139. Heterocyclic Spiro-naphthalenones. Part II. Synthesis and Reactions of some Spiro[tetrahydrofuran-2,1'-(2'*H*-naphthalene)]-2',5-diones and Spiro[tetrahydrofuran-2,2'-(1'*H*-naphthalene)]-1',5-diones

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Summary

The spiro-lactone **3** was obtained by *N*-bromosuccinimide (NBS) oxidation of the carboxylate **2** at −20°. When **2** was oxidized at 10° the spiro-lactone **4** was the main product. Compound **4** was rearranged with triethylamine to the spiro-lactone **9** whereas the stereoisomeric spiro-lactones **14** and **15** were obtained by NBS oxidation of the carboxylate **13**. The ketones **3**, **4**, **9**, **14** and **15** were reduced with $NaBH_4$ to the corresponding alcohols **5**, **6**, **10**, **16** and **18** respectively; these were hydrogenated to the alcohols **7**, **8**, **11** and **20**. The allylic alcohols **5** and **6** gave the benzochromanone **1** when heated in polyphosphoric acid whereas the benzochromanones **12** and **21** were obtained from the alcohols **10** and **16** respectively.

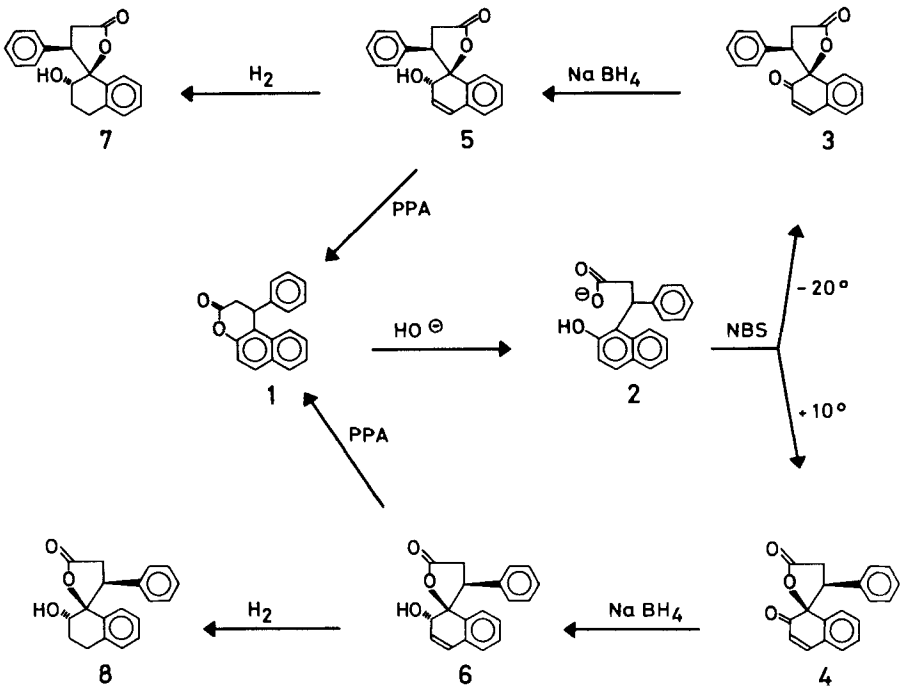
Introduction. – In part I of this study we reported the synthesis and reactions of some spiro[1*H*-naphthalene-1,3'-piperidin]-2-ones [1] prepared *via* an intramolecular *Mannich* condensation. We present now the stereoselective synthesis of a few spiro[tetrahydrofuran-2,1'-(2'*H*-naphthalene)]-2',5-diones and spiro[tetrahydrofuran-2,2'-(1'*H*-naphthalene)]-1',5-diones, by an oxidative cyclization procedure. An interesting conversion of the first to the second type of spiro[tetrahydrofuran-naphthalene] and other reactions of these spiro-lactones are also reported.

