Articles

gem-Difluorination vs 1,3-Dithiolane–Dihydro-1,4-dithiin Rearrangement. The Role of Benzylic Carbons[1]

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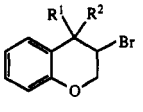
1,3-Dithiolanes bearing a phenyl or substituted aromatic group and a methyl (or methylene) group attached to C-2 cannot be *gem*-difluorinated with 1,3-dibromo-5,5-dimethylhydantoin (DBH) (or NBS) + HF/pyridine because a rapid 1,3-dithiolane–dihydro-1,4-dithiin rearrangement takes place instead.

Our continuing interest in the synthesis of benzopyran derivatives[2] has led us to the attempted application of a recently reported[3] transformation of dithiolanes to *gem*-difluoro compounds.

Thus, chromanones **1a–d**[4,5] and **1g**[6] were prepared as described previously and transformed to the corresponding 1,3-dithiolane derivatives[7] **2a–d** and **2g**, respectively. These 1,3-dithiolanes were then treated with 1,3-dibromo-5,5-dimethylhydantoin (DBH) and pyridinium poly(hydrogen fluoride).[3] We observed in several experiments that novel sulphur-containing products were formed instead of the *gem*-difluorochromanes (**3**). In addition, these products contained no fluorine. These findings prompted us to study the possibility of *gem*-difluorination (of our model chromanones) by this method and elucidate the structures of the novel products.

It is known that *N*-haloamides facilitate the rearrangement of suitably substituted 1,3-dithiolanes to dihydro-1,4-dithiins.[8] A similar rearrangement of the 1,3-dithiolane (**7b**) formed from a bromochromanone (**7a**) to **8a** (and **8b**) has also been described.[9] These findings and literature data suggest that the choice between the two alternative reaction pathways is determined by the substituents of the starting carbonyl compounds (or dithiolanes).



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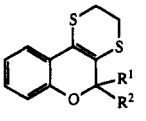
a) $R^1 + R^2 = O$

b) $R^1 + R^2 = -SCH_2CH_2S-$



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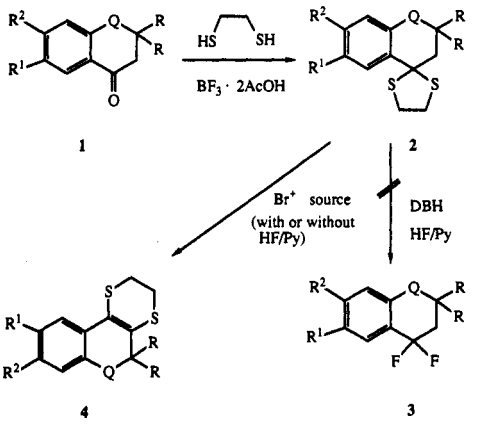
a) $R^1 = R^2 = H$

b) $R^1 + R^2 = O$

In further experiments we have found that this reaction takes place upon treatment with 2 equiv of DBH alone.

In order to find an explanation for the difference in the behavior of our dithiolanes from those reported we prepared and transformed dithiolanes (**2e,f,h, 5a–c**). In the case of 2,2-diphenyl-1,3-dithiolane (**5b**) and cyclododecanone ethylene dithioketal (**5c**) *gem*-difluorination took place (giving **6**) as reported.[3] There was no 1,3-dithiolane → dihydro-1,4-dithiin rearrangement in these cases even when the reaction was attempted with NBS or DBH without the fluorination agent (HF–pyridine).

