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SYNTHESIS OF CYCLIC SULPHONIUM SALTS INVOLVING REARRANGEMENT OF CARBONIUM IONS.

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The synthesis of thiachromans, thianaphthalenium salts and thiacyanine dyes by interaction of β-arylmercaptoethyl methyl ketones and 4-methylthiachroman-4-ols with acids (polyphosphoric, perchloric or sulphuric) has been reported by us earlier[1,2]. These reactions involve acid catalysed intermolecular hydride shift from the intermediate Δ^3-thiachromenes which are formed <u>in situ.</u>

In order to study the structural and stereochemical factors which govern these hydride transfers, acid induced cyclization of a series of 3-oxoalkylphenyl sulphides and 3-oxoalkylaryl phenyl sulphides was studied. Whereas details of this work will be published elsewhere, presently the cyclodehydration of two ketones and a secondary alcohol containing an iso-propyl and a tert-butyl group is now reported. These cyclizations involve an interesting rearrangement of the incipient carbonium

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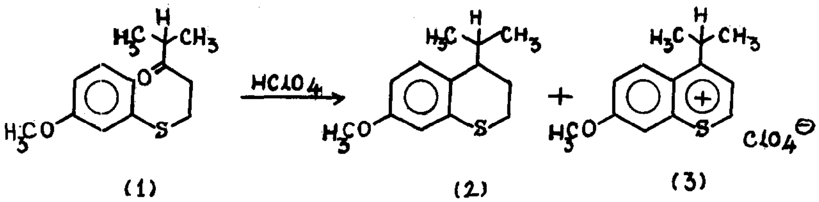
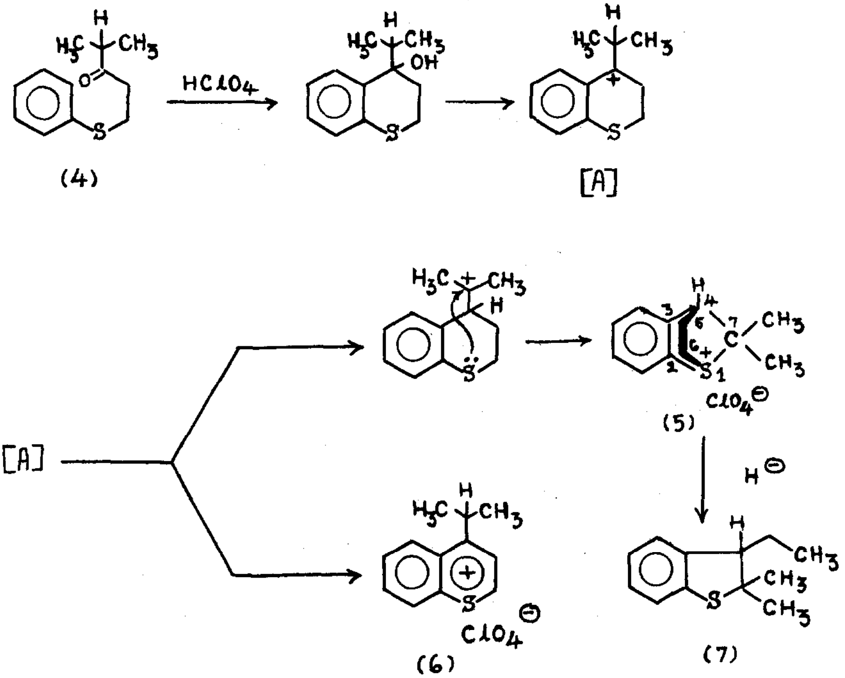
ions which are formed by protonation of the respective starting materials.

When 3-oxo-4-methyl-1-pentyl m-methoxyphenyl sulphide (1) was treated with 60% aqueous perchloric acid (at 27-28°; 3 hours), 4-isopropyl-7-methoxythiachroman (colourless liquid, b.p. 125-130° 0.7 mm. yield 38%) (2) and 4-isopropyl-7-methoxythianaphthalenium perchlorate, m.p. 140° (yellow needles, yield 32%) (3) were obtained as expected by disproportionation involving hydride transfer.



In contrast with the above cyclization, 3-oxo-4-methyl-1-pentyl phenyl sulphide (4), on treatment with 60% aqueous perchloric acid (3 hours at 27-28° and then 70-80° for 45 minutes), gave a colourless crystalline perchlorate, m.p. 140° (5) (plates from ACOH/$HClO_4$; yield, 22%). The latter was obtained by removal of unreacted (4) and diphenyl disulphide by means of petroleum ether and subsequent dilution of the perchloric acid solution with diethyl ether. Absorption spectrum of the perchloric acid mother liquor left after removal of (5) revealed the presence of a thianaphthalenium salt (probably 6), which was, however, not isolated.

