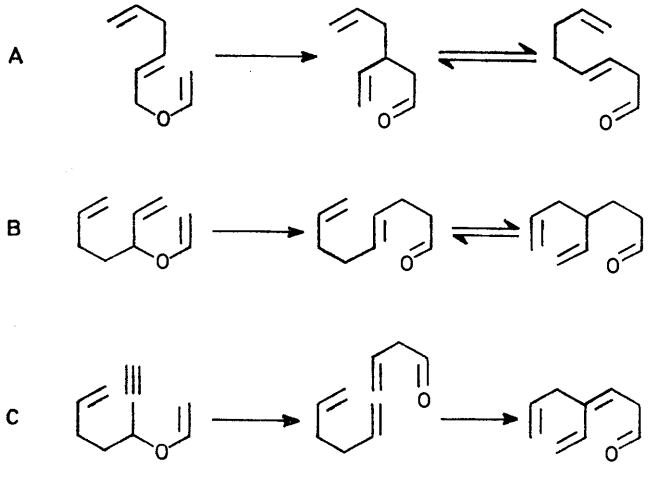
Sequential Claisen and Cope Rearrangements: the Propenyl Ether and Acetate of 3-Methylhept-6-en-1-yn-3-ol

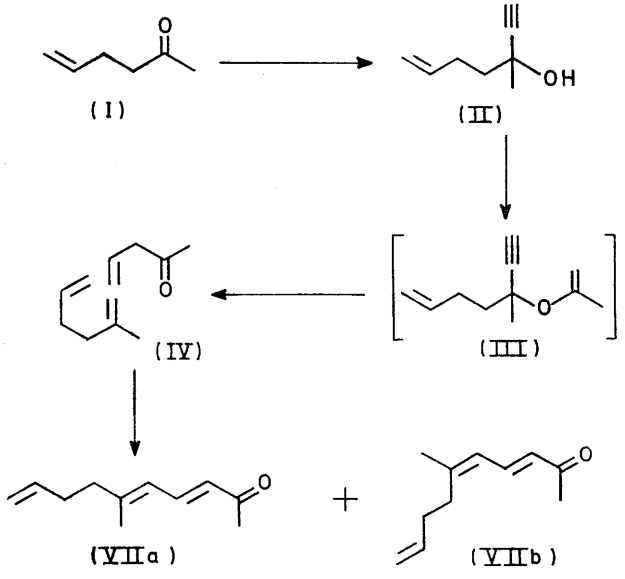
By **Bruce Bowden, Richard C. Cookson,*** and **Harry A. Davis,** Chemistry Department, Southampton University, Southampton SO9 5NH

The synthetic potential of a Claisen followed by a Cope rearrangement is illustrated by the reactions of 3-methylhept-6-en-1-yn-3-ol (II). This propargylic alcohol (II) condenses with methyl isopropenyl ether with Claisen rearrangement to give 6-methyldeca-4,5,9-trien-2-one (IV), which isomerises in boiling xylene through the product of Cope rearrangement (V) to 5-isopropylideneocta-*trans*-3,7-dien-2-one (VI). The acetate (IX) of the alcohol (II) undergoes an analogous series of rearrangements to the allenyl acetate (X) and the dienyl acetate (XII).

THERE are two classes of allylic alcohol containing a second double bond the enol ethers of which could undergo a Claisen rearrangement followed by a Cope rearrangement. In the first (A) the double bond



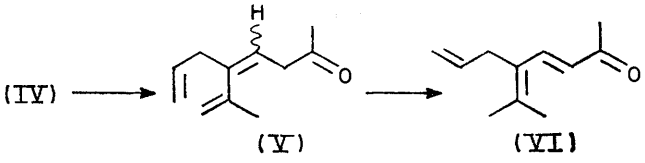
involved in the Claisen rearrangement moves away from the one intended to participate with it in the Cope rearrangement, and in the second (B) it moves towards the other double bond. Examples of class A will be described in a future publication.



