The value of magnetic moment (μ_{eff}) of these complexes are in the range of 5·05 to 5·19 BM.[3], suggesting the presence of three unpaired electrons and hence the complexes are spin-free with octahedral stereochemistry.

The infrared spectrum of the parent complexes has confirmed the presence of coordinated water molecules ~3,450 cm^{-1}, while the complexes derived from 8-hydroxyquinoline do not show absorption in this region. This indicates that these mixed ligand complexes are anhydrous. The significant bands ν(C–N) and ν(C–O) due to coordinated 8-hydroxyquinoline occurs around 1590 cm^{-1} and 1095 cm^{-1} respectively[4]. The bands ν(C–O), ν(C–C) and ν(M–O) due to coordinated acetylacetone[5], methylacetoacetate and ethylacetoacetate[6] have been given in Table I.

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5-SUBSTITUTED-1, 3, 4-THIADIAZOLYL-2-DITHIOCARBAMYL-(N,N,N-TRIALKYL) ETHYL AMMONIUM IODIDES AS ANTI-ACETYL-CHOLINESTERASES

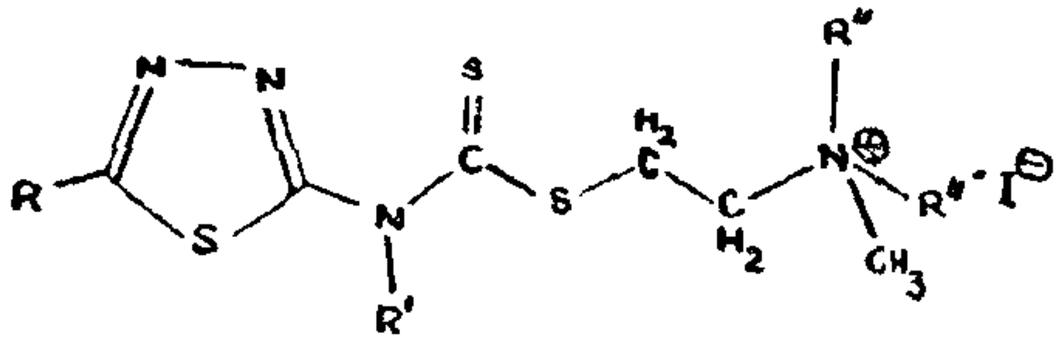
QUATERNARY ammonium salts have been found active as cholinergics[1] as well as anti-cholinergics[2,3]. In the last communication[4], a few title compounds were described to be the CNS excitants. This indicated a cholinergic mechanism of action of these quaternary ammonium compounds on the central nervous system of mice. To substantiate this observation, the title compounds have been screened out for anti-acetyl-cholinesterase activity on isolated brain tissues of rats. The compounds have been found to possess good anti-acetyl-cholinesterase activity.

The method of Parmar *et al*[5] was adopted to estimate anti-acetyl-cholinesterase activity of the compounds. The substrate used was acetyl-thiocholine iodide. The 'sulfhydryl' content of the thiocholine, liberated after enzymatic hydrolysis, was determined colorimetrically in a spectrophotometer at a wavelength of 520 mμ. The reduction in the 'Sulfhydryl' content, when the title compounds took part in the reaction, marked the anti-acetyl-cholinesterase activity of the test compounds.

The anti-acetyl-cholinesterase activity of the title compounds are listed in Table I.

TABLE I

Anti-acetyl-cholinesterase activity of 5-substituted-1, 3, 4-thiadiazolyl-2-dithiocarbamyl-(N, N, N-trialkyl)- ethyl ammonium iodides



Sl. No.	R	R′	R″	Anti-acetyl-cholinesterase activity (% inhibition)
1.	–H	$-CH_3$	$-CH_3$	55
2.	$-CH_3$	$-CH_3$	$-CH_3$	50
3.	$-C_2H_5$	$-CH_3$	$-CH_3$	42
4.	$-n\cdot C_3H_7$	$-CH_3$	$-CH_3$	35
5.	$-n\cdot C_4H_9$	$-CH_3$	$-CH_3$	34
6.	$-C_6H_5$	$-CH_3$	$-CH_3$	25
7.	$-SCH_3$	$-C_6H_5$	$-CH_3$	25
8.	$-SCH_3$	$o-CH_3.C_6H_4-$	$-CH_3$	25
9.	$-SCH_3$	$m-CH_3.C_6H_4-$	$-CH_3$	51
10.	$-SCH_3$	$p-CH_3.C_6H_4-$	$-CH_3$	66
11.	$-C_6H_5$	$-CH_3$	$-C_2H_5$	25
12.	$-SCH_3$	$-C_6H_5$	$-C_2H_5$	28
13.	$-SCH_3$	$o-CH_3.C_6H_4-$	$-C_2H_5$	30
14.	$-SCH_3$	$m-CH_3.C_6H_4-$	$-C_2H_5$	64
15.	$-SCH_3$	$p-CH_3.C_6H_4-$	$-C_2H_5$	85

Discussion.—From the results (Table I) the following are evident :

1. Comparing the activity of compounds 6–10 with compounds 11–15, in the light of their structure at the substituent R", it is clear that the replacement of 'CH_3' group on the cholinic nitrogen atom by 'C_2H_5' group slightly increases the antiacetylcholinesterase activity.

