ as the base peak (100%). Surprisingly, when **15b** was crystallized from ethanol it gave the ethoxythiadiazoline **16b**. This means that the chlorine atom can be easily replaced by a nucleophile. So, when **15a–c** were boiled in ethanol for $\frac{1}{2}$ h they gave the ethoxythiadiazolines **16a–c** (Scheme 3). The structures of the latter compounds were verified by microanalytical data and spectral data. By X-ray analysis of a single crystal, the *S* configuration of **16b** (Fig. 1, Table 1) was established. The ^{1}H NMR spectrum of the compound **16a** showed the presence of the two diasteriomers (see Experimental Section). To our knowledge, these types of chlorothiadiazoline derivatives **15a–c** and consequently the ethoxythiadiazoline derivatives **16a–c** have not been reported in the literature.

EXPERIMENTAL

The melting points are uncorrected. Microanalyses were performed by the Central Services Laboratory, National Research Centre, Cairo. ^{1}H NMR spectra were taken in a Varian Gemini 200 MHz spectrometer with $CDCl_3$ and DMSO-d_6 as solvents (Cairo University, Faculty of Science). EI (70 eV). Mass spectra were recorded on a G. C. MSQP 1000 Ex Shmadzu spectrometer, National Research Centre. IR spectra were obtained with PU 9712 infrared spectrophotometer for neat samples (for liquids) or KBr wafers (for solid); National Research Centre, Dokki, Cairo).

TABLE 1 Crystal Data, Bond Lengths, and Bond and Torsion Angles of **16b**

Crystal data	
Crystal system	Triclinic
Space group	P1
a (Å)	7.3610 (5)
b (Å)	11.3212 (6)
c (Å)	13.1357 (7)
α (°)	103.445
β (°)	105.962
γ (°)	108.238
V (Å^3)	936.79 (9)
Z	2
D_X(g cm^{-3})	1.366
R	0.048
wR	0.057
Bond length (Å)	
O2—C17	1.4072 (6)
N4—N7	1.3615 (6)
N4—C13	1.2877 (6)
N5—O6	1.2255 (6)
N5—O12	1.2226 (6)
N5—C16	1.3833 (6)
Bond and Torsion angles (°)	
N7—N4—C13	111.11 (4)
N4—C13—C8	125.11 (5)
N4—C13—C17	118.77 (5)
O2—C17—C13	111.80 (5)
N4—N7—C15	121.23 (4)
N5—C16—C11	119.37 (6)
N5—C16—C20	119.27 (5)
N7—N4—C13—C8	−176.44 (8)
C13—N4—N7—C15	−168.47 (7)
N7—N4—C13—C7	6.06 (5)

The single crystal for the X-ray diffraction analysis of **16b** was obtained by slow evaporation of the corresponding ethanol solution. The X-ray determination was performed by the Central Services Laboratory, National Research Centre, Cairo.

Preparation of Hydrazones **12a–c**

A solution of the ketone **11a–c** (0.01 mol) and hydrazine hydrate 99% (0.01 mol) in absolute ethanol (Merck) was heated under gentle reflux for 3 h. Evaporation of the solvent under reduced pressure gave the hydrazones **12a–c**.

*3-Ethyl-3-methyl-1,2,3,4-tetrahydronaphthalen-1-one Hydrazone (***12a***).* Colorless oil (1.50 g, 75%) purified by column chromatography (silica gel, Merck 60, particle size 0.06–0.20 mm, ethyl acetate/petroleum ether 40–60°C 1:10). Anal calcd for $C_{13}H_{18}N_2$ (202.29): C, 77.18%; H, 8.96; N, 13.84%. Found: C, 77.48; H, 8.79; N, 13.78%. IR (neat): ν_{NH2} 3320, 3285; $\nu_{C=N}$ 1600 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.89