Results. – The benzochromanone **1** [2] was opened with aqueous NaOH to the carboxylate **2** which was then oxidized with NBS at −20° to the spiro-lactone **3**. When **2** was treated with NBS at 10°, the stereoisomeric spiro-lactone **4** was the main product. No clear explanation could be given for this stereospecificity. The isomers **3** and **4** were differentiated by NMR. spectroscopy; in the spectrum of **3** both olefinic protons were shifted to a higher field compared to those of **4**. This up-field shift is explained by the plane of the phenyl ring of the isomer **3** being approximately parallel and above the plane of the double bond, as can be seen from molecular models. Both spiro-lactones **3** and **4** have practically superimposable absorptions between 1350 and 4000 cm^{-1} in their IR. spectra.

The unsaturated ketones **3** and **4** were reduced with $NaBH_4$. This reagent presumably attacked the carbonyl group from the side not hindered by the lactone

phenyl ring, and gave the allylic alcohols **5** and **6**, respectively, with the OH group *trans* to the C(2)–O(1) bond of the lactone[1]). The allylic alcohols **5** and **6** were hydrogenated to **7** and **8**. When heated in polyphosphoric acid (PPA) both **5** and **6** gave the benzochromanone **1**.

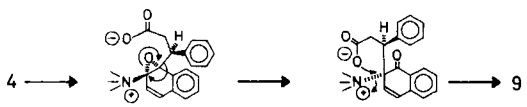
The spiro-lactone **4** when refluxed in CH_3OH and triethylamine underwent an unusual rearrangement, giving selectively the spiro-lactone **9**[2]). No rearrangement product could be obtained from the stereoisomeric lactone **3**. The unsaturated ketone **9** was reduced with $NaBH_4$ which, as before, attacked the carbonyl group from the less hindered side to give the benzylic alcohol **10**, with the OH group *trans* to the C(2)–O(1) bond of the spiro-lactone. The alcohol **10** could be hydrogenated to **11** or rearranged to the benzochromanone **12** when heated in PPA. The proton H–C(1′), of both alcohols **10** and **11** treated with D_2O, appeared in the NMR. spectra as a singlet proving the disubstitution of C(2′), whereas H–C(2′) was seen as a multiplet in spectra of the alcohols **5**, **6**, **7** and **8**.

