Tetrahedron Vol. 37, pp. 743 to 746
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0040-4020/81/0215 0743/$02.00/0

A NOVEL THERMAL REARRANGEMENT OF THE 2-THIABICYCLO[3, 1, 0]HEX-3-ENE SYSTEM. THE CRYSTAL AND MOLECULAR STRUCTURE OF ETHYL-2,4-DICHLORO-5-HYDROXY-6-METHYLBENZOATE

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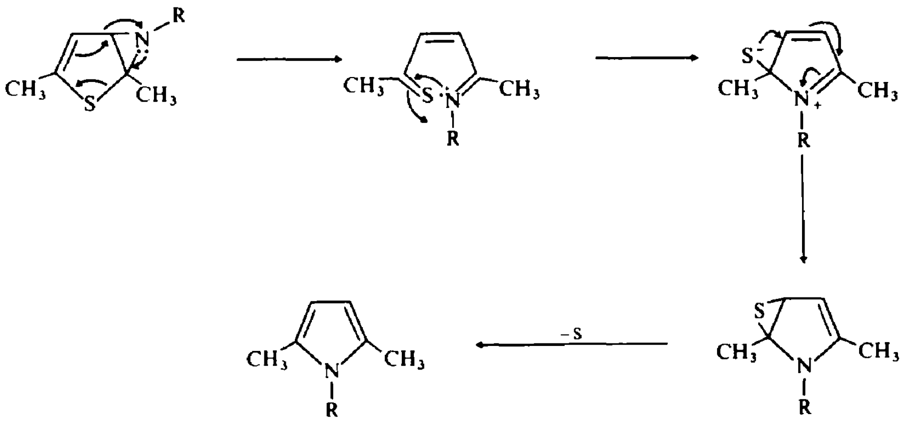
(*Received in France* 5 *March* 1980)

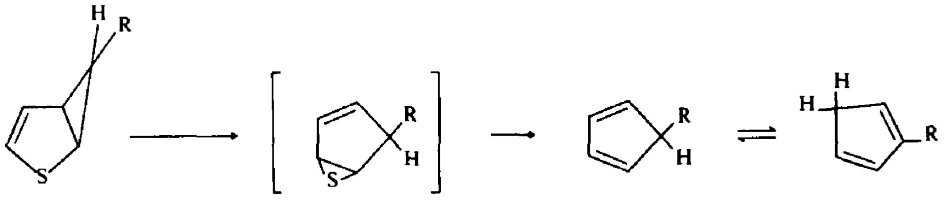
Abstract—Thermal rearrangement of 1,3-dichloro-6-ethoxycarbonyl-2-thiabicyclo[3,1,0]hex-3-ene does not follow the anticipated course, but leads instead to ethyl-2,4-dichloro-5-hydroxy-6-methylbenzoate, whose structure has been confirmed by an X-ray crystal structure determination.

During the course of a systematic investigation of the reactions of diazoalkanes[1] with thiophen and its derivatives we have had cause to note[2] the apparent thermal instability of the 2-thiabicyclo[3,1,0]-hex-3-ene ring system. Thus, for example, prolonged heating of the ester (1, $R=CO_2Et$, $R^1=H$) during distillation results in extensive decomposition with the formation of a number of unidentified products. In view of the potential importance of (1, $R=CO_2Et$, $R^1=H$) as an intermediate in the synthesis of 2-(3-thienyl)-acetic acid[2] we considered it important to gain more information about the possible rearrangement pathways available to this bicyclic system.

A consideration of the possible modes of thermal decomposition of **1** and its derivatives suggests two probable decomposition pathways. The analogy with the 2-thia-6-azabicyclo[3,1,0]hex-3-ene system[3] (Scheme 1) (which has been shown to yield 1-substituted pyrroles[4] on thermal rearrangement), suggests that reaction of **1** might lead to cyclopentadiene derivatives. Subsequent participation in numerous secondary reactions would then lead to the observed mixture of products. Similarly, a vinylcyclopropane rearrangement[5] of **1** would be expected to result in the formation of an unstable episulphide (Scheme 2). Sulphur extrusion would then result in the



Scheme 1.



Scheme 2.

