577. *Synthesis of Thia*cyclo*alk-2-enes.*

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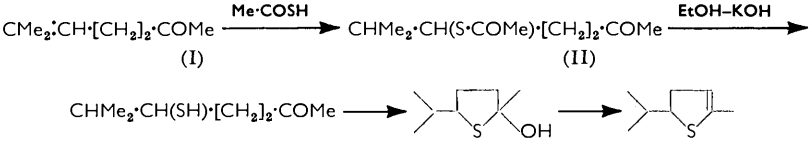
Substituted thia*cyclo*alk-2-enes have been synthesized by intramolecular condensation of suitably spaced thiol and keto-groups. Attempts to prepare unsubstituted thia*cyclo*alk-2-enes by analogous reactions involving aldehyde groups were unsuccessful.

Sulphuration of alka-1 : 5-dienes, typified in rubber vulcanization, leads to sulphur-bridged intermolecular compounds and to cyclic sulphides.[1] In order to determine the composition of the latter series (cf. refs 2—4) it became necessary to obtain various thia*cyclo*alkenes so that the effect of unsaturation pattern and substitution on their chemical and spectroscopic properties could be ascertained.

Thia*cyclo*hex-3-enes have previously been obtained by reduction of thia*cyclo*hexan-3-ones and dehydration of the resulting thia*cyclo*hexanols,[5, 6] and by deacetylation of 3-acetoxythia*cyclo*hexanes.[7] Thia*cyclo*alk-2-enes have been less readily accessible. Replacement of the oxygen in the corresponding dihydropyran by sulphur at high temperature in the presence of hydrogen sulphide yields impure material,[5, 8] and the reduction of thiophens with sodium and liquid ammonia gives rather poor yields of mixtures of thia*cyclo*pent-2- and -3-enes which are difficult to separate.[9] The present paper [10] reports new syntheses of pure thia*cyclo*alk-2-enes in good yields by intramolecular condensation of suitably spaced thiol and keto-groups under acidic or basic conditions. Concurrent polycondensation occurs to an extent varying from system to system.

2-Methyl-5-*iso*propylthia*cyclo*pent-2-ene (V) was obtained in 45% overall yield from the common methylheptenone (I) by the annexed reactions:



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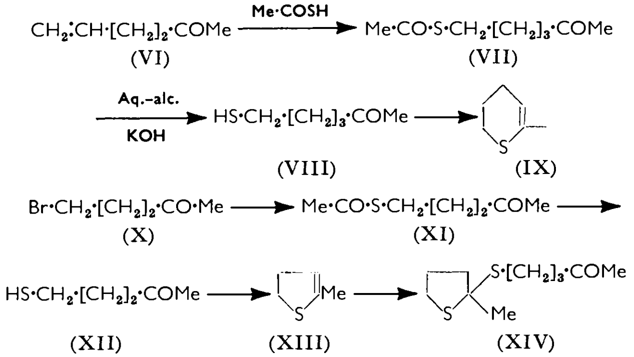
[1] Farmer and Shipley, *J.*, 1947, 1519.
[2] Glazebrook and Saville, *J.*, 1954, 2094.
[3] Bateman, Glazebrook, Moore, and Saville, Proc. 3rd Rubber Tech. Conf., London, 1954, p. 298.
[4] Bateman, Glazebrook, and Moore, *J.*, 1958, 2846.
[5] Naylor, *J.*, 1949, 2749.
[6] Fehnel and Lackey, *J. Amer. Chem. Soc.*, 1951, **73**, 2473.
[7] Olsen and Rutland, *Chem. Ber.*, 1953, **86**, 361.
[8] Yur'ev, Dubrovina, and Tregubov, *J. Gen. Chem. U.S.S.R.*, 1946, 843.
[9] Birch and McAllan, *J.*, 1951, 2256, 3411.
[10] Cf. Bateman and Glazebrook, *Chem. and Ind.*, 1951, 1093.

Hydrolysis of the ester (II), whose structure follows from the known " abnormal " addition of thiolacetic acid to olefins under the conditions used,[11] gave either the thiol (III) or the dihydrothiophen (V), depending on the severity of the procedure; the possible intermediate (IV) was never isolated.