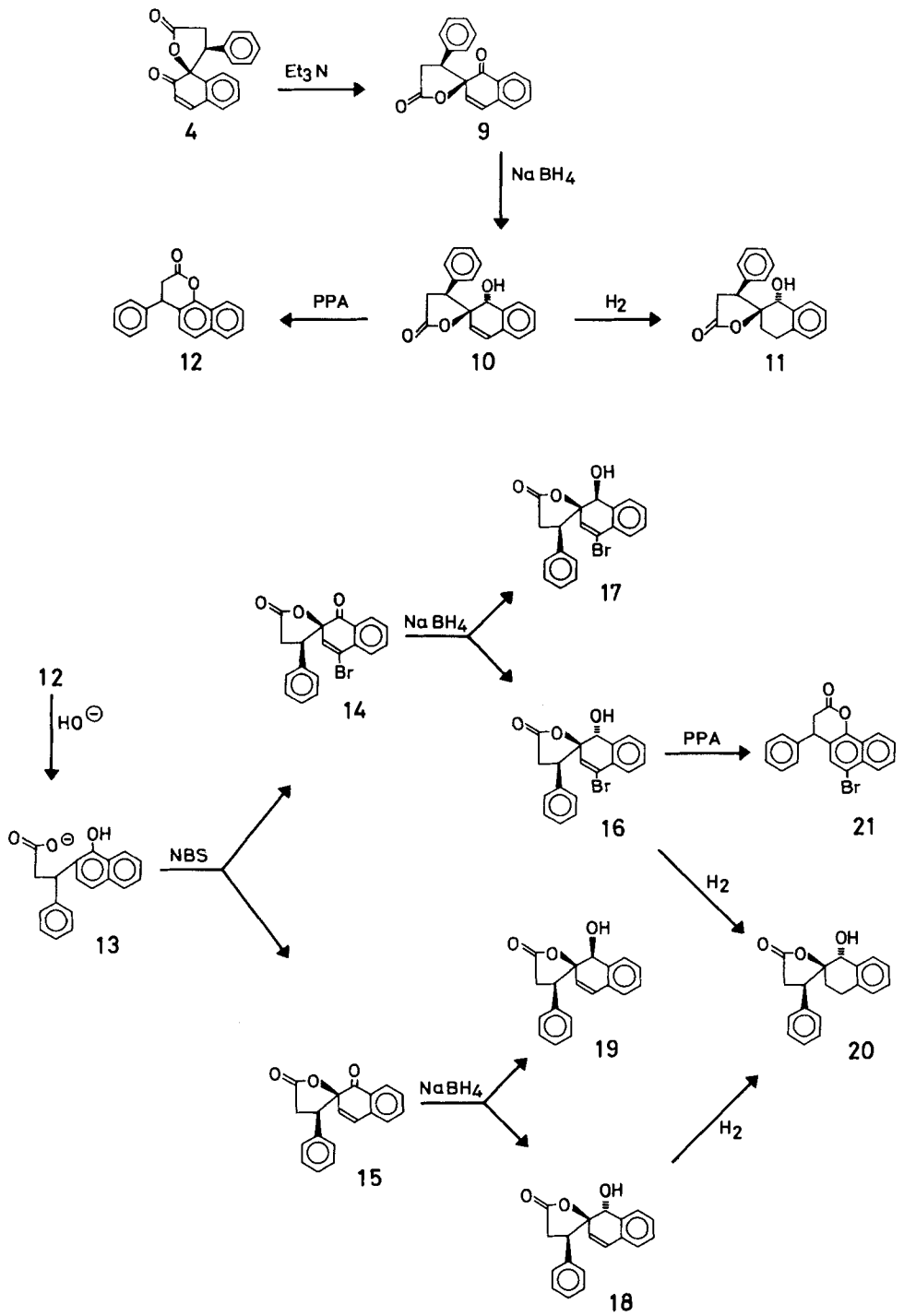


7 5 3 1 2 8 6 4

[1]) The X-ray crystal structure analysis of *2′-hydroxy-3-(4-chlorophenyl)spiro[tetrahydrofuran-2,1′-(2′H-naphthalen)]-5-one*, obtained by a similar route to that used for the synthese of **5**, showed that its configuration was identical with that proposed for the allylic alcohol **5** [3].

[2]) Although experimental support is lacking the reaction is considered to proceed as follows:




Et3N
4
9
NaBH4
PPA
H2
12
10
11
OH
Br
17
14
NaBH4
12
HO⊖
PPA
16
21
NBS
13
H2
19
20
NaBH4
15
H2
18

The lactone **12** [4] was opened with aqueous NaOH to the sodium salt **13** which was treated with 1 mol-equiv. of NBS to give mainly the brominated spiro-lactone **14** and a small amount of the unbrominated spiro-lactone **15** isolated by TLC. When 2 mol-equiv. of NBS were used the sole product isolated was **14**.

In the NMR. spectrum of **15** both olefinic protons appeared shifted to a higher field compared to those of **9**. As for the spiro-lactone **3**, the cause of this shift was attributed to the presence of the phenyl ring in the neighbourhood of the olefinic protons. Spiro-lactones **9** and **15** have practically superimposable absorptions between 1350 to 4000 cm^{-1} in their IR. spectra. However these are quite different from those of **3** and **4**.

Both unsaturated ketones **14** and **15** were reduced with $NaBH_4$ to give in each case 2 isomeric benzylic alcohols. Compound **16**[3]) and a smaller amount of **17** were obtained from **14** and were separated by crystallization.

The unsaturated ketone **15**, on the other hand, gave **18** and a smaller amount of the isomeric alcohol **19**. The mixture was separated by TLC.

The allylic alcohols **5**, **6** or the benzylic alcohols **10**, **16** and **18** presented a very similar NMR. pattern for the 3 protons of their lactone rings. By contrast the NMR. pattern of the lactone ring of **17** and **19** was totally different from that of the above alcohols. This difference was assumed to be due to the different geometrical position of the OH group. As can be seen from models the OH group of **5**, **6**, **10**, **16** and **18** but not of **17** and **19** stands above the plane of the lactone ring.

In agreement with the proposed configuration the hindered ketone **9** gave only the alcohol obtained by attack of $NaBH_4$ from the less hindered side whereas the much less hindered ketones **14** and **15** gave in addition to the main products some amounts of alcohols obtained by attack from the more hindered side.