(t, $J = 8.00$ Hz, 3H, CH_3CH_2), 0.98 (s, 3H, CH_3), 1.22 (q, $J = 8.00$ Hz, 2H, CH_2CH_3), 2.55 (d, $J = 18.00$ Hz, 1H, 4-CH_aH$_b$), 2.63 (d, $J = 18.00$ Hz, 1H, 4-CH$_a$$H_b$), 3.45 (s, 2H, CH_2), 5.34 (br s, 2H, NH_2, exchangeable with D_2O), 7.28–7.42 (m, 3H, ArH), 8.23 ppm (d, $J = 8.00$ Hz, 1H, ArH). MS (EI): *m/z* (%) 202 (M, 100), 187 (8), 173 (37), 156 (30), 143 (13), 128 (16), 116 (13), 91 (60).

*2,2-Dimethylchroman-4-one Hydrazone (***12b***).* Colorless oil (1.10 g, 60%), purified by column chromatography (silica gel, Merck 60, particle size 0.06–0.20 mm, ethyl acetate/petroleum ether 40–60°C 1:10). Anal calcd for $C_{11}H_{14}N_2O$ (190.24): C, 69.44; H, 7.41; N, 14.72%. Found: C, 69.14; H, 7.39; N, 14.65%. IR (neat): ν_{NH2} 3310, 3275; $\nu_{C=N}$ 1595 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.40 (s, 6H, 2 CH_3), 2.70 (s, 2H, CH_2), 5.37 (br s, 2H, NH_2, exchangeable with D_2O), 7.26–7.31 (m, 3H, ArH), 8.14 ppm (d, $J = 8.05$ Hz, 1H, ArH). MS (EI): *m/z* (%) 190 (M, 91), 176 (37), 161 (100), 121 (52), 92 (35).

*Spirochroman(2,1′)cyclohexane-4-one Hydrazone (***12c***).* Colorless crystals (1.80 g, 80%), crystallized from *n*-hexane; mp 73–75°C. Anal calcd for $C_{14}H_{18}N_2O$ (230.30): C, 73.01; H, 7.87; N, 12.16%. Found: C, 72.91; H, 7.80; N, 12.01%. IR (KBr): ν_{NH2} 3295, 3215; $\nu_{C=N}$ 1605 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.16–1.90 (m, 10H, $(CH_2)_5$), 2.70 (s, 2H, CH_2), 5.35 (br s, 2H, NH_2, exchangeable with D_2O), 7.26–7.32 (m, 3H, ArH), 8.10 ppm (d, $J = 8.05$ Hz, 1H, ArH). MS (EI): *m/z* (%) 230 (M, 66), 214 (100), 199 (13), 187 (30), 172 (44), 156 (17), 135 (15), 120 (20), 91 (19).

Preparation of Ketazines **13a–c**

A solution of the ketone **11a–c** (0.01 mol) and hydrazine hydrate 99% (0.01 mol) in absolute ethanol (Merck) was heated under brisk reflux for 6 h. Evaporation of the solvent and crystallization of the residue from ethanol afforded the pure ketazines **13a–c**.

*3-Ethyl-3-methyl-1,2,3,4-tetrahydronaphthalen-1-azine (***13a***).* Dark yellow crystals (3.1 g, 85%), mp 117–119°C. Anal calcd for $C_{26}H_{32}N_2$ (372.54): C, 83.82; H, 8.66; N, 7.52%. Found: C, 83.72; H, 8.61; N, 7.39%. IR (KBr): $\nu_{C=N}$ 1605 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.87 (t, $J = 8.00$ Hz, 6H, 2 CH_3CH_2), 0.98 (s, 6H, 2 CH_3), 1.20 (q, $J = 8.00$ Hz, 4H, 2 CH_2CH_3), 2.54 [d, $J = 18.00$ Hz, 2H, 2 (4- & 4′-CH_aH$_b$)], 2.63 [d, $J = 18.00$ Hz, 2H, 2 (4- & 4′-CH$_a$$H_b$)], 3.44 (s, 4H, 2 CH_2), 7.28–7.44 (m, 6H, ArH), 8.23 ppm (d, $J = 8.00$ Hz, 2H, ArH). MS (EI): *m/z* (%) 273 (M + H, 88), 372 (M, 78), 357 (92), 344 (84), 343 (69), 329 (18), 315 (18), 301 (32), 287 (15), 186 (62), 158 (100), 143 (91), 128 (85), 115 (86).