Scheme I



1 **2** **4** **3**

in **1, 2, 3, 4**:

a) R = Me, R^1 = H, R^2 = OMe, Q = O

b) R = Me, R^1 = H, R^2 = OEt, Q = O

c) R = Me, R^1 = OMe, R^2 = OMe, Q = O

d) R = Me, R^1 = OMe, R^2 = OEt, Q = O

e) R = R^1 = R^2 = H, Q = O

f) R = Me, R^1 = R^2 = H, Q = O

g) R = Me, R^1 = H, R^2 = OMe, Q = S

h) R = R^2 = H, R^1 = OMe, $Q = CH_2$

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a) R^1 = Me, R^2 = Ph

b) $R^1 = R^2$ = Ph

c) $R^1 + R^2 = (CH_2)_{11}$

6

a) $R^1 = R^2$ = Ph

b) $R^1 + R^2 = (CH_2)_{11}$

in **4i** and **4j** (from **2a** and **2b**, respectively):

4i R = Me, R^1 = Br, R^2 = OMe, Q = O

4j R = Me, R^1 = Br, R^2 = OEt, Q = O

Attempted transformation of the 7-methoxychromanone derivative **2a** using a variety of conditions (2 equiv of DBH + HF/py[3], −78 °C to +25 °C; 2 equiv of NBS + HF/py,

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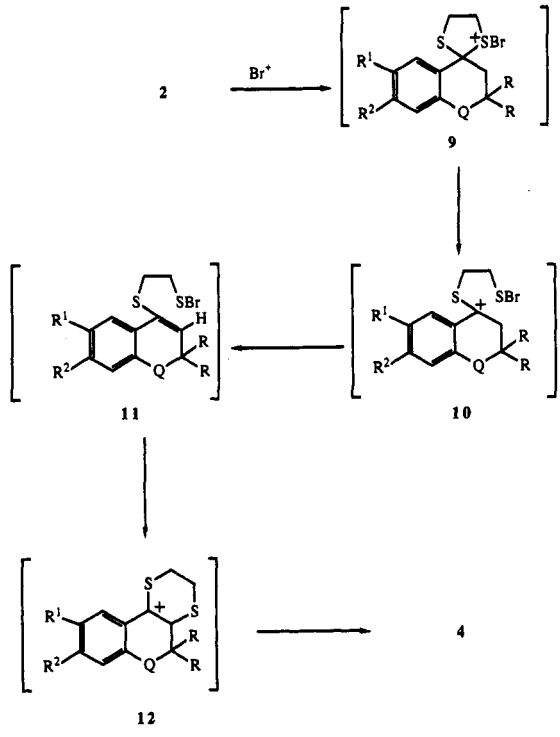
Scheme II

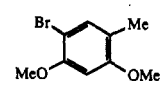


-78 °C to +25 °C; 2 equiv of DBH or NBS; 1 equiv of DBH or NBS; 1 mol of Br_2/mol of **2a**, etc.) gave either **4a** (R^1 = H, R^2 = OMe) or the corresponding ring-brominated derivative **4i** (R^1 = Br, R^2 = OMe). These compounds were characterized by elemental analysis, IR, ^1H NMR, and MS data. Thus, this reaction did not require the presence of fluoride ion, since the formation of fluorine-containing products was not observed, and 1 equiv of DBH or NBS or 1 mol of Br_2/mol of dithiolane was sufficient for the 1,3-dithiolane → dihydro-1,4-dithiin rearrangement. GC and HPLC study of the same reaction in the presence of less than 1 equiv of DBH or NBS, or less than 1 equiv of Br_2 showed that the amount of rearranged product was proportional to the amount of brominating agent (45–50% with 0.5 equiv, 5–10% with 0.1 equiv of DBH or NBS).

A presumed mechanism involves—as proposed earlier for the fluorination[3] reaction—a bromosulfonium compound (**9**), which is transformed subsequently to the sulfur-stabilized carbocation **10**, a sulfenyl bromide intermediate (Scheme II).

Since no incorporation of fluoride occurs even in the presence of 20 equiv of hydrogen fluoride–pyridine, one may presume that the deprotonation, ring closure, and second deprotonation must take place in very fast reaction. Indeed, the reaction of **2b** in a 1×10^{-5} M chloroform solution was complete in 10–15 s; the characteristic UV maximum of **2b** at 302.4 nm disappeared in 10–15 s and a new maximum of higher intensity appeared at 340.8 nm characteristic of the dihydrodithiin derivative **4b**. No further changes were observed in the spectra in repeated scans.