The brominated compound **16** rapidly absorbed 2 mol-equiv. of H_2 to give **20** identical with the compound obtained by hydrogenation of **18**, thus proving that the spiro-lactones **14** and **15** had identical configurations.

Experimental Part

General. – For general remarks on NMR. spectra and microanalysis see part I [1]. IR. spectra: the maxima of absorption are given in cm^{-1}.

cis-*3-Phenylspiro[tetrahydrofuran-2,1'-(2'H-naphthalene)]-2',5-dione* (**3**). The benzochromanone **1** [2] (58.5 g, 0.2 mol) was suspended in methanol (600 ml) and 2N NaOH (100 ml) was added. The mixture was refluxed until all the lactone was dissolved, then cooled to −20° and solid NBS (36 g, 0.2 mol) added portionwise during a period of 30 min. The temperature was slowly brought to RT. and the solution was poured into water (2000 ml) and extracted with $CHCl_3$. The extract was washed with water, dried (Na_2SO_4) and evaporated to dryness. The oily residue was crystallized from ether/pet. ether giving 27.8 g (48%) of the spiro-lactone **3**, m.p. 146–149°. – IR.: 1390, 1410, 1450, 1500, 1570, 1615, 1675, 1790. – NMR.: 6.95 (*d*, *J* = 10, H–C(4')), 5.6 (*d*, *J* = 10, H–C(3')). – $C_{19}H_{14}O_3$: C,H.

trans-*3-Phenylspiro[tetrahydrofuran-2,1'-(2H-naphthalene)]-2',5-dione* (**4**). The benzochromanone **1** [2] (110 g, 0.37 mol) was suspended in methanol (600 ml). Water (400 ml) and 2N NaOH (200 ml) were added and the mixture was refluxed for 30 min, then cooled to 5–10°, while solution of NBS (72 g, 0.4 mol) in methanol (1200 ml) and water (120 ml) was added during a period of 1.5 h. The temperature

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[3]) The X-ray crystal structure analysis of **16** was in agreement with our proposed configuration [3].

was maintained between 5 and 10° another hour and the reaction mixture was poured into H_2O (3000 ml) and extracted with $CHCl_3$. The extract was washed with water, dried and evaporated to dryness. The oily residue was crystallized from ether/petroleum ether to give 57.1 g (52%) of **4**, m.p. 142–145. – IR.: 1390, 1420, 1455, 1500, 1570, 1615, 1685, 1790. – NMR.: 7.4 (*d*, J = 10, H–C(4')), 6.2 (*d*, J = 10, H–C(3')). – $C_{19}H_{14}O_3$: C,H.

*(2*RS,*2'*RS,*3*SR*)-2'-Hydroxy-3-phenylspiro[tetrahydrofuran-2,1'-(2'*H*-naphthalen)]-5-one* (**5**). A solution of the spiro-lactone **3** (20.3 g) in methanol (2000 ml) was cooled to 5° and $NaBH_4$ (700 mg) was added in small portions. After 45 min the solution was poured into water (5000 ml) and extracted with $CHCl_3$ which was washed with H_2O, dried and evaporated to dryness. The residue was crystallized from toluene to give 17.1 g (83%) of the allylic alcohol **5**, m.p. 215–218°. – NMR. ($CDCl_3/D_2O$): 5.2 (*m*, H–C(2')). – $C_{19}H_{16}O_3$: C,H.

*(2*RS,*2'*RS,*3*RS*)-2'-Hydroxy-3-phenylspiro[tetrahydrofuran-2,1'-(2*H*-naphthalen)]-5-one* (**6**). Spirolactone **4**, treated as **3** in the previous experiment gave **6** (74%), m.p. 165–168°. – NMR. ($CDCl_3/D_2O$): 5.2 (*m*, H–C(2')). – $C_{19}H_{16}O_3$: C,H.

*(2*RS,*2'*RS,*3*SR*)-2'-Hydroxy-3-phenylspiro[tetrahydrofuran-2,1'-(1',2',3',4'-tetrahydronaphthalen)]-5-one* (**7**). The allylic alcohol **5** (8.7 g) was dissolved in methanol (500 ml) and Pd/C 5.4% (850 mg) was added. After hydrogenation under normal conditions the filtrate was evaporated to dryness and the residue crystallized from ether/pet. ether giving 6.9 g (78%) of the alcohol **7**, m.p. 220–224°. – NMR. ($CDCl_3/D_2O$): 4.2 (*m*, H–C(2')). – $C_{19}H_{18}O_3$: C,H.

