Tetrahedron Vol 44, No 7, pp 2063 to 2066, 1988
Printed in Great Britain.

0040-4020/88 $3.00+ 00
Pergamon Press plc

PENTATHIOMONOORTHOOXALATES[x]

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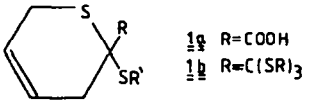
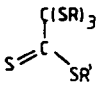
(*Received in UK 29 December 1987*)

Summary: Reaction of trialkyl trithioorthoformate anions with carbon disulphide and subsequent methylation of the products gave methyl tris-alkylthio-dithioacetates (pentathiomonoorthooxalates). Attempted Diels-Alder reaction of this new species gave rise to open-chain hexa-1,4Z-dienes 6a-c instead of the expected thiopyran adducts.

Our synthetic studies required thiopyrancarboxylic derivatives of type 1a, having the carboxylic function in a masked form permitting carbanionic manipulations on the heterocyclic ring. Since such unsaturated thianes can easily be prepared using hetero-Diels-Alder reactions of thiocarbonyl compounds[1-3] we chose a properly functionalised dithiocarboxylate for this purpose. As a trithio-orthoester function satisfies the conditions for the masked, easily regenerable carboxyl we thought that a tris-alkylthio-dithioacetic ester 2 (a pentathio-monoorthooxalate) could be the compound of choice.

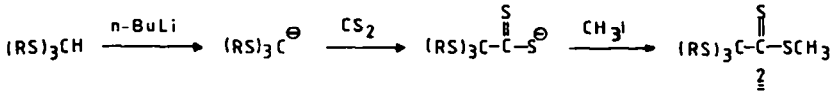


1a R=COOH
1b R=C(SR)$_3$



2a R=R'=CH$_3$
2b R=C$_2$H$_5$ R'=CH$_3$
2c R=CH$_2$C$_6$H$_5$ R'=CH$_3$

We have prepared three derivatives of 2 using methyl, ethyl and benzyl trithioorthoformate anions obtained from the appropriate thioorthoformates by lithiation[4]. Reaction of these anions with carbon disulphide and subsequent methylation with methyl iodide afforded the expected products 2a-c as unstable oils.



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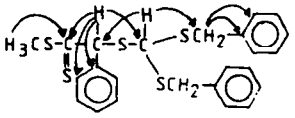
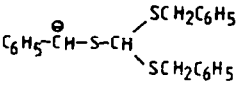
[x] Dedicated to Professor Rezső Bognár on the occasion of his 75th birthday.

In the case of 2c we could isolate a crystalline side product from the reaction mixture. The structure of this compound was deduced completely from NMR measurements. The ^{1}H-NMR spectrum indicated the presence of two methylene groups and two isolated CH-protons with distinctly different chemical shifts instead of the expected three CH_2S signals. The dithiocarboxylate group was identified on the basis of a quaternary carbon resonance at 233.56 ppm, characteristic[5] for the C=S in such systems. On the other hand, the chemical shift of the CH-carbon at 52.19 ppm is characteristic for trithioorthoformates[6]. Consequently, the structure of 3 was inferred from the evidence above. The correctness of this assumption was demonstrated by selective INEPT measurements[7]. Pathways, indicated be arrows of selective ^{1}H-^{13}C magnetisation transfer experiments permitted an unambigous selection of structure 3 as the correct one among the six alternative structures that are also compatible with the ^{1}H- and ^{13}C-NMR shifts.



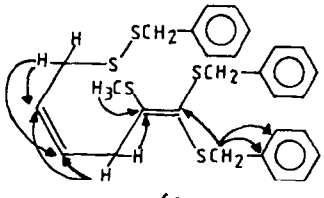
3



4

Formation of 3 can be attributed to a concurrent deprotonation of a benzylic methylene or a rearrangement of the intermediate orthoformate anion to give 4. Existence of 4 can be explained by steric compression of the tribenzyl trithioorthoformate anion.

In order to study the reactivities of 2a-c they were reacted with 1,3-butadiene at 100°, but unfortunately instead of the expected 5a-c another type of compounds have been obtained. Structure elucidation of these products required extensive NMR studies. The ^{1}H-NMR spectrum of 6c displayed two groups of SCH_2 singlets in a 2:1 ratio at 4.00 and 3.57 ppm, respectively. This is clearly incompatible with structure 5c. The ^{13}C-NMR data were also at variance with this structure since two quaternary carbon resonance occurred at 140.84 and 135.96 ppm instead of around 60 ppm expected for 5c. This indicated the presence of two quaternary sp^2-carbons. Structure 6c could than be unequivocally established from a series of selective INEPT measurements[7] as indicated in the scheme below.