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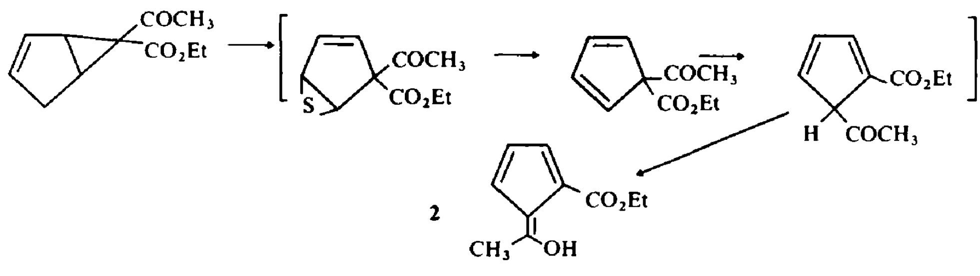
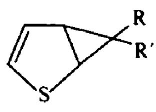


Scheme 3.

formation of a substituted cyclopentadiene which in turn would be expected to be in a fluxional equilibrium by successive 1,5-sigmatropic shifts,[6] and undergo facile Diels–Alder reactions, again leading to a mixture of products.

In an attempt to throw some light on the decomposition of the 2-thiabicyclo-3[3,1,0]hex-3-ene system we have sought to examine the thermal decomposition of a suitable derivative of **1**. Both suggested modes of decomposition lead to cyclopentadiene derivatives and if secondary transformations are to be avoided, halting the decomposition at this stage might be accomplished by a careful choice of substituents R and R′. We considered that the thermal decomposition of (**1**, R=CO_2Et, R′=$COCH_3$) might furnish a 1,1-disubstituted cyclopentadiene which by a single [1,5]-sigmatropic shift should yield the fulvene **2** (Scheme 3), which we would expect to be stable under the reaction conditions.

Initial attempts to prepare (**1**, R=CO_2Et, R^1=$COCH_3$) were unsuccessful since the reaction of thiophen with ethyl diazoacetoacetate produces almost exclusively the 2-insertion product **3**. However, 2,5-dichlorothiophen reacted readily to product **4** (as a mixture of C-6 epimers) in excellent yield, which has the additional advantage of having the chlorine substituents as X-ray markers. As expected **4** proved to be thermally labile and controlled decomposition to a single product was readily achieved by refluxing **4** in toluene for 38 h. The crystalline product **5** was obtained in 86% yield and mass spectral and microanalytical data confirmed a molecular formula of $C_{10}H_{10}Cl_2O_3$ corresponding to loss of sulphur from **4**. The ^1H NMR spectrum of the product showed two one-proton singlets at τ 2.85 and 4.25, a three-proton singlet at τ 7.80 along with the characteristic ethyl triplet at 8.60 and quartet at 5.65 (J = 7 Hz) and the IR spectrum showed signals at 3450, 1725 and 1595 cm^{-1}. On the basis of the spectral data, unambiguous structural assignment was not possible and the product was subjected to an X-ray crystallographic analysis.



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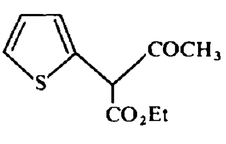

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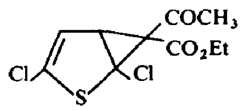

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EXPERIMENTAL

Crystals of **5** are monoclinic, space group $P2_1/c$, $a = 7.41(1)$, $b = 15.95(2)$, $c = 11.18(1)$Å, $\beta = 121.26(1)$, $U = 1134$ Å,^{3} $Z = 4$, $F(000) = 512$, $\mu(MoK\bar{\alpha}) = 4.95\ cm^{-1}$. Data were collected for $h0$-$12l$ with $\theta_{max} = 25^\circ$ on a Stoe STADI-2 2-circle diffractometer (graphite monochromated Mo$K\bar{\alpha}$ radiation). This gave 1620 data of which 1301 unique reflexions with $I > 3\sigma(I)$ were used in subsequent calculations. Lorentz and polarization corrections (but none for extinction or absorption) were applied and the data scaled by a Wilson plot. The structure was solved by direct phasing methods with the SHELX-76 system of crystallographic programs, which was used for all calculations. Complex neutral atomic scattering factors were taken from International tables for X-ray crystallography. Weighted full-matrix least squares refinement (including isotropic hydrogen atoms) converged at $R = 0.0327$ for 1301 observed reflexions ($R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$); $R_w = 0.0334$ ($R_w = \Sigma(||F_o| - |F_c||.w^{\frac{1}{2}})/\Sigma(F_o|.w^{\frac{1}{2}})$, $w = 3.5/(\sigma^2(F_o) + 0.00017F_o^{\ 2})$. Positional parameters are given in Table 1, bond distances Table 2 and bond angles in Table 3.†