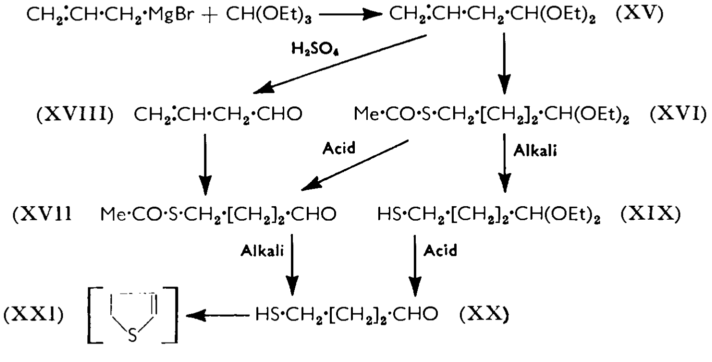
2-Methylthia*cyclo*hex-2-ene (IX) was obtained similarly:



In this case, hydrolysis of the ester (VII) gave the cyclized product (IX) directly, none of the intermediate thiol (VIII) being isolated.

The analogous preparation of 2 : 3-dimethylthia*cyclo*hex-2-ene differs from the previous examples in that the thiol corresponding to (VIII) requires treatment with cold sulphuric acid for dehydration and cyclization.

Unsuccessful attempts were made to apply this synthesis to 2-methylthia*cyclo*pent-2-ene (XIII). The thioester (XI) was obtained in good yield, but on hydrolysis by boiling ethanolic potassium hydroxide or cold dilute methanolic sodium methoxide gave a product which on the basis of elementary analysis, molecular weight, carbonyl content, and absence of thiol function is identified as 2-methyl-2-(4-oxopentylthio)-thia*cyclo*pentane (XIV), which presumably results from interaction of the products (XII) and (XIII) under alkaline conditions. An alternative route to the simple product (XIII)—addition of thiolacetic acid to pent-4-en-2-one—proved impracticable owing to the inaccessibility of this ketone, which could not be prepared by the reaction of dimethylcadmium with but-3-enoyl chloride or of allylmagnesium bromide with acetic anhydride.[12]



The synthesis of thia*cyclo*alk-2-enes unsubstituted at the 2-position by intramolecular condensation of thiol and aldehyde groups could not be realized, partly because of the difficulty of introducing a thiol group into an aldehyde in a suitable position, and partly because of the preferential polymerization of aldehydes under the condition of condensation.

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[11] Cunneen, *J.*, 1947, 134.

[12] Newman and Booth, *J. Amer. Chem. Soc.*, 1945, **67**, 154.

For example, attempts to synthesize thia*cyclo*pent-2-ene (XXI) by the procedures in the reaction scheme failed at different stages.

But-3-enal (XVIII), obtained from of 4 : 4-diethoxybut-1-ene (XV), was readily converted into 4-acetylthiobutanal (XVII), which was unaffected by cold methanolic sodium methoxide and was polymerized in hot ethanolic sodium hydroxide. Addition of thiolacetic acid to the acetal (XV) was normal, giving the thioester (XVI), which partly polymerized on treatment with sulphuric acid and gave the thiol (XIX) on alkaline hydrolysis, but with sulphuric acid this gave only involatile products.

The thia*cyclo*alk-2-enes described were colourless, stable liquids, giving well-defined solid sulphones and sulphidimines by conventional methods.

EXPERIMENTAL

6-Methylhept-5-en-2-one (I), prepared by the alkaline cleavage of citral,[13] had b. p. 65—66°/10 mm., n_D^{20} 1·4412.