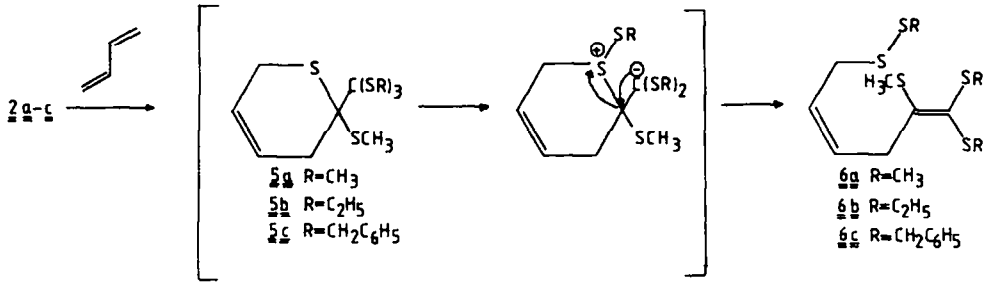


6c

The lack of the long-range connectivity across the sulphur atom with SCH_2 protons at 3.57 ppm establishes the disulphide bond. 6a and 6b displayed ^{1}H- and ^{13}C-NMR spectra very similar to those of 6c, in accordance with the analogous ketene dithioacetal structure.

We could not isolate a normal Diels-Alder adduct from the reaction mixtures because under milder conditions no reaction can be observed. However, the intermediacy of 5a-c must be considered.

We postulate that because of the high steric compression in the trithio-orthoester grouping of the presumed 1b one of the alkylthio groups migrates onto the sulphur of the ring, and the decomposition of the intermediate thiasulphonium derivative leads to compounds 6a-c.



EXPERIMENTAL

General methods: Solutions were concentrated at 40° (bath) at ca. 17 mmHg. Chromatography was performed on Kieselgel 60. ^{1}H- and ^{13}C-NMR spectra were recorded with a Bruker WP-200 SY spectrometer for solutions in $CDCl_3$. Mass spectra were obtained by using a VG-7035 GC/MS/DS instrument (70 eV).

Preparation of pentathiomonoorthooxalates 2a-c: The appropriate trithio-orthoformate[8,9] (1 mM) in dry tetrahydrofuran (5 mL) was treated with 1mM of n-butyllithium (1.6 M solution in hexanes) at -78° under nitrogen athmosphere. After 15 minutes 1.1 mM of carbon disulphide was added and the mixture was stirred for 30 minutes while the temperature was allowed to rise to -20°. Then methyl iodide (1.1 mM) was added and stirred for another 1h at the same temperature. After bringing to room temperature the solvent was evaporated, the residue was extracted with ether, the etheral extract washed with water, dried ($MgSO_4$) and evaporated to give the crude product as a red oil. This was chromatographed using a hexanes-$CHCl_3$ 8:2 mixture as eluent.

Methyl tris-methylthiodithioacetate 2a. Yield: 71.8 %. ^{1}H-NMR (200 MHz, $CDCl_3$) δ 2.14 (s, 9H, 3xSCH_3); 2.63 (s, 3H, SCH_3) ppm. MS m/e 244 (M^+); 197 (M^+-SCH_3); 153 (M^+-$CSSCH_3$); 91 (M^+-$C(SCH_3)_3$). Anal.:Calc. for $C_6H_{12}S_5$: S, 65.58; Found: S, 65.23.

Methyl tris-ethylthiodithioacetate 2b. Yield: 71.8 %. ^{1}H-NMR (200 MHz) δ 1.28 (t, 9H, 3x$SCH_2\underline{CH_3}$); 2.61 (s, 3H, SCH_3); 2.71 (q, 6H, 3x$S\underline{CH_2}CH_3$) ppm. MS m/e 286 (M^+); 225 (M^+-SCH_2CH_3); 195 (M^+-$CSSCH_3$). Anal.: Calc. for $C_9H_{18}S_5$: S, 55.95; Found: S, 55.81.

Methyl tris-benzylthiodithioacetate 2c. Yield: 60.8 %. ^{1}H-NMR (200 MHz) δ 2.60 (s, 3H, SCH_3); 3.68 (s, 2H, SCH_2); 3.98 (s, 4H, 2xSCH_2); 7.1-7.3 (m, 15H,aromatic) ppm. MS m/e 473 (M^+); 381 (M^+-$CSSCH_3$). Anal.: Calc. for $C_{24}H_{24}S_5$: S, 33.91; Found: S, 33.68.