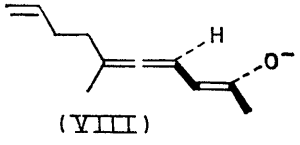
In class B the occurrence of Cope rearrangement in the parent system will not be favoured kinetically or

thermodynamically, although the reaction might be driven to the right by appropriate substitution. We have chosen a different method of imposing the Cope rearrangement, by using a propargyl rather than an allyl ether, the resulting allene then forcing the Cope rearrangement to give the conjugated diene (C).

3-Methylhept-6-en-1-yn-3-ol (II), made by addition of acetylene to hex-5-en-2-one (I), condensed with methyl isopropenyl ether to give the allene (IV) through the intermediate enol ether (III).[1] In boiling xylene compound (IV) rearranged into the isomeric conjugated ketone (VI), identified by its spectroscopic properties, and evidently formed by a 1,5-prototropic shift in the primary product (V) of the Cope rearrangement.



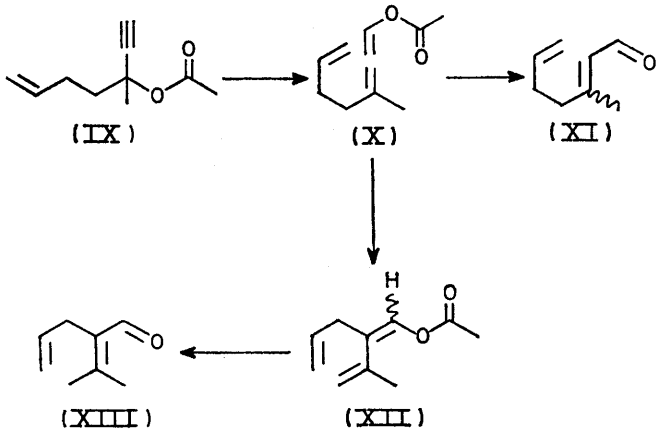
The allene (IV) was isomerised by dilute alkali into a mixture containing predominantly one isomer of the conjugated ketone (VII), the n.m.r. spectrum indicating the *trans*-5-configuration which would have arisen from protonation of the enolate (VIII) from the same side as



the methyl group rather than the larger allyl group. An attempt to purify the product by preparative g.l.c. at 210° caused equilibration to approximately equal proportions of the *cis*-5 (VIIb) and the *trans*- (VIIa) isomer.

Helg *et al.*[2] have reported the synthesis of compound (VII) by a much longer sequence also starting with the propargyl alcohol (II). Our *trans*-5-isomer (VIIa) yielded a 2,4-dinitrophenylhydrazone of m.p. 161—163° (lit.,[2] 162—164°), and a semicarbazone, m.p. 160—161° (lit.,[2] 159—161°). On the other hand the *cis*-5-isomer formed a 2,4-dinitrophenylhydrazone and a semicarbazone as gums, both of which crystallised slowly; on repeated recrystallisation each gave the same derivative as the *trans*-isomer. Evidently the derivatives of Helg *et al.*[2] were also derived from the *trans*-isomer (VIIa).

The analogous sequence of structural changes was carried out on the system containing an oxygen atom in place of the methylene group of the enol ether (*i.e.* on the acetate). When the acetate (IX) was heated in butan-2-one containing a catalytic amount of silver perchlorate[3] it rearranged quantitatively to the allenyl acetate (X). This underwent mild hydrolysis to the conjugated aldehyde (XI), which, from from its n.m.r. spectrum, seemed to be a mixture of about 70% of the *trans*-isomer and about 30% of the *cis*.



In boiling xylene the allenyl acetate (X) rearranged to give a mixture of two new compounds in approximately equal amounts (g.l.c.), presumably the *cis*- and *trans*-isomers of the Cope product (XII). Chromatography on silica gel produced little separation, but some hydrolysis. The mixture was therefore hydrolysed directly to the isopropylidene aldehyde (XIII).

EXPERIMENTAL

N.m.r. spectra were measured on a Perkin-Elmer R12 instrument; *S* values quoted are peak separations (in Hz). Tetramethylsilane was used as internal standard.