In the ^1H NMR spectra the most characteristic sign of transformation was the disappearance of the signals of the C-3 protons. ^{13}C NMR spectra, recorded with the attached proton test (APT) gave the number of carbons and the number of protons attached to them. These were in accordance with the proposed structures (**4**). An $^1H\{^1H\}$ NOE study of **4i** showed only a 6.8% NOE on the C-7 proton upon irradiating on the methoxy group. The lack of NOE between the *gem*-dimethyl groups at C-5 and the methylene groups of the dihydro-1,4-dithiin (C2–C3) excluded one of the four possible conformers. The higher field aromatic proton was assigned to C-7. Long-range INEPT experiments helped us to assign all the carbons of the new dithiins. In the case of **4i** all the carbons but C-9 and C-10a were assigned in this way. We calculated for a model compound (**13**) 117.0 ppm for C-10a and 100.8 ppm for C-9. (Found: 116.87 and 102.30 ppm, respectively).



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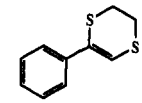

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The mass spectra gave molecular ions and fragmentation patterns, characteristic of 2,2-dimethyl-2*H*-chromenes and aromatic methoxy compounds. It is worth noting that a very broad metastable peak can be observed in the normal mass spectrum of **4i** due to a retro hetero-Diels–Alder reaction leading to vicinal dithiones. This finding corroborates the proposed dihydro-1,4-dithiin structure. It is also of interest that the following double charged ions can also be observed: M^{2+} (3.6%), $[M - CH_3]^{2+}$ (2.7%), $[M - CH_3 - C_2H_4]^{2+}$ (1.6%) and $[M - CH_2O]^{2+}$ (4%).

To substantiate the novel, stable 2,3-dihydro-1,4-dithiin structure, an X-ray diffraction analysis[10] of the product **4i** has been also carried out.

These findings made it certain that the products of this rearrangement were 2,3-dihydro-1,4-dithiins (**4**) as shown in Scheme I.

Conclusion

We have found that 1,3-dithiolanes formed on a carbon attached directly to an aromatic ring undergo a rapid, high-yield rearrangement leading to dihydro-1,4-dithiin derivatives, provided that a methyl- or methylene group is available in the other α-position. Consequently, in the case of starting dithiolanes with these structural features, no *gem*-difluorination can be expected with the DBH (or NBS) + HF/pyridine reagent system. Our finding provides a one-step, fast and convenient, high-yielding alternative of the existing methods for dihydro-1,4-dithiin synthesis.[11-16]

Experimental Section

Caution. Pyridinium poly(hydrogen fluoride), while more convenient to use than anhydrous hydrogen fluoride, requires similar safety precautions. This reagent should only be used in a well-ventilated hood with the user wearing protective clothing and a full-face shield. It is extremely corrosive to human tissue, and contact with the skin, even in dilute concentrations, can result in painful, slow-healing burns which may not be visible for several hours.[17]

General Methods. Melting points were determined with a Kofler hot-stage melting point apparatus and are uncorrected. Analytical thin-layer chromatography was performed on precoated aluminum-backed 0.2-mm silica gel plates (E.M. Science 5554, Kieselgel 60F 254). Column chromatography was carried out with Kieselgel 60 silica gel (Reanal, Hungary). Solvents were used either as purchased or dried and purified by standard methodology. Starting materials and reference compounds were pur-

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chased from Aldrich Chemical Co., Inc., Milwaukee, WI. Organic solutions were dried over anhydrous Na_2SO_4 and concentrated below 50 °C under reduced pressure. IR spectra were recorded on a Perkin Elmer 283B spectrophotometer. ^1H and ^{13}C NMR spectra were determined for solutions in deuteriochloroform with TMS internal reference at ambient temperature on a Bruker WP-200 SY instrument. Mass spectra were obtained on a VG 7035 instrument in the EI mode (70 eV, direct inlet). Gas chromatography measurements were performed on a Fractovap 2300 gap chromatograph (Carlo-Erba). UV spectra were detected on a Hitachi 150-20 spectrophotometer. HPLC studies were carried out on a Hewlett-Packard 1090 M liquid chromatograph. Microanalyses were performed by the Microanalysis Laboratory, Department of Chemistry, L. Kossuth University (Debrecen, Hungary).