*2,2-Dimethylchroman-4-azine (***13b***).* Dark yellow crystals (2.60 g, 76%), mp 191–193°C. Anal calcd for $C_{22}H_{24}N_2O_2$ (348.43): C, 75.83; H, 6.94; N, 8.04%. Found: C, 75.55; H, 6.82; N, 7.85%. IR (KBr): $\nu_{C=N}$ 1600 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.40 (s, 12H, 4 CH_3), 3.00 (s, 4H, 2 CH_2), 6.88–7.01 (m, 4H, ArH), 7.26–7.35 (m, 2H, ArH), 8.16 ppm (d, $J = 8.18$ Hz, 2H, ArH). MS (EI): *m/z* (%) 348 (M, 41), 333 (100), 173 (24), 160 (29), 120 (11), 91 (19).

*Spirochroman(2,1′)cyclohexane-4-azine (***13c***).* Dark yellow crystals (3.3 g, 80%), mp 174–177°C. Anal calcd for $C_{28}H_{32}N_2O_2$ (428.56): C, 78.46; H, 7.52; N, 6.53%. Found: C, 78.28; H, 7.48; N, 6.51%. IR (KBr): $\nu_{C=N}$ 1600 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.24–1.94 (m, 20H, 2 $(CH_2)_5$), 2.95 (s, 4H, 2 CH_2), 6.91–7.00 (m, 4H, ArH), 7.26–7.36 (m, 2H, ArH), 8.13 ppm (d, $J = 8.18$ Hz, 2H, ArH). MS (EI): *m/z* (%) 428 (M, 74), 413 (60), 213 (100), 199 (40), 172 (60), 156 (17), 120 (25), 91 (30).

Preparation of Arylhydrazones **14a–f**

A solution of the ketones **11a–c** (0.01 mol) and the arylhydrazine (0.01 mol) in ethanol (100 ml) containing glacial acetic acid (1 ml) was boiled under reflux for 6 h. After cooling, the solid was collected and crystallized from ethanol to give the hydrazones **14a–f**.

*3-Ethyl-3-methyl-1,2,3,4-tetrahydronaphthalen-1-one (4-Nitrophenyl)hydrazone (***14a***).* Yellowish-brown crystals (2.00 g, 62.5%), mp 168–170°C. Anal calcd for $C_{19}H_{21}N_3O_2$ (323.38): C, 70.56; H, 6.54; N, 12.99%. Found: C, 70.32; H, 6.48; N, 12.69%. IR (KBr): ν_{NH} 3345; $\nu_{C=N}$ 1608 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.83 (t, $J = 8.00$ Hz, 3H, CH_3CH_2), 0.92 (s, 3H, CH_3), 1.33 (q, $J = 8.00$ Hz, 2H, CH_2CH_3), 2.53 (d, $J = 18.00$ Hz, 1H, 4-CH_aH$_b$), 2.65 (d, $J = 18.00$ Hz, 1H, 4-CH$_a$$H_b$), 3.37 (s, 2H, CH_2), 7.17–7.41 (m, 6H, ArH), 8.13 ppm (d, $J = 8.00$ Hz, 2H, ArH), 10.30 (s, H, NH, exchangeable with D_2O). MS (EI): *m/z* (%) 323 (M, 100), 299 (4), 170 (5), 156 (15), 130 (15), 116 (21), 91 (8).

*3-Ethyl-3-methyl-1,2,3,4-tetrahydronaphthalen-1-one (2,4,6-Trichlorophenyl)hydrazone (***14b***).* The compound (purified by column chromatography on silica gel, Merck 60, particle size 0.06–0.20 mm, ether/petroleum ether 40–60°C 1:10) was isolated (2.20 g, 60%) as a brownish oil. Anal calcd for $C_{19}H_{19}Cl_3N_2$ (381.73): C, 59.77; H, 5.01; N, 7.34%.