The perchlorate (5) has been assigned the structure 2,3-benzo-7,7-dimethyl-bicyclo- [2.2.1] -heptene-1-sulphonium perchlorate, and its formation from (4) and its reaction with sodium bdrohydride to give 2,2-dimethyl-3-ethyl-2,3-dihydrobenzo-b-thiophene (7) is rationalised as follows :-

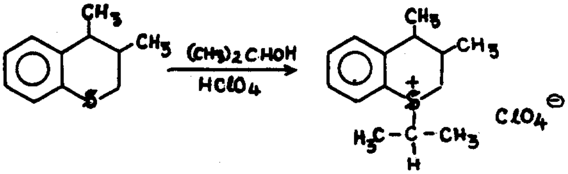


The structure (5) for the above perchlorate is assigned on the basis of the following evidence and arguments:-

(1) C, H, S and Cl content.

(2) Solubility in water, ethanol and acetic acid; it explodes on heating.

(3) Its U.V. spectrum λ max (mμ) (log ϵ) :- 276 (2.89), 268 (2.95), S 263 (2.84) is different from that expected for thianaphthalenium salts, and was very similar to that of 1-isopropyl-3,4-dimethylthiachromanyl sulphonium perchlorate (9), m.p. 143-144° [λ max (mμ) (log ϵ) :- 280 (3.08), 273 (3.12), S 263 (3.04)]. The latter was prepared by treating 3,4-dimethylthiachroman (8)[3] with isopropyl alcohol and perchloric acid.



(8) (9)

(4) Bicyclic sulphonium salts have been prepared earlier by interaction of cyclic sulphides with a carbonium ion generated at a suitable location[4].

(5) NMR spectrum (in trifluoroacetic acid) showed the following characteristics :-

- (a) Two methyl singlets at δ 1.47 and δ 1.85.
- (b) A band for $-S-CH_2-$ protons centered at δ 4.0.
- (c) A complex broad band centered at δ 3.0 (benzylic methine proton)
- (d) Four aromatic protons centered at δ 7.7. The paramagnetic shift of aromatic protons is ascribed to the delocalised positive charge on the sulphur atom.

The structure (5) for the perchlorate is further supported by its conversion to (7) by interaction with sodium borohydride. The latter structure for the reduction product (homogeneous as shown by VPC) was assigned on the basis of the following data :-

a) Analysis corresponds to $C_{12}H_{16}S$; Molecular Wt. by mass spectrum 192 (Calculated, 192).

b) Its U.V. spectrum [λ max (mμ) (log ϵ) :- S 300 (3,04), S 288 (3,19), S 265 (3.69), 250 (3.97)] is different from that of thiachromans.

c) NMR spectrum of (7) showed the following characteristics:-

  (a) Two methyl singlets at δ 1.35 and δ 1.45 (gem-dimethyl)

  (b) A triplet at δ 2.65 (J = 7 cps) (benzylic methine proton).

  (c) An ethyl group with methyl triplet at δ 0.95 and a - CH_2 - band centered at δ 1.7.

  (d) Four proton aromatic band centered at δ 6.9.

Interaction of 3-oxo-4,4-dimethyl-1-pentyl phenyl sulphide (10), containing a tertiary butyl group, with 70% aqueous perchloric acid (10 hrs at 27-28° and then 2 hours at (60-70°) gave on saturation with diethyl ether and cooling to 0° for 24 hours, a colourless crystalline perchlorate m.p. 173° (needles from $ACOH/HClO_4$) (yield 20%). The latter is assigned the structure 2,3-benzo-4,7,7-trimethyl-bicyclo-[2.2.1]-heptene-1-sulphonium perchlorate (11) because of its close similarity [water solubility, elementary analysis, U.V. spectrum: λ max (mμ) (log ϵ) :- 276 (2.96), 269 (3,05), S 262 (2.99)] with the perchlorate (5). The structure (11) was further confirmed by its NMR spectrum (in trifluoroacetic acid) which showed the following characteristics :-

a) Three methyl singlets at δ1.32, δ1.71, δ1.8.

b) Broad bands between δ2 - δ4 for four ($-S-CH_2-CH_2$) protons.

c) Four aromatic protons centered at δ7.75.

As in the case of (5), sodium borohydride reduction of (11) gave 3-ethyl-2,2,3-trimethyl-2,3-dihydrobenzo-b-thiophene (12). The structure for the latter follows from the following evidence :-

1) U.V. Spectrum λ max (mμ) (logϵ) :- S 300 (3.05), S 290 (3.25), S 265 (3.45), 252 (3.78).

