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SYNTHESIS AND CONVERSIONS OF THE DIMER OF 2-METHYLENE-5,6-BENZOCYCLOHEXAN-1-ONE INDUCED BY H_2S AND ACIDS

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Reaction of 5,6-benzocyclohexan-1-one with formaldehyde in the presence of bases gives the Diels–Alder dimer of the intermediate 2-methylene-5,6-benzocyclohexan-1-one and the expected methylenebis-5,6-benzocyclohexan-1-one. The optimal conditions for the formation of the dimer and its conversion into the hydroxy-1,6-diketone are found. The reactions of these products with H_2S and acids are studied. The structures of the newly prepared compounds are confirmed by ^{13}C NMR.

Carbonyl-substituted condensed 5,6-dihydrospirochromanes containing two reaction centers are valuable intermediates in fine organic synthesis. They can be generated during the preparation of dimethylaminomethylcyclanones [1], during thermal decomposition of the latter in the presence of hydroquinone [2], or during their acetolysis [3].

In continuation of studies on the synthesis and characterization of carbonyl-substituted spirohydrochromanes with H_2S and acids, we obtained new data on the reactivity and structures of the starting materials and final products. The structures of the synthesized compounds were found by using ^{13}C NMR.

Thus, spirane I was unexpectedly isolated in 9% yield during vacuum distillation of the reaction mixture following condensation of the α-tetralone with formaldehyde (2:1) in 50% NaOH. It apparently forms by competitive Diels–Alder dimerization of the corresponding 2-methylene-1-tetralone. The desired product, methylenebis-2,2′-(1,2,3,4-tetrahydronaphthalen-1-one) (II) was obtained in 57% yield as a mixture of the threo- and erythroisomers in a 2:1 ratio. These had the same melting point (107°C) as I.

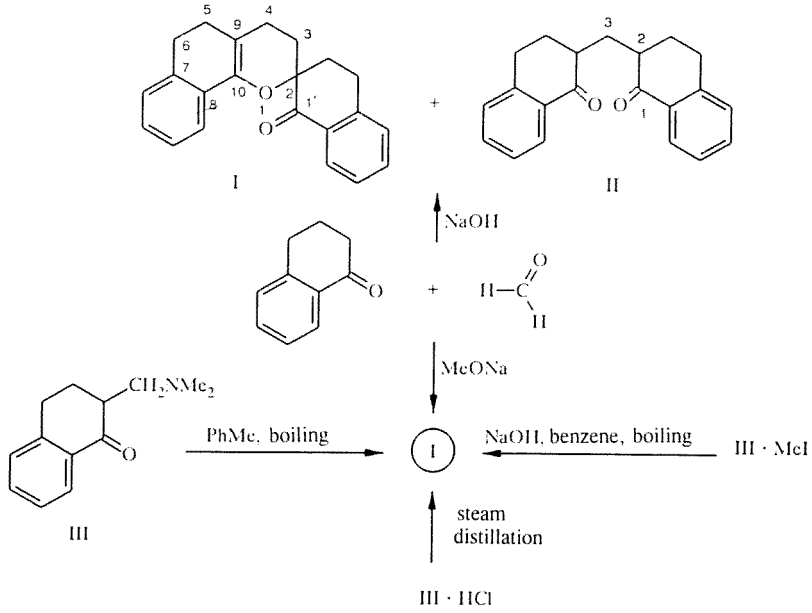

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TABLE 1. ^{13}C NMR Spectra of I, IV, and VI

Compound	Chemical shifts, δ, ppm							
	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$C_{(9)}$	$C_{(10)}$	$C_{(1)}$
I	77,08	26,34	23,05	25,55	27,91	107,09	142,04	195,36
IV	50,72	30,37	31,23	25,37	27,73	119,57	130,18	194,36
V*	87,14	67,40	26,64	25,12	40,90	...	...	...