Table 1. Fractional atomic coordinates × 10000 with e.s.d.'s in brackets

C(1)	1879(3)	3881(2)	1982(2)
C(2)	4046(3)	3830(2)	2569(2)
C(3)	4923(4)	3192(2)	2216(2)
C(4)	3618(4)	2607(2)	1232(2)
C(5)	1446(3)	2653(2)	0597(2)
C(6)	0565(3)	3299(2)	0970(2)
C(7)	0968(3)	4521(2)	2510(2)
C(9)	−0250(5)	5930(2)	2344(4)
C(10)	−2568(6)	5869(3)	1547(5)
C(15)	−1806(4)	3360(3)	0265(4)
CL(12)	5687(1)	4569	3803(1)
CL(13)	4696(1)	1788	0783(1)
O(8)	0673(3)	5267(1)	1909(2)
O(11)	0552(3)	4361(1)	3392(2)
O(14)	0111(3)	2101(2)	−0394(2)
H(3A)	6416(44)	3161(16)	2629(27)
H(9A)	0263(43)	5858(18)	3311(34)
H(9B)	0196(42)	6441(21)	2140(29)
H(10A)	−3191(63)	6377(28)	1692(40)
H(10B)	−3000(50)	5365(26)	1791(38)
H(10C)	−3069(61)	5824(25)	0552(47)
H(21A)	0661(49)	1748(21)	−0523(33)
H(16A)	−2393(59)	3496(24)	−0676(45)
H(16B)	−2163(55)	3698(24)	0743(38)
H(16C)	−2479(62)	2848(27)	0101(42)

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†Structure factors and anisotropic temperature factors have been deposited in Cambridge.

Table 2. Bond distances (A) with e.s.d.'s in brackets

C(1)–C(2)	1.392(3)
C(1)–C(6)	1.396(3)
C(1)–C(7)	1.506(3)
C(2)–C(3)	1.373(3)
C(2)–CL(12)	1.742(2)
C(3)–C(4)	1.384(3)
C(4)–C(5)	1.388(3)
C(4)–CL(13)	1.737(3)
C(5)–C(6)	1.396(3)
C(5)–O(14)	1.359(3)
C(6)–C(15)	1.516(3)
C(7)–O(8)	1.327(3)
C(7) O(11)	1.205(3).
C(9)–C(10)	1.477(5)
C(9)–O(8)	1.474(3)

Table 3. Bond angles (degrees) with e.s.d.'s in brackets

C(6) –C(1)–C(2)	119.7(2)
C(7) –C(1)–C(2)	120.1(2)
C(7) –C(1)–C(6)	120.1(2)
C(3) –C(2)–C(1)	120.9(2)
CL(12)–C(2)–C(1)	119.9(2)
CL(12)–C(2)–C(3)	119.2(2)
C(4) –C(3)–C(2)	119.1(2)
C(5) –C(4)–C(3)	121.4(2)
CL(13)–C(4)–C(3)	119.9(2)
CL(13)–C(4)–C(5)	118.7(2)
C(6) –C(5)–C(4)	119.2(2)
O(14) –C(5)–C(4)	123.1(2)
O(14) –C(5)–C(6)	117.7(2)
C(5) –C(6)–C(1)	119.6(2)
C(15) –C(6)–C(1)	121.0(3)
C(15) –C(6)–C(5)	119.5(2)
O(8) –C(7)–C(1)	113.5(2)
O(11) –C(7)–C(1)	122.4(3)
O(11) –C(7)–O(8)	124.1(2)
O(8) –C(9)–C(10)	110.6(3)
C(9) –O(8)–C(7)	117.3(2)

Table 4. Selected torsion angles (0°), (e.s.d.'s 0.4°)

C(2)–C(1)–C(7)–O(8)	85.5°
C(2) –C(1)–C(7)–O(11)	–94.6°
C(6) –C(1)–C(7)–O(8)	–98.9°
C(6) –C(1)–C(7)–O(11)	80.8°
C(1) –C(7)–C(8)–C(9)	178.9°
O(11)–C(7)–O(8)–C(9)	–0.8°
C(10)–C(9)–O(8)–C(7)	–84.5°