General Procedure for the Synthesis of Dithiolanes from Ketones. 2,2-Dimethyl-7-methoxy-4-chromanone Ethylene Dithioketal (2a). 2,2-Dimethyl-7-methoxy-4-chromanone (2.06 g, 10.0 mmol) and 1.7 mL (20 mmol) of 1,2-ethanedithiol were combined under nitrogen and stirred, followed by the addition of 1.40 mL (10.0 mmol) of BF_3·2HOAc. The solution was allowed to stir for 1 h. The mixture was diluted with hexane (30 mL) and washed with three 30-mL portions each of saturated $NaHCO_3$ solution, 10% NaOH solution, and brine. The organic layer was dried and concentrated. Purification by column chromatography (benzene) yielded 2.34 g (83%) of dithiolane **2a** as a white crystalline solid: mp 71–72 °C; ^1H NMR δ 1.41 (s, 6 H), 2.64 (s, 2 H), 3.31–3.64 (m, 4 H), 3.74 (s, 3 H), 6.23 (d, 1 H), 6.50 (dd, 1 H), 7.65 (d, 1 H); mass spectrum, m/z (rel intensity) 282 (64, M^+), 267 (97), 254 (15), 239 (33), 221 (20), 207 (100). Anal. Calcd for $C_{14}H_{18}O_2S_2$: C, 59.53; H, 6.42; S, 22.70. Found: C, 59.49; H, 6.59; S, 22.49.

2,2-Dimethyl-7-ethoxy-4-chromanone Ethylene Dithioketal (2b). Recrystallization from ethanol provided a 82% yield of dithiolane **2b**: mp 88–89 °C; ^1H NMR δ 1.38 (t, 3 H), 1.40 (s, 6 H), 2.65 (s, 2 H), 3.33–3.64 (m, 4 H), 3.96 (q, 2 H), 6.21 (d, 1 H), 6.52 (dd, 1 H), 7.65 (d, 1 H); mass spectrum, m/z (rel intensity) 296 (44, M^+), 281 (100), 268 (15), 253 (33), 235 (18), 221 (90). Anal. Calcd for $C_{15}H_{20}O_2S_2$: C, 60.77; H, 6.80; S, 21.63. Found: C, 60.75; H, 6.78; S, 21.51.

2,2-Dimethyl-6,7-dimethoxy-4-chromanone Ethylene Dithioketal (2c). Recrystallization from ethanol provided 84% yield of dithiolane **2c**: mp 99–101 °C; ^1H NMR δ 1.44 (s, 6 H), 2.64 (s, 2 H), 3.34–3.65 (m, 4 H), 3.80 (s, 3 H), 3.86 (s, 3 H), 6.24 (s, 1 H), 7.21 (s, 1 H); mass spectrum, m/z (rel intensity) 312 (59, M^+), 297 (93), 294 (29), 284 (8), 251 (17), 227 (100). Anal. Calcd for $C_{15}H_{20}O_3S_2$: C, 57.66; H, 6.45; S, 20.52. Found: C, 57.37; H, 6.42; S, 20.41.

2,2-Dimethyl-6-methoxy-7-ethoxy-4-chromanone Ethylene Dithioketal (2d). Recrystallization from ethanol provided 78% yield of dithiolane **2d**: mp 63–65 °C; ^1H NMR δ 1.39 (s, 6 H), 1.43 (t, 3 H), 2.64 (s, 2 H), 3.35–3.64 (m, 4 H), 3.84 (s, 3 H), 4.04 (q, 2 H), 6.24 (s, 1 H), 7.20 (s, 1 H); mass spectrum, m/z (rel intensity) 326 (77, M^+), 311 (100), 298 (9), 283 (25), 265 (10), 251 (74), 223 (24). Anal. Calcd for $C_{16}H_{22}O_3S_2$: C, 58.86; H, 6.79; S, 19.64. Found: C, 58.77; H, 6.82, S, 19.81.