Found: C, 59.38; H, 4.86; N, 7.20%. IR (neat): ν_{NH} 3342; $\nu_{C=N}$ 1598 cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.82 (t, $J = 8.00$ Hz, 3H, CH_3CH_2), 0.98 (s, 3H, CH_3), 1.41 (q, $J = 8.00$ Hz, 2H, CH_2CH_3), 2.55 (d, $J = 18.00$ Hz, 1H, 4-CH_aH$_b$), 2.59 (d, $J = 18.00$ Hz, 1H, 4-CH$_a$$H_b$), 3.40 (s, 2H, CH_2), 7.10–7.43 (m, 5H, ArH), 8.13 (d, $J = 8.00$ Hz, 1H, ArH), 10.08 ppm (s, H, NH, exchangeable with D_2O). MS (EI): *m/z* (%) 386 (M, 3 Cl^{37}, 25), 384 (M, 2 Cl^{37} Cl^{35}, 80), 382 (M, Cl^{37} 2 Cl^{35}, 90), 380 (M, 3 Cl^{35}, 98), 371 (4), 369 (12), 367 (28), 365 (40), 357 (5), 355 (23), 353 (34), 351 (49), 346 (98), 315 (44), 274 (26), 208 (40), 195 (97), 187 (25), 170 (97), 167 (95), 159 (23), 143 (96), 131 (40), 128 (100), 110 (86), 89 (47).

*2,2-Dimethylchroman-4-one (4-Nitrophenyl)hydrazone (***14c***).* Dark yellow crystals (2.69 g, 85%), mp 192–194°C (literature [11] 193–194°C). Anal calcd for $C_{17}H_{17}N_3O_3$ (311.33): C, 65.57; H, 5.50; N, 13.49%. Found: C, 65.35; H, 5.40; N, 13.28%. IR (KBr): ν_{NH} 3355; $\nu_{C=N}$ 1616 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.45 (s, 6H, 2 CH_3), 2.72 (s, 2H, CH_2), 6.98–7.43 (m, 6H, ArH), 8.09 (d, $J = 8.01$ Hz, 2H, ArH) 10.12 ppm (s, 1H, NH, exchangeable with D_2O). MS (EI): *m/z* (%) 311 (M, 80), 296 (100), 281 (60), 235 (40), 159 (28), 121 (52), 91 (35).

*2,2-Dimethylchroman-4-one (2,4,6-Trichlorophenyl)hydrazone (***14d***).* Yellowish-green crystals (2.90 g, 83%), mp 138–140°C. Anal calcd for $C_{17}H_{15}Cl_3N_2O$ (369.68): C, 55.22; H, 4.09; N, 7.57%. Found: C, 55.01; H, 3.98; N, 7.52%. IR (KBr): ν_{NH} 3355; $\nu_{C=N}$ 1616 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.46 (s, 6H, 2 CH_3), 2.72 (s, 2H, CH_2), 6.84–6.96 (m, 3H, ArH), 7.19–7.34 (m, 2H, ArH), 7.98 (d, $J = 8.01$ Hz, 1H, ArH) 10.01 ppm (s, 1H, NH, exchangeable with D_2O). MS (EI): *m/z* (%) 374 (M, 3 Cl^{37}, 4), 372 (M, 2 Cl^{37} Cl^{35}, 31), 370 (M, Cl^{37} 2 Cl^{35}, 98), 368 (M, 3 Cl^{35}, 100), 357 (7), 355 (28), 353 (28), 333 (25), 194 (10), 174 (11), 159 (12).