2-*Methyl*-5-iso*propylthia*cyclo*pent*-2-*ene* (V).—The ketone (I) (42 g.) reacted exothermically with freshly distilled thiolacetic acid (25 g.); the product, after being warmed on the steam-bath for 1 hr., gave on distillation 5-*acetylthio*-6-*methylheptan*-2-*one* (II) (51 g., 77%), b. p. 134°/10 mm., n_D^{20} 1·4786 (Found: C, 59·3; H, 9·0; S, 15·4. $C_{10}H_{18}O_2S$ requires C, 59·5; H, 8·95; S, 15·75%). Refluxing this thiolester (II) (51 g.) with potassium hydroxide (40 g.) in aqueous ethanol (400 ml.; 50% v/v) for 1 hr. gave 5-*mercapto*-6-*methylheptan*-2-*one* (III), which crystallized as colourless needles [from light petroleum (b. p. <40°)], m. p. 66—68° (C, 59·6; H, 10·0; S, 20·0. $C_8H_{16}OS$ requires C, 60·0; H, 10·0; S, 20·0%). This thiol slowly eliminated water at room temperature. In another experiment, extraction of the hydrolysis product with benzene, followed by distillation, gave 2-*methyl*-5-iso*propylthia*cyclo*pent*-2-*ene* (V) [42·4 g., 45% based on (I)], b. p. 65—67°/10 mm., which on elution through an alumina column with light petroleum (b. p. <40°) had b. p. 63—64°/10 mm., n_D^{20} 1·4932, $\lambda_{max.}$ 2400 Å (ε 2800) (Found: C, 67·5; H, 9·8; S, 22·7. $C_8H_{14}S$ requires C, 67·6; H, 9·8; S, 22·5%). Heating the thiol (III) (5·0 g.) with boric acid (1·0 g.) at 160° for 15 min. gave the product (V) (3·0 g., 68%), b. p. 63°/10 mm., n_D^{20} 1·4933 (Found: C, 67·2; H, 9·8; S, 23·0%). Oxidation of this compound in glacial acetic acid with 30% hydrogen peroxide at room temperature for 2—3 days [14] gave 2-*methyl*-5-iso*propylthia*cyclo*pent*-2-*ene* 1 : 1-*dioxide* as colourless needles [from light petroleum (b. p. 80—100°)], m. p. 66·5—67·5° (Found: C, 55·3; H, 8·2; S, 18·3. $C_8H_{14}O_2S$ requires C, 55·2; H, 8·0; S, 18·4%). Shaking the sulphide (V) with an aqueous solution of chloramine-T gave the *sulphidimine* as colourless prisms (from ethanol), m. p. 120—121° (Found: C, 57·9; H, 6·9; N, 4·5; S, 20·6. $C_{15}H_{21}O_2NS_2$ requires C, 57·9; H, 6·7; N, 4·5; S, 20·6%).

2-*Methylthia*cyclo*hex*-2-*ene* (IX).—Hex-5-en-2-one (VI), prepared from allyl bromide and ethyl acetoacetate,[15] had b. p. 32—33°/10 mm., n_D^{20} 1·4213 (Found: C, 73·3; H, 10·2. Calc. for $C_6H_{10}O$: C, 73·5; H, 10·2%). Reaction of this (98 g.) with thiolacetic acid (76 g.) as described above gave 6-*acetylthiohexan*-2-*one* (VII) (158 g., 91%), b. p. 133°/10 mm., n_D^{20} 1·4812 (Found: C, 55·0; H, 8·0; S, 18·4. $C_8H_{14}O_2S$ requires C, 55·2; H, 8·0; S, 18·7%). The thiolester (VII) (158 g.), on refluxing under nitrogen for 1 hr. with a solution of potassium hydroxide (100 g.) in aqueous ethanol (1 l., 50% v/v), followed by acidification with acetic acid and extraction with benzene, gave a high-boiling product from which 2-*methylthia*cyclo*hex*-2-*ene* (IX) (25 g., 24%) was obtained by distillation *in vacuo*. Elution of this material through alumina with light petroleum (b. p. <40°) followed by distillation of the eluate gave pure (IX), b. p. 50°/10 mm., n_D^{20} 1·5262, $\lambda_{max.}$ 2275 Å (ε 5160), with inflexion at λ 2450 Å (ε 2400) (Found: C, 63·1; H, 9·0; S, 28·1. $C_6H_{10}S$ requires C, 63·2; H, 8·8; S, 28·0%). The *sulphone* was obtained as prisms (from ethanol), m. p. 41—42° (Found: C, 49·3; H, 7·0; S, 21·7. $C_6H_{10}O_2S$ requires C, 49·3; H, 6·85; S, 21·9%). The *sulphidimine derivative* was obtained as needles (from ethanol), m. p. 119·5—120° (Found: C, 55·1; H, 6·2; N, 5·0; S, 22·5. $C_{13}H_{17}O_2NS_2$ requires C, 55·1; H, 6·0; N, 4·95; S, 22·6%).