1,3-*Dichloro-6-acetyl-6-ethoxycarbonyl-2-thiabicyclo-*[3.1.0]*hex-3-ene*

To a solution of $Rh_2(OAc)_4$ (0.005 g) in 2,5-dichlorothiophen (10 ml) was added dropwise ethyl diazoacetoacetate (1.56 g; 10 mmol) and the mixture was stirred at room temperature for 20 h until the peak for the diazo group was no longer present in the IR spectrum. The excess 2,5-dichlorothiophen was removed under reduced pressure and the crude product subjected to preparative TLC (light petroleum/ether 4:1) to yield the title compound 1.9 g, 67%, as a pale yellow oil, b.p. 94° (at 1 Torr); ν_{max} 2960, 1710, 1625, 1600, 1370, 1300, 1245 (broad), 1080, 1060, 940 and 895 cm^{-1}, $\tau(CDCl_3)$ 3.35 (1 H, d, J = 5 Hz), 4.15 (1 H, d, J = 5 Hz), 5.8 (2 H, q, J = 7 Hz), 7.65 (3 H, s) and 8.7 (3 H, t, J = 7 Hz). Found M^+ 279.9755. $C_{10}H_{10}Cl_2O_3S$ requires M^+ 279.9728.

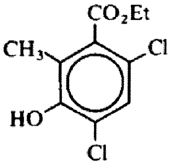
Thermal rearrangements of 1,3-*dichloro-6-acetyl-6-ethoxycarbonyl-2-thiabicyclo*[3.1.0]*hex-3-ene*

Distillation of the above compound resulted in some decomposition to ethyl 2,4-dichloro-5-hydroxy-6-methylbenzoate but the reaction was incomplete.

Generally the most satisfactory procedure for the thermal rearrangement was as follows. The title compound (0.50 g; 1.80 mmol) was heated under reflux in toluene (10 ml) for 38 h after which time TLC indicated no residual starting material. The solvent was removed under reduced pressure and the product purified by column chromatography (light petroleum/ethyl acetate, 9:1) to yield ethyl-2,4-dichloro-5-hydroxy-6-methylbenzoate (0.39 g, 86%) as a colourless solid, m.p. (toluene) 92.5–93 C; $\nu_{max}^{CHCl_3}$ 3540, 2900, 1725, 1595, 1440, 1290, 1235 (br), 1145, 1055 and 865 cm^{-1}, $\tau CDCl_3$ 2.85 (1 H, s) 4.25 (1 H, s, exchanges with D_2O), 5.65 (2 H, q, J = 7 Hz), 7.8 (3 H, s), and 8.6 (3 H, t, J = 7 Hz), found M^+ 248.0005: $C_{10}H_{10}Cl_2O_3$ requires 248.0007.

DISCUSSION

The X-ray analysis shows unequivocally that the product of rearrangement **5** is a pentasubstituted benzene derivative. It is interesting to note that *ab initio* elucidation of this relatively simple structure is almost impossible by spectroscopic means and would require extensive classical degradative and/or synthetic work. The formation of **5** by thermal rearrangement from **4** is difficult to rationalize, particularly the *meta* arrangement of the chlorine atoms and the *ortho* arrangement involving methyl and hydroxyl groups. The reaction paths suggested in Schemes 1 and 2 do not seem relevant, in spite of literature precedent. Although it is possible to conjecture a number of plausible schemes leading to **5**, they all involve many steps and a large number of intermediates and seem improbable in view of the high yield of **5**; however a plausible mechanism is illustrated in Scheme 4.



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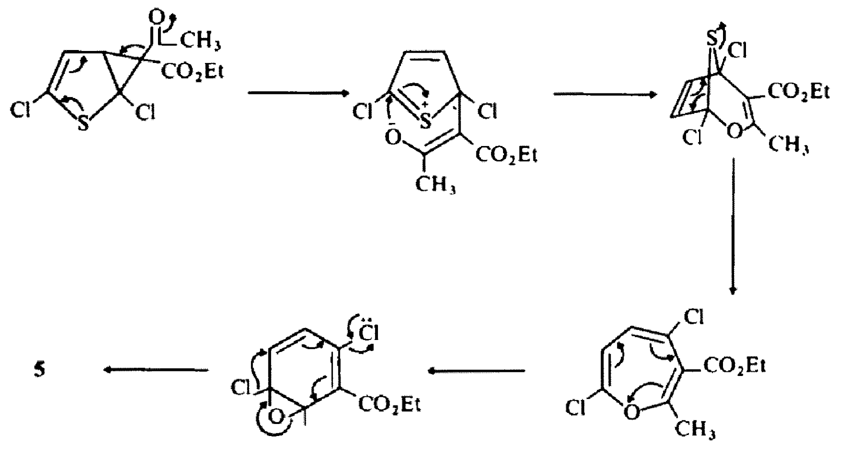
The crystal structure (Fig. 1) consists of hydrogen bonded chains [O(14)–H(21)A——O(11)] $(x, \frac{1}{2} - y, z - \frac{1}{2}) = 2.801(3)$ Å.