4-Chromanone Ethylene Dithioketal (2e). Recrystallization from pentane provided 83% yield of dithiolane **2e**: mp 52–53 °C; ^1H NMR δ 2.55 (m, 2 H), 3.38–3.69 (m, 4 H), 4.34 (m, 2 H), 6.73 (dd, 1 H), 6.91 (m, 1 H), 7.11 (m, 1 H), 7.84 (dd, 1 H); mass spectrum, m/z (rel intensity) 224 (100, M^+), 196 (50), 195 (26), 163 (87), 131 (57). Anal. Calcd for $C_{11}H_{12}OS_2$: C, 58.89; H, 5.39; S, 28.58. Found: C, 58.75; H, 5.65, S, 28.65.

2,2-Dimethyl-4-chromanone Ethylene Dithioketal (2f). Recrystallization from diethyl ether/pentane provided 81% yield of dithiolane **2f**: mp 59–61 °C; ^1H NMR δ 1.43 (s, 6 H), 2.67 (s, 2 H), 3.36–3.68 (m, 4 H), 6.70 (dd, 1 H), 6.91 (m, 1 H), 7.10 (m, 1 H), 7.75 (dd, 1 H); mass spectrum, m/z (rel intensity) 252 (54, M^+), 237 (87), 224 (22), 209 (38), 191 (15), 177 (100). Anal. Calcd for $C_{13}H_{16}OS_2$: C, 61.86; H, 6.39; S, 25.41. Found: C, 61.74; H, 6.57; S, 25.44.

2,2-Dimethyl-7-methoxy-4-thiochromanone Ethylene Dithioketal (2g). Recrystallization from pentane provided 80% yield of dithiolane **2g**: mp 47–49 °C; ^1H NMR δ 1.49 (s, 6 H), 2.80 (s, 2 H), 3.38–3.64 (m, 4 H), 3.78 (s, 3 H), 6.53 (d, 1 H), 6.68 (dd, 1 H), 7.87 (d, 1 H); mass spectrum, m/z (rel intensity) 298 (33, M^+), 283 (10), 237 (100), 223 (30), 214 (13). Anal. Calcd for $C_{14}H_{18}OS_3$: C, 56.33; H, 6.07; S, 32.22. Found: C, 55.98; H, 6.39; S, 32.00.

7-Methoxy-1-tetralone Ethylene Dithioketal (2h). Recrystallization from diethyl ether/pentane provided 72% yield of dithiolane **2h**: mp 38–40 °C; ^1H NMR δ 1.87–2.03 (m, 2 H), 2.29–2.45 (m, 2 H), 2.70 (t, 2 H), 3.31–3.61 (m, 4 H), 3.75 (s, 3 H), 6.68 (dd, 1 H), 6.86 (d, 1 H), 7.47 (d, 1 H); mass spectrum, m/z (rel intensity) 252 (81, M^+), 224 (13), 193 (63), 192 (100), 191 (48), 159 (82), 158 (27). Anal. Calcd for $C_{13}H_{16}OS_2$: C, 61.86; H, 6.39; S, 25.41. Found: C, 62.10; H, 6.32; S, 25.72.

2-Methyl-2-phenyl-1,3-ditholane (5a).[18] Column chromatography (benzene) yielded 75% of dithiolane **5a** as an oily product: ^1H NMR δ 2.11 (s, 3 H), 3.25–3.52 (m, 4 H), 7.16–7.37 (m, 3 H), 7.73 (m, 2 H); mass spectrum, m/z (rel intensity) 196 (54, M^+), 181 (93), 168 (54), 167 (74), 136 (38), 121 (100), 103 (76). Anal. Calcd for $C_{10}H_{12}S_2$: C, 61.17; H, 6.16; S, 32.66. Found: C, 61.31; H, 6.21; S, 32.50.