*(2*RS,*2'*RS,*3*RS*)-2'-Hydroxy-3-phenylspiro[tetrahydrofuran-2,1'-(1',2',3',4'-tetrahydronaphthalen)]-5-one* (**8**). Compound **6**, hydrogenated as **5**, gave **8** (85%), m.p. 168–172°. – NMR. ($CDCl_3/D_2O$): 4.3 (*m*, H–C(2')). – $C_{15}H_{18}O_3$: C,H.

1-Phenylbenzo[f]*chroman-3-one* (**1**). – 1) *From the allylic alcohol* **5**. The allylic alcohol **5** (200 mg) was added to PPA (5 g). The mixture was heated 15 min at 100° and then poured into ice/water which was extracted with $CHCl_3$. The extract was dried and evaporated to dryness. The residue crystallized from ether/petroleum ether. Yield 190 mg (95%), m.p. 115–118° (lit. [2] 116–117°). – NMR.: superimposable with that of **1** obtained as described [2]. 4.8 (*t*, J = 4, H–C(1)), 3.1 (*d*, J = 4, 2 H–C(2)). – $C_{19}H_{14}O_2$: C,H.

2) *From the allylic alcohol* **6**. As above from **5**; quantitative yield.

cis-*3-Phenylspiro[tetrahydrofuran-2,2'-(1'*H*-naphthalen)]-1',5-dione* (**9**). The spiro-lactone **4** (58 g) was dissolved at 30° in methanol (4000 ml) and triethylamine (20.2 g) was added. The mixture was refluxed for 2.5 h and evaporated to dryness. The oily residue was crystallized from 2-propanol giving 26.9 g (46.4%) of the rearranged product **9**, m.p. 169–170°. – IR.: 1415, 1455, 1485, 1500, 1600, 1690, 1790. – NMR.: 6.7 (*s*, J = 10, H–C(4')), 6.3 (*s*, J = 10, H–C(3')). – $C_{19}H_{14}O_3$: C,H.

*(1'*SR,*2*RS,*3*RS*)-1'-Hydroxy-3-phenylspiro[tetrahydrofuran-2,2'-(1'*H*-naphthalen)]-5-one* (**10**). The ketone **9** treated as **3** with $NaBH_4$ gave the benzylic alcohol **10** (61%), m.p. 188–192°. – NMR. ($CDCl_3/D_2O$): 5.3 (*s*, H–C(1')). – $C_{19}H_{16}O_3$: C,H.

*(1'*SR,*2*RS,*3*RS*)-1'-Hydroxy-3-phenylspiro[tetrahydrofuran-2,2'-(1',2',3',4'-tetrahydronaphthalen)]-5-one* (**11**). The olefinic product **10**, hydrogenated as described above for **5**, gave **11** (81%), m.p. 173–176°. – NMR. ($CDCl_3/D_2O$): 4.3 (*s*, H–C(1')). – $C_{19}H_{18}O_3$: C,H.

4-Phenylbenzo[h]*chroman-2-one* (**12**). Compound **10** heated 5 min at 100° in PPA (as for the preparation of **1** from **5**) gave the lactone **12** (71%), m.p. 110–111° (lit. [4] 112–113°). – NMR.: 4.4 (*t*, H–C(4)); 3.0 (*d*, 2 H–C(3)). – $C_{19}H_{14}O_2$: C,H.

trans-*4'-Bromo-3-phenylspiro[tetrahydrofuran-2,2'-(1'*H*-naphthalen)]-1',5-dione* (**14**). The lactone **12** was treated with 2 equiv. of NBS instead of 1 mol-equiv. for the oxidation of **1** to **3**. The bromo-compound **14** was obtained in 26% yield, m.p. 150–153°. – NMR.: 5.9 (*s*, H–C(3')). – $C_{19}H_{13}BrO_3$: C, H, Br.