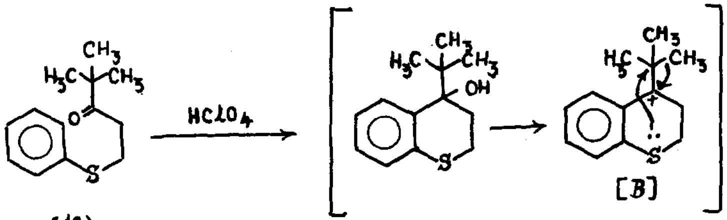
2) Its NMR spectrum showed the following characteristics :-

   a) Three methyl singlets (gem-dimethyl) and C_3-methyl at δ1.18, δ1.35 and δ1.38.

   b) An ethyl group with methyl triplet centered at δ0.7 ($J = 7.5$ cps) and a $-CH_2-$ band centered at δ1.9. The higher chemical shift of the methyl triplet is due to long-range shielding by the phenyl ring (as shown by a Dreiding model).

   c) Four aromatic protons multiplet centered at δ6.95.

The synthesis of (11) from (10) and of (12) from (11) may be rationalised as follows :-



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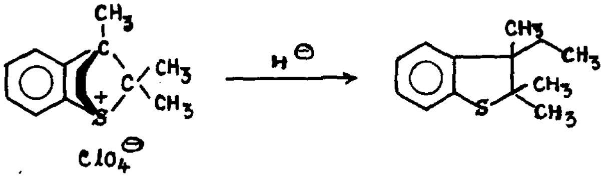


(11) (12)

Finally, the cyclization of 3-hydroxy-4-methyl-1-pentyl phenyl sulphide (13) (by interaction with 60% aqueous perchloric acid (4 hours at 27-28° and 1 hour at 70-80°) was studied. Work up of the mixture by saturation with diethyl ether gave a colourless perchlorate (14) which crystallised from $ACOH/HClO_4$ in needles, m.p. 135-136°, (yield, 50%).

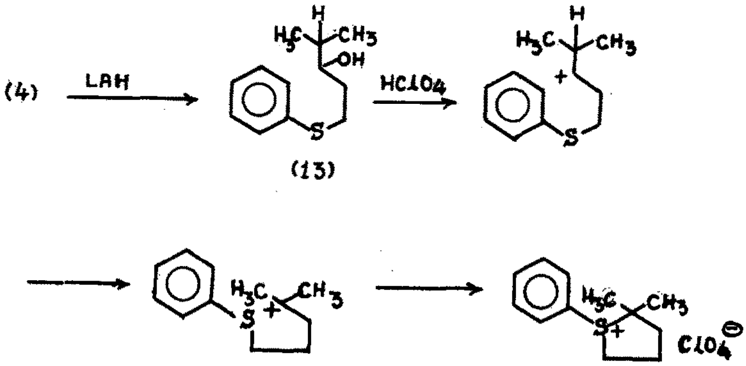
The perchlorate has been assigned the structure of 2,2-dimethyl-1-phenyl-2,3,4,5-tetrahydrothiophenium perchlorate (14) on the basis of its elementary analysis, solubility in water, U.V. spectrum λ max (mμ) (logϵ) :- 277 (2.72), 270 (2.95), 263 (3.0), 261 (3.03), 258 (3.04), S 255 (3.06) and NMR spectrum. The latter shows the following characteristics :-

a) Two methyl singlets at δ 1.35 and δ 1.85.

b) A band for $-S-CH_2-$protons centered at δ 4.15.

c) A complex broad band between δ 2 to δ 3 for four protons. ($-CH_2-CH_2-$)

d) A five proton phenyl peak at δ 7.82.



(13)

(14)

Whereas cyclic sulphonium perchlorates have been prepared earlier by interaction of the sulphur atom in saturated heterocyclics[5] with a carbonium ion derived from a leaving group such as ~~k~~ a hydroxyl or a halogen atom, the present work appears to illustrate the first example of :-

a) The synthesis of bicyclic sulphonium perchlorates with sulphur atom at a bridgehead and containing a fused aromatic ring and (b) the synthesis of cyclic sulphonium perchlorates involving a rearrangement of the carbonium ions in a manner more suited for participation of the sulphur atom in forming a bicyclic sulphonium salt. The driving force for the latter rearrangement seems to be the relief of steric strain (between the isopropyl or t-butyl group and the peri-hydrogen atom in the ions A and B) following rearrangement together with the facile participation of the S-atom in the newly-formed tertiary carbonium ion. However, when the ions (e.g. A,B) are further stabilised by a p-methoxy group, no rearrangement was observed (cf. formation of 3 from 1).

It is hoped th synthesise other complex bicyclic sulphonium salts with or without fused aromatic rings and containing an additional heteroelement such as nitrogen. The broad spectrum biological activity of the bicyclic sulphonium salts and their derivatives is also under investigation.

Compounds (1) (4) and (10) were prepared by the condensation of the relevant arylmercaptans with mannich bases obtained from methyl isopropyl ketone and methyl tert-butyl ketone (using morpholine as base). Compound (13) was obtained by lithium aluminium hydride reduction of the ketone (4).

The elementary analysis of the compounds described are in conformity with the structures assigned.

ACKNOWLEDGEMENT.

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