*Spirochroman(2,1′)cyclohexane-4-one (4-Nitrophenyl)hydrazone (***14e***).* Yellowish-brown crystals (2.80 g, 80%), mp 245–248°C. Anal calcd for $C_{20}H_{21}N_3O_3$ (351.39): C, 68.35; H, 6.02; N, 11.96%. Found: C, 68.10; H, 5.92; N, 11.75%. IR (KBr): ν_{NH} 3322; $\nu_{C=N}$ 1598 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.33–1.77 (m, 10H, $(CH_2)_5$), 2.62 (s, 2H, CH_2), 6.90–7.03 (m, 3H, ArH), 7.19–7.27 (m, 3H, ArH), 8.20 (d, $J = 8.00$ Hz, 2H, ArH), 10.38 ppm (br s, 1H, NH, exchangeable with D_2O). MS (EI): *m/z* (%) 351 (M, 100), 335 (24), 326 (11), 306 (15), 284 (13), 277 (17), 260 (11), 134 (15), 115 (25), 91 (9).

*Spirochroman(2,1′)cyclohexane-4-one (2,4,6-Trichlorophenyl)hydrazone (***14f***).* The compound (purified by column chromatography on silica gel, Merck 60, particle size 0.06–0.20 mm, ether/petroleum ether 40–60°C 1:10) was isolated (2.80 g, 76%) as brownish oil. Anal calcd for $C_{20}H_{19}Cl_3N_2O$ (409.74): C, 58.62; H, 4.67; N, 6.83%. Found: C, 58.35; H, 4.60; N, 6.79%. IR (neat): ν_{NH} 3315; $\nu_{C=N}$ 1600 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.32–1.77 (m, 10H, $(CH_2)_5$), 2.68 (s, 2H, CH_2), 6.91–7.02 (m, 3H, ArH), 7.19–7.35 (m, 2H, ArH), 8.10 (d, $J = 8.00$ Hz, 1H, ArH), 10.03 ppm (s, 1H, NH, exchangeable with D_2O). MS (EI): *m/z* (%) 414 (M, 3 Cl^{37}, 3), 412 (M, 2 Cl^{37} Cl^{35}, 14), 410 (M, Cl^{37} 2 Cl^{35}, 30), 408 (M, 3 Cl^{35}, 38), 216 (62), 190 (36), 185 (38), 179 (16), 173 (82), 159 (20), 145 (15), 131 (21), 121 (100), 91 (35).

Preparation of Chlorothiadiazolines **15a–c**

Hydrazone **14** (0.01 mol) was added portionwise to thionyl chloride (20 ml) with stirring. The mixture was stirred at room temperature for 10 h. The excess of thionyl chloride was removed under reduced pressure and recrystallization from ethyl acetate afforded the corrresponding chlorothiadiazolines **15a–c**.

(3aRS, 4RS) 3a-Chloro-4-ethyl-4-methyl-2-(4-nitrophenyl)-3a,4,5,9b-tetrahydronaphtho[1,2-d]-$\Delta^{1,9b}$*-[1,2,3]thiadiazoline (***15a***).* Yellow crystalline powder (3.50 g, 91%), mp 272–274°C. Anal calcd for $C_{19}H_{18}ClN_3O_2S$ (387.86): C, 58.83; H, 4.67; N, 10.83; S, 8.26%. Found: C, 58.74; H, 4.55; N, 10.62; S, 8.16%. IR (KBr): $\nu_{C=N}$ 1594 cm^{-1}. ^1H NMR (DMSO-d_6): δ 0.98 (t, $J = 8.00$ Hz, 3H, CH_3CH_2), 1.00 (t, $J = 8.00$ Hz, 3H, CH_3CH_2), 1.02 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.62–1.78 (m, 2H, CH_2CH_3), 1.81–2.00 (m, 2H, CH_2CH_3), 2.97 (d, $J = 18.00$ Hz, 1H, CH_aH$_b$), 3.00 (d, $J = 18.00$ Hz, 1H, CH_aH$_b$), 3.22 (d, $J = 18.00$ Hz, 1H, 5-CH$_a$$H_b$), 3.28 (d, $J = 18.00$ Hz, 1H, 5-CH$_a$$H_b$), 7.12–7.20 (m, 3H, ArH), 7.25–7.31 (m, 4H, ArH), 7.42–7.50 (m, 3H, ArH), 7.55–7.61 (m, 4H, ArH), 8.00 (d, $J = 8.00$ Hz, 1H, ArH), 8.21 (d, $J = 8.00$ Hz, 1H, ArH). MS (EI): *m/z* (%) 389 (M, Cl^{37}, 0.22), 387 (M, Cl^{35}, 0.62), 352 ($M^+ - Cl$, 100), 337 (50), 330 (35), 323 (60), 306 (10), 294 (4), 170 (5), 156 (15), 130 (20), 91 (40).