trans-*3-Phenylspiro[tetrahydrofuran-2,2'-(1'*H*-naphthalen)]-1',5-dione* (**15**). From 2.5 g of **12** (treated as for the oxidation of **1** to **3**), 60 mg of **15** were isolated on *Macherey-Nagel* Polygram TLC. plates (Sil G UV_{254}) eluted with heptane/$CHCl_3$/ethanol, 65:35:10; Rf 0.45. The compound was crystallized from petroleum ether giving pure **15**, m.p. 146–148°. – IR.: 1415, 1450, 1480, 1500, 1600, 1690, 1790. – NMR.: 6.4 (*d*, J = 5, H–C(4')); 5.5 (*d*, J = 5, H–C(4')). – $C_{19}H_{14}O_3$: C,H.

(1'RS, 2SR, 3RS)-4'-Bromo-1'-hydroxy-3-phenylspiro[tetrahydrofuran-2, 2'-(1'H-naphthalen)]-5-one (**16**) and its *(1'RS,2RS,3SR) stereoisomer* **17**. Compound **14** (1.8 g) reduced as **3** with $NaBH_4$ gave the isomers **16** and **17** in a 3:2 ratio (TLC.). Product **17** crystallized from ether/petroleum ether in the cold giving 220 mg pure product, m.p. 167–168°. – NMR. ($CDCl_3/D_2O$): 4.9 (*s*, H–C(1')), 4.2 (*t*, *J* = 4, H–C(3)), 2.95 (*d*, *J* = 4, 2 H–C(4)). – $C_{19}H_{15}BrO_3$: C, H, Br.

The mother liquor was evaporated to dryness and toluene was added from which 250 mg of **16** were isolated, m.p. 182–185°. – NMR. ($CDCl_3/D_2O$): 5.4 (*s*, H–C(1')), 4.0 (*d* × *d*, *J* = 6, 10, H–C(3)), 3.3 (*d* × *d*, *J* = 10, 16, H_A–C(4)), 2.7 (*d* × *d*, *J* = 6, 16, H_B–C(4)). – $C_{19}H_{15}BrO_3$: C, H, Br.

(1'RS,2SR,3RS)-1'-Hydroxy-3-phenylspiro[tetrahydrofuran-2, 2'-(1'H-naphthalen)]-5-one (**18**) and its *(1'RS,2RS,3SR) stereoisomer* **19**. As above from 100 mg of **15** about 100 mg of an oil were obtained containing a 3:2 ratio of **18** and **19** respectively (TLC.). Both products were separated on *Macherey-Nagel* precoated TLC. plates Sil G-100 UV_{254} eluted with heptane/$CHCl_3$/ethanol, 65:35:10. Product **18**, Rf 0.43, 50 mg, crystallized from ether, m.p. 165–169°. Product **19**, Rf 0.37, 38 mg, crystallized from ether/pet. ether, m.p. 142–144°.

(1'RS, 2SR, 3RS)-3, 3', 1'-Hydroxy-3-phenylspiro[tetrahydrofuran-2, 2'-(1', 2', 3', 4'-tetrahydronaphthalen)]-5-one (**20**). – 1) *From* **16**. The bromo-compound **16** (150 mg) hydrogenated as **5** gave **20** (35 mg), m.p. 150–151°. – NMR. ($CDCl_3/D_2O$): 4.8 (*s*, H–C(1')). – $C_{19}H_{18}O_3$: C, H.

2) *From* **18**. The olefinic compound **18** (50 mg) hydrogenated as **5** gave **20** (25 mg), m.p. 149–150°. – NMR.: superimposable with that of **20** obtained from **16**. – $C_{19}H_{18}O_3$: C, H.

6-Bromo-4-phenylbenzo[h]*chroman-2-one* (**21**). As for the preparation of **1** from **5**, compound **21** was obtained in quantitative yield from **16**, m.p. 158–160°. – NMR.: 7.3 (*s*, H–C(5)), 4.4 (*t*, *J* = 6, H–C(4)), 3.1 (*d*, *J* = 6, H–C(3)). – $C_{19}H_{13}BrO_2$: C, H, Br.

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140. A Short Synthesis of 3,5-Dimethyl-1,2,4-trithiolane

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Summary

A short synthesis of 3,5-dimethyl-1,2,4-trithiolane (**1**), a well-known constituent of processed meat, is described.

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