Methyl bis-benzylthiomethylthio-phenyldithioacetate 3. Yield: 23.0 %. ^{1}H-NMR (200 MHz) δ 2.51 (s, 3H, SCH_3); 3.66 (s, 2H, SCH_2); 3.68 (s, 2H, SCH_2); 4.15 (s, 1H, $HC\lesssim^{S}_{S}$); 5.43 (s, 1H, CH-S); 6.75-7.35 (m, 15H, aromatic) ppm. ^{13}C-NMR (50.3 MHz) δ 19.98 (SCH_3); 36.43; 36.50 (SCH_2); 52.19 ($C\lesssim^{S}_{S}$); 66.74 (C -$CSSCH_3$); 126.77; 126.87; 127.94; 128.12; 128.43; 128.49; 128.83; 128.88 (CH, aromatic); 137.41; 137.61 (benzylthio C_q); 138.16 (C_6H_6, C_q); 233.56 (SC=S) ppm. MS m/e 426 (M^+-SCH_3) 382 (M^+-$CSSCH_3$); 292 (M^+-$H_3CSC(S)CHC_6H_5$). Anal.: Found for $C_{24}H_{24}S_5$: S, 34.08. m.p. 106-107°.

Preparation of 6a-c: Compounds 2a-c were heated with excess of 1,3-butadiene in benzene at 80-100° in a sealed tube for 12h. The solvent was evaporated, the residue was chromatographed using hexanes-$CHCl_3$ 8:2 mixture as eluent.

1,1,2-Tris-methylthio-6-methyldithio-hexa-1,4Z-diene 6a. Yield: 74.8 %. ^{1}H-NMR (200 MHz) δ 1.99 (s, 3H, $SSCH_3$); 2.37; 2.40; 2.41 (ss, 9H, 3xSCH_3); 3.04 (m, 2H, H-6,6'); 3.50 (m, 2H, H-3,3', $J_{3,4}$= 5.0 Hz); 5.57 (m, 2H, H-4,5) ppm. ^{13}C-NMR (50.3 MHz) δ 14.14 (SCH_3); 18.25 (SCH_3); 35.20 (C-6); 36.76 (C-3); 127.71; 129.21 (C-4, C-5); 135.28 (C-1). 140.14 (C-2) ppm. MS m/e 298 (M^+); 251 (M^+-SCH_3); 219 (M^+-$SSCH_3$). Anal.: Calc. for $C_{10}H_{18}S_5$: S, 53.70; Found: S, 53.40.

1,1-Bis-ethylthio-2-methylthio-6-ethyldithio-hexa-1,4Z-diene 6b. Yield: 65.3 %. ^{1}H-NMR (200 MHz) δ 1.26 (t, 9H, 3x$CH_2\underline{CH_3}$); 2,50 (q, 2H, $SS\underline{CH_2}CH_3$); 2.88 (q, 4H, 2x$S\underline{CH_2}CH_3$); 3.10 (d, 2H, H-6,6'); 3.52 (d, 2H, H-3,3'); 5.60 (m, 2H, H-4,5) ppm. ^{13}C-NMR (50.3 MHz) δ 14.39 ($SSCH_2\underline{CH_3}$); 14.60; 14.66 ($SCH_2\underline{CH_3}$); 18.49 (SCH_3); 24.61 ($SS\underline{CH_2}CH_3$); 29.46 ($S\underline{CH_2}CH_3$); 32.94 (C-6); 37.13 (C-3); 127.72; 129.80 (C-4, C-5); 137.32 (C-1); 138.06 (C-2) ppm. MS m/e 340 (M^+); 279 (M^+-SCH_2CH_3). Anal.: Calc. for $C_{13}H_{24}S_5$: S, 47.07; Found: S, 47.43.

1,1-Bis-benzylthio-2-methylthio-6-benzylthio-hexa-1,4Z-diene 6c. Yield: 42.2 %. ^{1}H-NMR (200 MHz) δ 2.20 (s, 3H, SCH_3); 2.92 (d, 2H, H-6,6'); 3.33 (d, 2H, H-3,3'); 3.60 (s, 2H, $SS\underline{CH_2}C_6H_5$); 4.05 (s, 4H, 2x$S\underline{CH_2}C_6H_5$); 5.48 (m, 2H, H-4,5, $J_{4,5}$= 5.0 Hz); 7.2 (m, 18H, aromatic) ppm. ^{13}C-NMR (50.3 MHz) δ 18.45 (SCH_3); 32.51 (C-6); 34.80 ($SS\underline{CH_2}C_6H_5$); 37.07 (C-3); 39.68 ($S\underline{CH_2}C_6H_5$); 128.01 (C-5); 129.35 (C-4); 135.96 (C-1); 140.84 (C-2) ppm. MS m/e 528 (M^+). Anal.: Calc. for $C_{28}H_{30}S_5$: S, 30.43; Found: S, 30.46.

Acknowledgments: This work was financially supported by the Hungarian Academy of Sciences through a grant TPB KKFA. The authors are indebted to the analytical laboratory for the elemental analyses and to Dr. Z. Dinya for the mass spectra.

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