2,2-Diphenyl-1,3-dithiolane (5b). Recrystallization from ethanol provided a 83% yield of dithiolane **5b** as a white crystalline solid: mp 103–104 °C. The spectral data is consistent with literature values.[3]

Cyclodecanone Ethylene Dithioketal (5c). Recrystallization from diethyl ether and pentane provided a 77% yield of dithiolane **5c** as a colorless platelets: mp 83–84 °C; spectral data is consistent with literature values.[19]

General Procedure for the Preparation of Dihydro-1,4-dithiins. 2,3-Dihydro-5,5-dimethyl-8-methoxy-5*H*-benzo[*b*]pyrano[3,4-*b*][1,4]dithiin (4a). *N*-Bromosuccinimide (1.78 g, 10.0 mmol) was dissolved in 10 mL of dry CH_2Cl_2 and allowed to stir under nitrogen at room temperature. The solution of dithiolane **2a** (2.82 g, 10.0 mmol) in 10 mL CH_2Cl_2 was then added within 5 min. After 15 min, the reaction mixture was diluted with hexane (50 mL) and washed with three 100-mL portions, each of saturated $NaHCO_3$ solution, water, and brine. The organic layer was dried and concentrated. Purification by column chromatography (benzene) yielded 2.2 g (78%) of dithiin **4a**: mp 72–74 °C; ^1H NMR δ 1.48 (s, 6 H), 3.22 (s, 4 H), 3.78 (s, 3 H), 6.41 (d, 1 H), 6.48 (dd, 1 H), 7.23 (d, 1 H); mass spectrum, m/z (rel intensity) 280 (26, M^+), 265 (100), 237 (17). Anal. Calcd for $C_{14}H_{16}O_2S_2$: C, 59.96; H, 5.75; S, 22.87. Found: C, 60.18; H, 5.83; S, 22.50.

2,3-Dihydro-5,5-dimethyl-8-ethoxy-5*H*-benzo[*b*]pyrano[3,4-*b*][1,4]dithiin (4b): yield 90%; mp 120–121 °C; ^1H NMR δ 1.38 (t, 3 H), 1.48 (s, 6 H), 3.25 (s, 4 H), 4.00 (q, 2 H), 6.40 (d, 1 H), 6.46 (dd, 1 H), 7.19 (d, 1 H); mass spectrum, m/z (rel intensity) 294 (27, M^+), 279 (100), 251 (28), 223 (11). Anal. Calcd for $C_{15}H_{18}O_2S_2$: C, 61.19; H, 6.16; S, 21.78. Found: C, 61.37; H, 6.19; S, 21.40.

2,3-Dihydro-5,5-dimethyl-8,9-dimethoxy-5*H*-benzo[*b*]pyrano[3,4-*b*][1,4]dithiin (4c): yield 82%; mp 97–99 °C; ^1H NMR δ 1.44 (s, 6 H), 3.24 (s, 4 H), 3.84 (s, 3 H), 3.86 (s, 3 H), 6.44 (s, 1 H), 6.85 (s, 1 H); mass spectrum, m/z (rel intensity) 310 (27, M^+), 295 (100). Anal. Calcd for $C_{15}H_{18}O_3S_2$: C, 58.03; H, 5.84; S, 20.66. Found: C, 58.02; H, 6.00; S, 20.63.

2,3-Dihydro-5,5-dimethyl-8-ethoxy-9-methoxy-5*H*-benzo[*b*]pyrano[3,4-*b*][1,4]dithiin (4d): yield 76%; mp 85–87 °C; ^1H NMR δ 1.41 (t + s, 3 H + 6 H), 3.23 (s, 4 H), 3.85 (s, 3 H), 4.05 (q, 2 H), 6.42 (s, 1 H), 6.85 (s, 1 H); mass spectrum, m/z (rel intensity) 324 (29, M^+), 309 (100), 281 (17), 251 (17), 235 (16). Anal. Calcd for $C_{16}H_{20}O_3S_2$: C, 59.22; H, 6.21; S, 19.76. Found: C, 59.30; H, 6.17; S, 19.70.

2,3-Dihydro-5*H*-benzo[*b*]pyrano[3,4-*b*][1,4]dithiin (4e): yield 85%, yellowish oil (decomposes upon standing); ^1H NMR δ 3.29 (s, 4 H), 4.51 (s, 2 H), 6.83 (m, 1 H), 6.94 (m, 1 H), 7.08 (m, 1 H), 7.28 (m, 1 H); mass spectrum, m/z (rel intensity) 222 (100, M^+), 221 (29), 194 (39), 193 (44), 162 (20), 136 (18), 108 (14). Anal. Calcd for $C_{11}H_{10}OS_2$: C, 59.42; H, 4.53; S, 28.84. Found: C, 59.58; H, 4.52; S, 28.94.