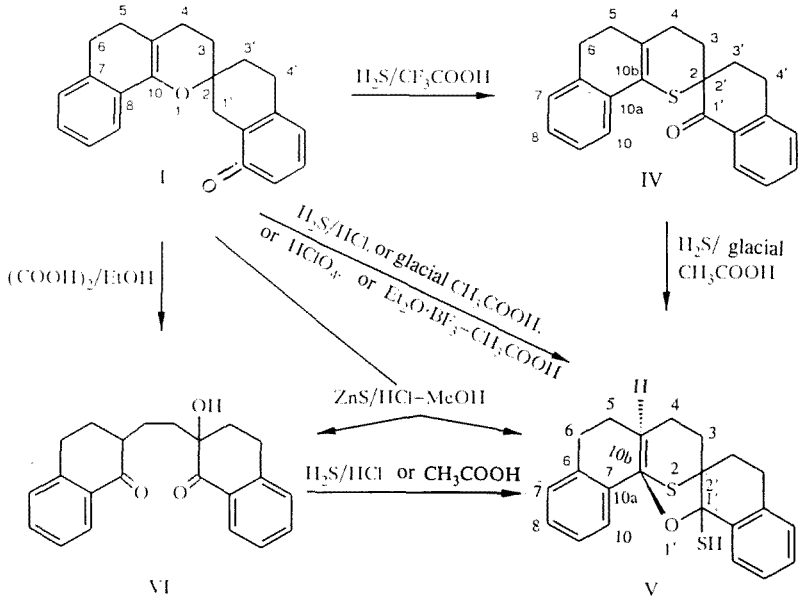
*$C_{(7)}$ 96.65 ppm.

In the ^{13}C NMR of II, only atoms $C_{(1)}$ (200.07 and 199.63 ppm, respectively), $C_{(2)}$ (45.32 and 44.45 ppm), and $C_{(3)}$ (30.31 and 29.63 ppm) show important differences between the threo- and erythroisomers. Characteristic peaks in the ^{13}C NMR spectrum of I are the C atoms of the double bond in the heterocycle, $C_{(9)}$ and $C_{(10)}$ (109.09 and 142.94 ppm, respectively), the spiro atom $C_{(2)}$ (77.08 ppm), and the carbonyl C (195.39 ppm) of the annelated benzene alicycle, which appears at stronger field than that in cyclohexanone (208.9 ppm).

We found that with a 1:1 α-tetralone:trioxane ratio the yield of I reaches 68% in the presence of NaOMe. Compound I is the principal product of boiling Mannich base III in toluene, steam distillation of the hydrochloride of III (III·HCl), or boiling of the methyl iodide of III (III·MeI) in benzene with NaOH.

The availability of I enabled a study of its reactions with H_2S and acids. The absence of systematic investigations of the chemistry of carbonyl-substituted spirohydrochromanes (-thiochromanes) is noteworthy. Only one publication in this area has appeared [4].

We first demonstrated the possibility in principle of recyclizing I by using H_2S. The nature of the protonating agent controls the subsequent S-heterocyclization. Spirothiochromane IV, which is stable under the reaction conditions, forms in 85% yield under the action of H_2S in absolute trifluoroacetic acid. Mineral acids (HCl and $HClO_4$) and boron trifluoride etherate in acetic acid cause a more extensive conversion of I into the polycyclic spiran V with yields of 61, 64, and 76%, respectively.



Spiran V was the principal product (56% yield) from the reaction of I and H_2S in situ (ZnS/HCl) in methanol. In this instance, a significant amount of hydroxy-1,6-diketone VI, which does not contain S, was also obtained. We confirmed the formation of VI by comparing it with a sample prepared by heating I with oxalic acid in aqueous alcohol. Its presence in the reaction mixture and special experiments on the conversion by H_2S and HCl into the mercapto derivative V provided a basis for suggesting a possible mechanism of the above reactions. Recyclization of I to VI, which is stable to acid hydrolysis,

probably occurs first. This agrees with the literature data [3]. Then, VI reacts with the nucleophile H_2S. This is accompanied by cyclization into IV or double cyclization involving the carbonyl of the spirocyclic fragment. The conversion of IV into V under analogous conditions confirms this sequence.