2 : 3-*Dimethylthia*cyclo*hex*-2-*ene*.—Reaction of ethyl allylacetoacetate with methyl iodide

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[13] Cf. Barnard, Bateman, Harding, Koch, Sheppard, and Sutherland, *J.*, 1950, 915.

[14] Barker, Stevens, and Dost, *Rec. Trav. chim.*, 1948, **67**, 451.

[15] Schechter, Green, and LaForge, *J. Amer. Chem. Soc.*, 1949, **71**, 3165.

in the presence of potassium *tert.*-butoxide gave 3-methylhex-5-en-2-one, b. p. 61°/40 mm., $n_{\rm D}^{20}$ 1·4241 (Found: C, 74·7; H, 10·8. Calc. for $C_7H_{12}O$: C, 75·0; H, 10·7%). This ketone (46 g.) reacted with thiolacetic acid (35 g.) on irradiation with ultraviolet light for 2 hr. at room temperature, giving 6-*acetylthio*-3-*methylhexan*-2-*one* (60 g. 78%), b. p. 138—140°/10 mm., $n_{\rm D}^{20}$ 1·4802 (Found: C, 57·1; H, 8·7; S, 17·4. $C_9H_{16}O_2S$ requires C, 57·5; H, 8·5; S, 17·0%). The thiolester (60 g.) was refluxed under nitrogen for 1 hr. with potassium hydroxide (50 g.) in aqueous ethanol (500 ml.; 50% v/v). The product, on extraction as previously, gave 6-*mercapto*-3-*methylheptan*-2-*one* (40 g., 90%), b. p. 102—103°/10 mm., $n_{\rm D}^{20}$ 1·4800 (Found: C, 57·3; H, 9·6; S, 22·1. $C_7H_{14}OS$ requires C, 57·6; H, 9·6; S, 21·9%). Treatment of this thiol (27 g.) with ice-cold sulphuric acid (250 g., 60% w/w) for 1 hr., followed by ether-extraction and distillation of the product, gave 2 : 3-*dimethylthia*cyclo*hex*-2-*ene* (15 g., 63%). On purification as described above this had b. p. 65—66°/10 mm., $n_{\rm D}^{20}$ 1·5280, $\lambda_{\rm max.}$ 2280 Å (ε 6840) (Found: C, 65·4; H, 9·5; S, 25·2. $C_7H_{12}S$ requires C, 65·6; H, 9·4; S, 25·0%). The *sulphone* was obtained as needles [from light petroleum (b. p. 60—80°)], m. p. 74·5—75·0° (Found: C, 52·6; H, 7·6; S, 20·2. $C_7H_{12}O_2S$ requires C, 52·4; H, 7·5; S, 20·0%). The *sulphidimine derivative* formed plates (from aqueous ethanol), m. p. 138—139° (Found: C, 56·6; H, 6·5; N, 4·9; S, 21·5. $C_{14}H_{19}O_2NS_2$ requires C, 56·6; H, 6·4; N, 4·7; S, 21·5%).