(3aRS) 3a-Chloro-4,4-dimethyl-2-(4-nitrophenyl)-chromane[4,3-d]-$\Delta^{1,9b}$*-[1,2,3]thiadiazoline (***15b***).* Yellow crystalline powder (2.20 g, 60%), mp 247–248°C. Anal calcd for $C_{17}H_{14}ClN_3O_3S$ (375.81): C, 54.32; H, 3.75; N, 11.18; S, 8.53%. Found: C, 54.01; H, 3.68; N, 10.98; S, 8.46%. IR (KBr): $\nu_{C=N}$ 1605 cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.43 (s, 6H, 2 CH_3), 6.97–7.15 (m, 4H, ArH), 7.48–7.55 (m, 3H, ArH),

8.25 (d, $J = 8.00$ Hz, 1H, ArH). MS (EI): *m/z* (%) 377 (M, Cl^{37}, 0.21), 375 (M, Cl^{35}, 0.64), 340 (100), 325 (30), 310 (25), 308 (8), 264 (65), 194 (20), 174 (11), 159 (15), 89 (70).

*(3aRS) 3a-Chloro-2-(4-nitrophenyl)spirochromane(4,1′)cyclohexane[4,3-d]-$\Delta^{1,9b}$-[1,2,3]thiadiazoline (***15c***).* Yellow crystalline powder (3.40 g, 83%), mp 273–275°C. Anal calcd for $C_{20}H_{18}ClN_3O_3S$ (415.87): C, 57.75; H, 4.36; N, 10.10; S, 7.70%. Found: C, 57.55; H, 4.33; N, 10.00; S, 7.40%. IR (KBr): $\nu_{C=N}$ 1614 cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.19–2.22 (m, 10H, $(CH_2)_5$), 7.18–7.21 (m, 4H, ArH), 7.59–7.69 (m, 3H, ArH), 8.02 (d, $J = 8.00$ Hz, 1H, ArH). MS (EI): *m/z* (%) 417 (M, Cl^{37}, 0.11), 415 (M, Cl^{35}, 0.32), 380 (100), 358 (40), 344 (10), 326 (10), 306 (15), 284 (14), 277 (18), 260 (10), 213 (9), 115 (25), 91 (50).

Preparation of Ethoxythiadiazolines **16a–c**

Boiling of chlorothiadiazolines **15a–c** (0.01 mol) in 100 ml absolute ethanol was carried out for 1/2 h. The solvent was evaporated and crystallization of the residue from ethanol afforded the ethoxythiadiazolines **16a–c**.