The structures of the products are consistent with their spectra. In contrast with I (see Table 1), the signal of $C_{(2)}$ in IV occurs at stronger field (50.72 ppm). Substitution of the heteroatom affects the signals of the C atoms in the heterocyclic double bond, $C_{(9)}$ and $C_{(10)}$ (119.57 and 130.18 ppm, respectively). For V, the signals are assigned by using spectral parameters for thioacetals, acetals, and condensed oxacyclohexanes [5, 6]: $C_{(2)}$ 87.14, $C_{(3)}$ 67.40, $C_{(7)}$ 96.65 ppm. The signal of $C_{(6)}$ (40.90 ppm) indicates that the tetrahydrothiopyran ring and the alicycle are trans-bonded.

EXPERIMENTAL

Infrared spectra were obtained on a UR-20 spectrometer in KBr pellets and mineral oil. ^{13}C NMR spectra were recorded on a Varian FT-80A Fourier spectrometer at 30°C in $CDCl_3$ at a working frequency 20 MHz. The spectra were calibrated using $CDCl_3$. The course of the reaction and the purity of the products was followed by TLC on Silufol UV-254 plates (hexane–ether–acetone 4:1:1).

The elemental analyses of I-VI agree with those calculated.

Spiro[2,3,5,6-tetrahydro-7,8-benzo-1-chroman-2,2′-(1′,2′,3′,4′-tetrahydronaphthalen-1′-one)] (I, $C_{22}H_{20}O_2$) and methylenebis-2,2′-(1,2,3,4-tetrahydronaphthalen-1-one) (II). A. Sodium hydroxide (2 ml, 50% solution) was added to a mixture of 1,2,3,4-tetrahydronaphthalen-1-one (58.4 g, 0.40 mole), 40% formalin (30 g, 0.40 mole), ethanol (130 ml), and water (70 ml). The mixture was stored for 48 h with subsequent treatment with water (250 ml) and ether (2 × 50 ml). Vacuum distillation gave the 1,5-diketone II (30 g, 57%), bp 110-115°C (6.6 hPa), mp 107°C (ethanol) and I (4.2 g, 9%), bp 135-140 °C (6.6 hPa), mp 106-107°C (hexane). IR spectrum: 1150, 1080, 1065 (C–O–C), 1620 (C=C), and 1725 cm^{-1} (C=O).

B. A mixture of 1,2,3,4-tetrahydronaphthalen-1-one (9 g, 0.06 mole), trioxane (1.83 g, 0.06 mole), and 2 N NaOMe (8.2 ml) was kept at 40-50°C for 12 h. Neutralization with HCl gave I (6.8 g, 68%).

C. A mixture of 2-N,N-dimethylaminomethyl-1,2,3,4-tetrahydronaphthalen-1-one (III, 7 g, 0.04 mole) and hydroquinone (0.005 g) was boiled in absolute toluene (50 ml) for 7-10 h with subsequent vacuum distillation of the solvent. Crystallization of the residue from hexane gave I (3.5 g, 57%).

D. The hydrochloride of 2-N,N-dimethylaminomethyl-1,2,3,4-tetrahydronaphthalen-1-one (III·HCl, 15 g, 0.08 mole) was dissolved in water (300 ml). Hydroquinone (0.015 g) was added. The mixture was steam distilled. The distillate was extracted with ether (3 × 50 ml). The residue after evaporation and combination of the extract crystallized from cold hexane to give I (6.4 g, 58%).