2,3-Dihydro-5,5-dimethyl-5*H*-benzo[*b*]pyrano[3,4-*b*][1,4]dithiin (4f): yield 68%, yellow oil; ^1H NMR δ 1.47 (s, 6 H), 3.22 (s, 4 H), 6.78 (dd, 1 H), 6.88 (m, 1 H), 7.08 (m, 1 H), 7.28

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(dd, 1 H); mass spectrum, m/z (rel intensity) 250 (26, M^+), 235 (100), 207 (29). Anal. Calcd for $C_{13}H_{14}OS_2$: C, 62.36; H, 5.63; S, 25.61. Found: C, 62.64; H, 5.88; S, 25.90.

2,3-Dihydro-5,5-dimethyl-8-methoxy-5*H*-benzo[*b*]thiopyrano[3,4-*b*][1,4]dithiin (4g): yield 73%, yellow oil; ^1H NMR δ 1.48 (s, 6 H), 3.20 (s, 4 H), 3.79 (s, 3 H), 6.70 (dd, 1 H), 6.83 (d, 1 H), 7.62 (d, 1 H); mass spectrum, m/z (rel intensity) 296 (55, M^+), 281 (93), 255 (36), 235 (100). Anal. Calcd for $C_{14}H_{16}OS_3$: C, 56.71; H, 5.44; S, 32.44. Found: C, 56.52; H, 5.40; S, 32.61.

2,3,5,6-Tetrahydro-9-methoxynaphtho[1,2-*b*][1,4]dithiin (4h): yield 87%; mp 82–84 °C; ^1H NMR δ 2.40 (m, 2 H), 2.75 (m, 2 H), 3.20–3.38 (m, 4 H), 3.83 (s, 3 H), 6.68 (dd, 1 H), 7.03 (d, 1 H), 7.07 (d, 1 H); mass spectrum, m/z (rel intensity) 250 (100, M^+), 222 (13), 191 (16), 190 (14). Anal. Calcd for $C_{13}H_{14}OS_2$: C, 62.36; H, 5.63; S, 25.61. Found: C, 62.50; H, 5.76; S, 25.47.

2,3-Dihydro-5,5-dimethyl-8-methoxy-9-bromo-5*H*-benzo[*b*]pyrano[3,4-*b*][1,4]dithiin (4i): yield 83%; mp 132–134 °C; ^1H NMR δ 1.48 (s, 6 H), 3.23 (s, 4 H), 3.85 (s, 3 H), 6.43 (s, 1 H), 7.45 (s, 1 H); mass spectrum, m/z (rel intensity) 360 (25, M^+), 358 (22), 345 (100), 343 (92), 317 (14), 315 (14). Anal. Calcd for $C_{14}H_{15}BrO_2S_2$: C, 46.80; H, 4.21; Br, 22.24; S, 17.85. Found: C, 46.75; H, 4.34; Br, 22.30; S, 17.85.

2,3-Dihydro-5,5-dimethyl-8-ethoxy-9-bromo-5*H*-benzo[*b*]pyrano[3,4-*b*][1,4]dithiin (4j): yield 79%; mp 129–132 °C; ^1H NMR δ 1.42 (t, 3 H), 1.48 (s, 6 H), 3.24 (s, 4 H), 4.05 (q, 2 H), 6.41 (s, 1 H), 7.46 (s, 1 H); mass spectrum, m/z (rel intensity) 374 (35, M^+), 372 (33), 359 (100), 357 (97), 331 (29), 329 (29), 279 (48). Anal. Calcd for $C_{15}H_{17}BrO_2S_2$: C, 48.25; H, 4.59; Br, 21.40; S, 17.17. Found: C, 48.42; H, 4.79; Br, 21.61; S, 17.38.