2. Further, comparing the activity of compounds 1–6 in the light of their structures at R substituent, it is clear that increases in the bulk of R group at 2-position of thiadiazole ring in the title compounds, decreases the anti-acetylcholinesterase activity.

3. Change in the position of 'CH_3' group on the phenyl ring substituted on R' (compounds 8–10 and 13–15) is of high significance. As CH_3 group moves from 'o', 'm' to 'p'–position on phenyl ring, the activity increases in title compounds.

4. The good anti-acetyl-cholinesterase activity of the title compounds also gives, to some extent, the cholinergic mechanism of exciant action of these compounds on CNS[4].

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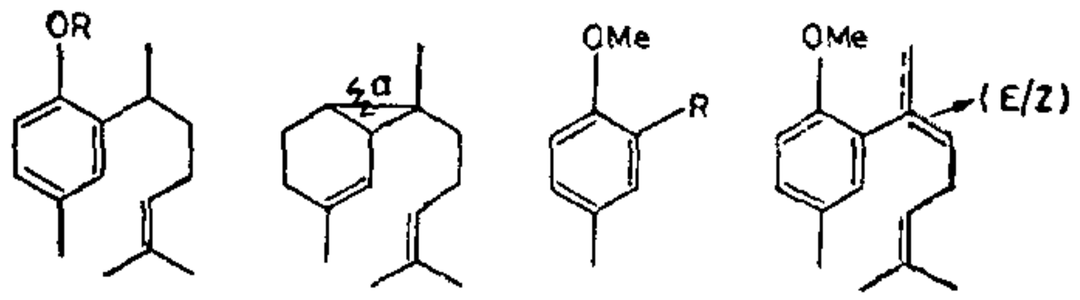
SYNTHESIS OF ELVIROL METHYL ETHER

BECAUSE of the biogenetic interest of the phenolic sesquiterpenoid elvirol[1] (I *a*), which we suggest, may originate from sesquicarene[2] (II) by oxidative ring fission (bond *a*) followed by aromatisation, several syntheses of the phenol and its methyl ether have been reported[3]. In continuation of our work on phenolic secosesquiterpenoids[4], a two-step synthesis[5] of elvirol methyl ether (I *b*) is described in this communication.

2-Bromo-4-methylanisole (III *a*) [NMR (60 MHz, CCl_4 + TMS): δ 2·16 (3H, s, Ar-Me), 3·5 (3H, s, Ar–OMe) and 6·53–7·33 (3H, m, Ar–H)] obtained either from *p*-cresol methyl ether by bromination in glacial acetic acid[6] or from 2-bromo-4-methyl phenol[7] by methylation with dimethyl sulphate in alkali, was reacted with lithium dust in ether under nitrogen to furnish 2-methoxy-5-methylphenyl lithium (III *b*). Treatment of 6-methylhept-5-en-2-one with the aryllithium (III *b*) in ether followed by work-up with aqueous hydrochloric acid (1 : 1), and chromatographic purification of the product (silica gel column-hexane gave the arylheptadiene (IV) in 90% yield [IR ν_{max} (neat): 1620 and 1605 cm^{-1} (aromatic and C=C); NMR (CCl_4): δ 1·70 (3H, bs,-vinyl-Me), 1·75 (3H, bs, vinyl-Me), 2·0 (bs, Ar-C(=)–Me), 2·3 (3H, s, Ar–Me), 2·35–3·00 (m, $>CH_2$), 3·75 (3H, s, Ar–OMe), 4·9–5·4 (m, vinyl-H) and 6·65–7·17 (3H, m, Ar–H)]. Identical diene (IV) (IR, NMR and TLC) was obtained by treatment of methylheptenone with 2-methoxy-5-methylphenylmagnesium bromide (III *c*).



I a, R = H
b, R = Me

II

III a, R = Br
b, R = Li
c, R = Mg Br

IV

The regioselective reduction of the styryl double bond in the diene (IV) by lithium in liquid ammonia[8] (dried over sodium), followed by decomposition with ammonium chloride and chromatographic purification of the product (silica gel column-hexane) gave elvirol methyl ether (I *b*) in 87% yield [IR (neat): 1605 and 1595 cm^{-1} (aromatic and C=C); NMR (CCl_4): δ 1·13 (3H, d, J = 7Hz, Ar-CHMe), 1·46 (3H, s, vinyl-Me), 1·60 (3H, s, vinyl-Me), 1·3–2·0 (4H, m, CH_2), 2·2 (3H, s, Ar-Me), 2·8–3·26 (1H, m, Ar-CHMe), 3·7 (3H, s, Ar-OMe), 5·05 (1H, m, vinyl-H) and 6·46–6·93 (3H, m, Ar-H)]. The spectral characteristics of the specimen agree with those reported for elvirol methyl ether[3] (I *b*). After completion of this work[5] our attention was drawn to an account of