E. The methyl iodide of 2-N,N-dimethylaminomethyl-1,2,3,4-tetrahydronaphthalen-1-one (III·MeI, 5 g, 0.014 mole) and NaOH (0.56 g, 0.014 mole) were boiled in benzene for 5 h. Subsequent distillation of the solvent gave I (2.5 g, 48%).

Spiro(2,3,5,6-tetrahydro-7,8-benzo-1-thiochroman)-2,2′-(1′,2′,3′,4′-tetrahydronaphthalen-1′-one) (IV, $C_{22}H_{20}O_3$). Absolute trifluoroacetic acid (50 ml) was saturated with H_2S for 1 h. Compound I (3.95 g, 0.01 mole) was added. The saturation with H_2S was continued until the reaction was complete (~6 h). Reaction mixture was treated with water (50 ml) and extracted with $CHCl_3$ (2 × 30 ml). Extract was washed with saturated Na_2CO_3 solution and water and dried. The solvent was evaporated to give IV (3.5 g, 85%), mp 147-148 °C (ether). IR spectrum: 1610 (C=C), 1680 cm^{-1} (C=O).

10b,1′-Oxido-1′-mercaptospiro-[(2,3,5,6-tetrahydro-7,8-benzo-1-thiochroman)-2,2′-(1′,2′,3′,4′-tetrahydronaphthalene)] (V, $C_{22}H_{22}O_2$). A. Analogously to the synthesis of IV, I (1.2 g, 0.003 mole) and BF_3 etherate (0.53 g, 0.003 mole) or $HClO_4$ (3 ml, 70%) in glacial acetic acid (50 ml) after saturation with H_2S gave V (0.9 g, 76% or 0.6 g, 64%, respectively), mp 154-155°C (hexane). IR spectrum: 1158, 1080, 1065 (C–O–C), 2540 cm^{-1} (S–H).

B. Glacial acetic acid was saturated with H_2S for 1 h. Compounds I, IV, or VI (0.01 mole) were added. The reaction mixture was simultaneously saturated with H_2S and HCl for 7 h until the reaction was complete. The crystals of V that formed were separated and washed with hexane.

C. A HCl solution (40 ml, 5 N) was added over 40 min to a stirred mixture of I (3.0 g, 0.008 mole) and ZnS (1.2 g, 0.012 mole) in absolute methanol. The crystals that formed were separated. The mixture was chromatographed on an Al_2O_3 column (III degree activity, 300 × 50 mm, 6:1 hexane:$CHCl_3$) to give V (2.8 g, 57%) and VI (0.6 g, 18%).

2-Hydroxy[ethylenebis-2,2′-(1,2,3,4-tetrahydronaphthalen-1-one)] (VI, $C_{22}H_{22}O_3$). A mixture of I (3.16 g, 0.01 mole) and oxalic acid (9 g, 0.1 mole) in ethanol (50 ml) was heated on a water bath for 10 h, diluted with water (100 ml), and

extracted with $CHCl_3$ (3 × 30 ml). The entire extract after removal of solvent gave VI (1.8 g, 53%), mp 201-202 °C. IR spectrum: 1660 (C=O), 3140-3160 cm^{-1} (O–H).

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REFERENCES

1. M. H. Holehosse and Z. J. Zostfler, J. Pharm. Sci., **6**, 715 (1982).
2. M. J. Roth and M. Haupt, Arch. Pharm., **4**, 241 (1975).
3. M. J. Roth and G. Dvorak, Arch. Pharm., **8**, 510 (1963).
4. S. Motoki and J. Wantonove, J. Org. Chem., **23**, 4151 (1979).
5. S. K. Klimenko, T. I. Tyrina, T. V. Stolbova, N. N. Sorokin, and V. G. Kharchenko, Khim. Geterotsikl. Soedin., No. 9, 1194 (1985).
6. L. M. Yudovich, N. S. Smirnova, G. I. Rybina, O. V. Bryukhanova, and V. G. Kharchenko, Zh. Org. Khim., **23**, 2333 (1987).