The ethoxycarbonyl group is not coplanar with the benzene ring (Table 4) because of steric hindrance from the 2,6-substituents. The conformation about the O–Et bond (Table 4, $\tau = 84.5°$) is neither *trans* nor *gauche*. We have recently made a study of the conformation of ethyl esters in the Cambridge Crystallographic Data File and of 101 examples the majority (74) had torsion angles ($RCOO-CH_2CH_3$) in the *trans* region (155–180°) as expected. A significant number (24) however, fell in the range (75–105°) with none in the gauche orientation (60°). The ethyl group in esters would thus seem to have a local energy minimum with a torsion angle of 85° which agrees very well with the gas-phase structure of ethyl formate.[7] This effect will be discussed in more detail elsewhere.

Acknowledgements—We thank the SRC and Pilot Chemical Company Ltd, for a CASE studentship (to RJG), Johnson and Matthey and Co. Ltd. for the loan of $Rh_2(OAc)_4$ and Dr. W. B. Motherwell, Dr. C. D. Maycock and Mr. S. Z. Zard for helpful discussions.



Scheme 4.

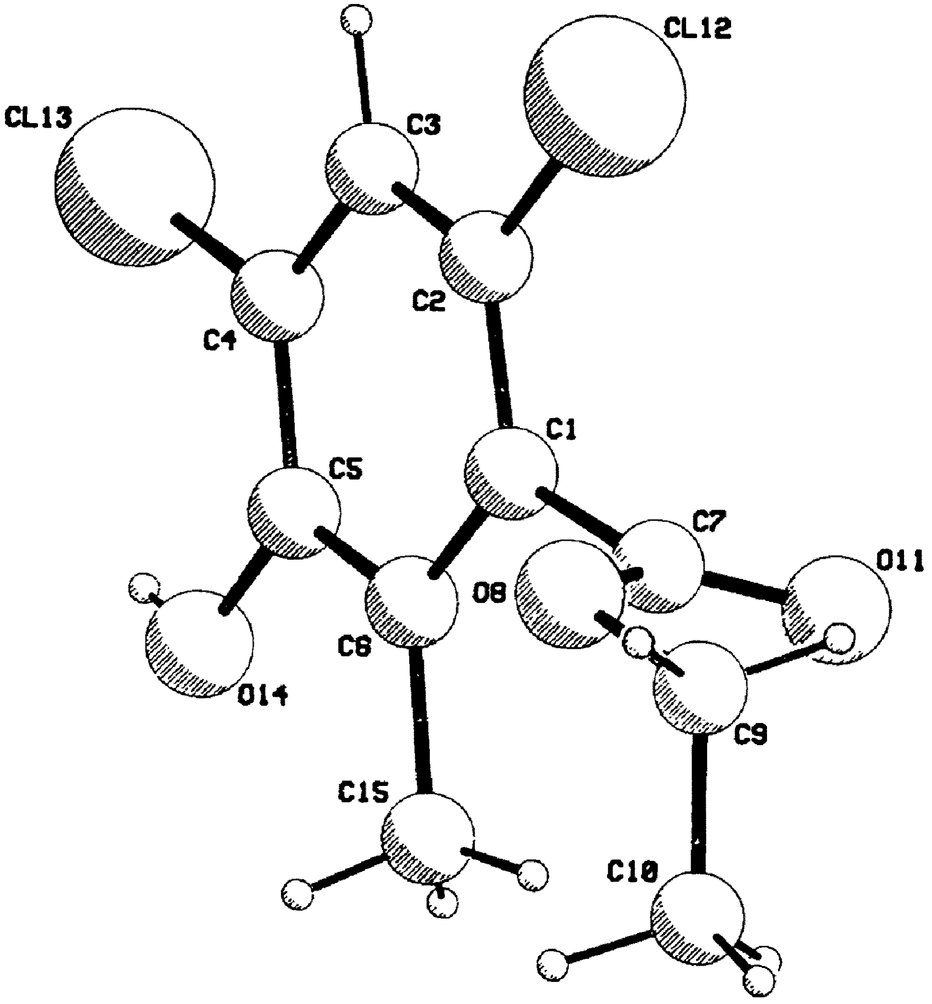


Fig. 1.

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