*(3aRS, 4RS)-3a-Ethoxy-4-ethyl-4-methyl-2-(4-nitrophenyl)-3a,4,5,9b-tetrahydronaphtho[1,2-d]-$\Delta^{1,9b}$-[1,2,3]thiadiazoline (***16a***).* Red crystals (2.7 g, 70%), mp 115–117°C. Anal calcd for $C_{21}H_{23}N_3O_3S$ (397.7): C, 63.45; H, 5.87; N, 10.57; S, 8.06%. Found: C, 63.15; H, 5.72; N, 10.39; S, 7.89%. IR (KBr): $\nu_{C=N}$ 1600 cm^{-1}. ^1H NMR (DMSO-d_6): δ 0.99 (t, $J = 8.00$ Hz, 3H, CH_3CH_2), 1.00 (t, $J = 8.00$ Hz, 3H, CH_3CH_2), 1.02 (s, 3H, CH_3), 1.21 (s, 3H, CH_3), 1.30 (t, $J = 8.00$ Hz, 3H, CH_3CH_2O), 1.42 (t, $J = 8.00$ Hz, 3H, CH_3CH_2O), 1.61–1.79 (m, 2H, CH_2CH_3), 1.81–2.05 (m, 2H, CH_2CH_3), 2.40 (q, $J = 8.00$ Hz, 2H, CH_3CH_2O), 2.66 (q, $J = 8.00$ Hz, 2H, CH_3CH_2O), 2.98 (d, $J = 18.00$ Hz, 1H, 5-CH_aH_b), 3.02 (d, $J = 18.00$ Hz, 1H, 5-CH_aH_b), 3.22 (d, $J = 18.00$ Hz, 1H, CH_aH_b), 3.28 (d, $J = 18.00$ Hz, 1H, CH_aH_b), 6.99–7.21 (m, 3H, ArH), 7.25–7.31 (m, 4H, ArH), 7.42–7.50 (m, 3H, ArH), 7.55–7.63 (m, 4H, ArH), 8.10 (d, $J = 8.00$ Hz, 1H, ArH), 8.21 (d, $J = 8.00$ Hz, 1H, ArH). MS (EI): *m/z* (%) 397 (M, 35), 368 (21), 352 (15), 323 (20), 294 (10), 170 (15), 130 (35), 91 (100).

*(3aRS) 3a-Ethoxy-4,4-dimethyl-2-(4-nitrophenyl)chromane[4,3-d]-$\Delta^{1,9b}$-[1,2,3]thiadiazoline (***16b***).* Red crystals (3.0 g, 80%), mp 135–137°C. Anal calcd for $C_{19}H_{19}N_3O_4S$ (385.42): C, 59.20; H, 4.96; N, 10.90; S, 8.31%. Found: C, 58.91; H, 4.91; N, 10.81; S, 8.21%. IR (KBr): $\nu_{C=N}$ 1587 cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.08 (t, $J = 8.00$ Hz, 3H, CH_3CH_2O), 1.56 (s, 3H, CH_3), 1.68 (s, 3H, CH_3), 3.02 (q, $J = 8.00$ Hz, 2H, CH_3CH_2O), 7.02–7.08 (m, 3H, ArH), 7.27–7.39 (m, 4H, ArH), 7.93 (d, $J = 8.00$ Hz, 1H, ArH). MS (EI): *m/z* (%) 385 (M, 56), 356 (24), 340 (18), 325 (23), 295 (16), 252 (17), 145 (19), 139 (11), 127 (78), 111 (36), 97 (55), 83 (59), 73 (50), 55 (100).

*(3aRS) 3a-Ethoxy-2-(4-nitrophenyl)spirochromane(4,1′)cyclohexane[4,3-d]-$\Delta^{1,9b}$-[1,2,3]thiadiazoline (***16c***).* Red crystals (3.40 g, 83%), mp 150–152°C. Anal calcd for $C_{22}H_{23}N_3O_4S$ (425.48): C, 62.09; H, 5.44; N, 9.87; S, 7.53%. Found: C, 61.85; H, 5.34; N, 9.68; S, 7.40%. IR (KBr): $\nu_{C=N}$ 1596 cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.07 (t, $J = 8.00$ Hz, 3H, CH_3CH_2O),1.15–2.25 (m, 10H, $(CH_2)_5$), 2.92 (q, $J = 8.00$ Hz, 2H, CH_3CH_2O), 7.18–7.22 (m, 4H, ArH), 7.59–7.69 (m, 3H, ArH), 8.00 (d, $J = 8.01$ Hz, 1H, ArH). MS (EI): *m/z* (%) 425 (M, 30), 396 (20), 380 (50), 358 (20), 326 (17), 277 (30), 260 (20), 115 (30), 89 (100).

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