2,3-Dihydro-5-phenyl-1,4-dithiin (14):[6] yield 79%; mp 54–55 °C; ^1H NMR δ 3.20–3.36 (m, 4 H), 6.39 (s, 1 H), 7.24–7.49 (m, 5 H); mass spectrum, m/z (rel intensity) 194 (68, M^+), 166 (38), 134 (24), 121 (100). Anal. Calcd for $C_{10}H_{10}S_2$: C, 61.81; H, 5.19; S, 33.00. Found: C, 61.72; H, 5.50, S, 32.68.

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Registry No. **1a**, 20321-73-7; **1b**, 76348-94-2; **1c**, 65383-61-1; **1d**, 65383-62-2; **1e**, 491-37-2; **1f**, 3780-33-4; **1g**, 64793-90-4; **1h**, 6836-19-7; **2a**, 136545-72-7; **2b**, 136545-73-8; **2c**, 136545-74-9; **2d**, 136545-75-0; **2e**, 7156-48-1; **2f**, 136545-76-1; **2g**, 136545-77-2; **2h**, 136545-78-3; **4a**, 136545-79-4; **4b**, 136545-80-7; **4c**, 136545-81-8; **4d**, 136545-82-9; **4e**, 104169-49-5; **4f**, 136545-83-0; **4g**, 136545-84-1; **4h**, 136545-85-2; **4i**, 131356-27-9; **4j**, 136545-86-3; **5a**, 5769-02-8; **5b**, 6317-10-8; **5c**, 16775-67-0; **14**, 35756-26-4; HF/Py, 32001-55-1; $SH(CH_2)_2SH$, 540-63-6; CH_3COPh, 98-86-2; PhCOPh, 119-61-9; cyclododecanone, 830-13-7.

2-Aza 1,3-Dienes: A New and Simple Method for the Synthesis of Functionalized Pyridine Derivatives

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The synthesis of 4(1*H*)-pyridones and 4-chloropyridines from 2-aza 1,3-dienes is described, using carbonic acid derivatives. The process involves a [5 + 1] heterocyclization reaction, with formation of two new carbon–carbon bonds.

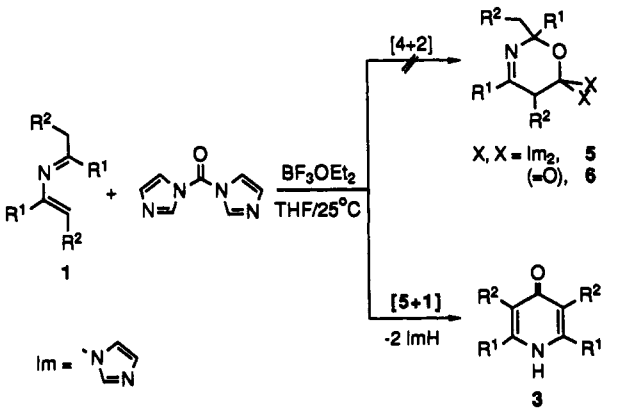
Introduction

Heterodienes have been extensively used in organic synthesis for the preparation of both open-chain functionalized compounds and heterocyclic systems. They have found important use in heterocyclic synthesis mainly due to their ability to take part in [4 + 2] cycloaddition reactions; other utilities are also known.[1] In this context, the synthetic possibilities of C-substituted 2-aza 1,3-dienes 1 have been well established in previous reports from these laboratories.[2] Thus, we have studied the behavior of compounds 1 in [4 + 2] cycloaddition reactions,[3] as well as their reactivity through either the nitrogen[4] or the C-α carbon atoms,[5] as outlined in Figure 1.

More recently, a new type of process which involves the participation of both the dienic system and the C_α-H hydrogen atom, i.e., a [5 + 1] formal cyclocondensation reaction (Figure 1), has also been described. For instance, the reaction of 1 with phosphorus(III) halide derivatives led, in a simple way, to λ^3- and λ^5-azaphosphinine derivatives 2 (Z = PR, OPR, Figure 2).[6]

This methodology was investigated as a simple route to several types of heterocycles 2 by replacing the halo-

Scheme I



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