Attempted Synthesis of 2-*Methylthia*cyclo*pent*-2-*ene* (XIII).—5-Bromopentan-2-one (X), prepared in a slightly impure state by Boon's method,[16] had b. p. 70·5°/10 mm., $n_{\rm D}^{20}$ 1·4700 (Found: C, 36·4; H, 5·6; Br, 47·6. Calc. for C_5H_9OBr: C, 36·4; H, 5·5; Br, 48·5%). The bromide (28 g.) was refluxed for 4 hr. with ethanolic sodium thiolacetate [from sodium hydroxide (10 g.), the acid (12 g.), and ethanol (100 ml.)]. Dilution of the product with water, followed by ether-extraction and distillation, gave 5-*acetylthiopentan*-2-*one* (XI) (18 g., 67%), b. p. 116—119°/10 mm., $n_{\rm D}^{20}$ 1·4890 (Found: C, 52·3; H, 7·7; S, 21·0. $C_7H_{12}O_2S$ requires C, 52·5; H, 7·5; S, 20·0%). This ester (37 g.) was kept overnight in methanol (400 ml.) containing a trace of sodium methoxide, after which the bulk of the solvent was removed, and the residue diluted with water, extracted with ether, and distilled, to give 2-*methyl*-2-(4-*oxopentylthio*)*thia*cyclo*pentane* (XIV) (15 g., 60%), b. p. 120—122°/0·01 mm., $n_{\rm D}^{20}$ 1·5324 (Found: C, 55·0; H, 8·4; S, 29·2%; *M*, 212. $C_{10}H_{18}OS_2$ requires C, 55·0; H, 8·3; S, 29·4%; *M*, 218). Its infrared spectrum showed the presence of one C=O group per molecule, the absence of thiol groups, and no detectable C:C-type unsaturation.

*Attempted Synthesis of Thia*cyclo*pent*-2-*ene* (XXI).—Ethyl orthoformate (60 g.) in ether (100 ml.) with allylmagnesium bromide [from allyl bromide (60 g.) and magnesium (38 g.) in ether (400 ml.)] under reflux for 6 hr. gave 4 : 4-diethoxybut-1-ene (XV) (22 g., 41%), b. p. 40°/10 mm., $n_{\rm D}^{20}$ 1·4096 (Found: C, 66·6; H, 11·2. Calc. for $C_8H_{16}O_2$: C, 66·7; H, 11·1%). Distillation of this from 2N-sulphuric acid gave an aqueous solution (75% w/w) of but-3-enal (XVIII), identified as the 2 : 4-*dinitrophenylhydrazone derivative* (red plates from ethanol), m. p. 186° (Found: C, 48·0; H, 4·1; N, 22·3. $C_{10}H_{10}O_4N_4$ requires C, 48·0; H, 4·0; N, 22·4%). The aqueous aldehyde (75% w/w; 5·0 g.) reacted exothermically with thiolacetic acid (5·0 g.), to give 4-*acetylthiobutanal* (XVII), b. p. 95—96°/10 mm., $n_{\rm D}^{20}$ 1·4850 (Found: C, 49·0; H, 6·8; S, 21·9. $C_6H_{10}O_2S$ requires C, 49·4; H, 6·8; S, 21·9%). This ester was recovered after being kept overnight in methanol contaning a trace of sodium methoxide; when refluxed for 5 min. under nitrogen with 10% aqueous-ethanolic (50% v/v) sodium hydroxide it yielded an undistillable oil.

Addition of thiolacetic acid (10 g.) during 45 min. to the acetal (XV) (20 g.) at 0° with ultraviolet irradiation gave 4-*acetylthio*-1 : 1-*diethoxybutane* (XVI) (16 g., 52%), b. p. 86°/0·01 mm., $n_{\rm D}^{20}$ 1·4627 (Found: C, 54·1; H, 9·0; S, 14·8. $C_{10}H_{20}O_3S$ requires C, 54·6; H, 9·1; S, 14·5%), treatment of which with 2N-sulphuric acid failed to give any steam-volatile material, the only isolable products being the unchanged ester (*ca.* 50%) and a non-volatile oil. The ester (21 g.) with potassium hydroxide (20 g.) in aqueous ethanol (50% v/v; 200 ml.) during 2 hr. at room temperature gave 4 : 4-*diethoxybutanethiol* (XIX) (15 g., 88%), b. p. 97°/10 mm., $n_{\rm D}^{20}$ 1·4515 (Found: C, 53·6; H, 10·1; S, 18·1. $C_8H_{18}O_2S$ requires C, 54·0; H, 10·1; S, 18·0%), whence 2N-sulphuric acid yielded only an undistillable oil.

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[16] Boon, B.P. 558,286/1943.