3-Methylhep-6-en-1-yn-3-ol (II).—To a stirred solution of iron(III) nitrate (0·2 g) in redistilled liquid ammonia (0·5 l) at −35°, sodium (11·7 g) was added in small pieces during 1 h. The solution was maintained at −35° until the blue colour had disappeared, then acetylene was passed through it for 6 h. Hex-5-en-2-one (50 g) was added and the solution was stirred for 4 h, then ether (400 ml) was added and the ammonia was allowed to escape. The solution was acidified and the ethereal phase was separated. The aqueous phase was extracted with ether (5 × 100 ml), and the combined ethereal extracts were dried ($MgSO_4$) and concentrated. The remaining oil was fractionated through a 10 in column packed with multi-helices, to yield 3-methylhep-6-en-1-yn-3-ol (36 g, 57%), b.p. 67—68° at 14 mmHg, n_D^{20} 1·4530 (lit.,[4] b.p. 56—58° at 10 mm Hg, n_D^{20} 1·4530; lit.,[5] b.p. 160—161°, n_D^{25} 1·4505), $\nu_{max.}$ (film) 3450—3250br, 3060, 1820br, 1640, 1460, 1380, 1120br, 1020, and 920 cm^{-1}; δ (CCl_4) 1·45 (3H, s, 3-Me), 1·45—1·85 (2H, m, 4-H_2), 2·05—2·45 (2H, m, 5-H_2), 2·33 (1H, s,

[1] *Cf.* G. Saucy and R. Marbet, *Helv. Chim. Acta*, 1967, **50**, 1158.

[2] R. Helg, F. Zobrist, A. Lauchenauer, K. Brack, A. Caliezi, D. Stauffacher, E. Zweifel, and H. Schinz, *Helv. Chim. Acta*, 1956, **39**, 1269.

[3] G. Saucy, R. Marbet, H. Lindlar, and O. Isler, *Helv. Chim. Acta*, 1959, **42**, 1945.

[4] I. N. Nazarov, B. P. Gusev, S. M. Makin, V. B. Mochalin, I. I. Nazarova, V. P. Vinogradov, B. K. Kruptsov, O. A. Shavrigina, and D. V. Nazarova, *Doklady Akad. Nauk S.S.S.R.*, 1957, **114**, 796.

[5] I. D. Papa, F. J. Villani, H. F. Hinsberg, *J. Amer. Chem. Soc.*, 1954, **76**, 4446.

1-H), 2·82 (1H, s, OH), 4·8—5·15 (2H, m, 7-H_2), and 5·55—6·2 (1H, m, 6-H).

6-*Methyldeca*-4,5,9-*trien*-2-*one* (IV).—A solution of 3-methylhept-6-en-1-yn-3-ol (II) (20 g, 0·162 mol), methyl isopropenyl ether (40 g, 0·56 mol), quinol (50 mg), and toluene-*p*-sulphonic acid (100 mg) in petroleum (200 ml; b.p. 80—100°) was heated under reflux for 24 h. The solvent was removed under reduced pressure, and the crude product was fractionated through a 6 in Vigreux column to yield 6-methyldeca-4,5,9-trienone (15 g, 57%), b.p. 105—109° at 15 mmHg (further impure ketone (6 g) was collected in the fraction of b.p. 109—120° at 15 mmHg), $\nu_{max.}$ (neat) 3050, 1965, 1710, 1640, 1570, 1440br, 1360, 1160, 1000, and 920 cm^{-1}, δ (CCl_4) 1·68 (3H, d, *S* 3, 6-Me), 2·07 (3H, s, 1-H_3), 1·7—2·3 (4H, m, 7- and 8-H_2), 2·96 (2H, d, *S* 7, 3-H_2), 4·75—5·45 (3H, m, 4-H and 10-H_2), and 5·45—6·2 (1H, m, 9-H).

6-*Methyldeca*-3,5,9-*trien*-2-*one* (VII).—A solution of 6-methyldeca-4,5,9-trien-2-one (5 g) in petroleum (100 ml; b.p. 40—60°) was stirred at 0° with 2% potassium hydroxide in methanol (10 ml) for 1 h. Water (20 ml) was added and the petroleum layer was separated. The aqueous layer was washed with petroleum (3 × 10 ml; b.p. 40—60°), and the combined extracts were dried, concentrated, and distilled to yield 6-methyldeca-3,5,9-trien-2-one (VII), b.p. 86—88° at 0·5 mmHg. G.l.c. analysis (5 ft 10% SE30 column; 118°) indicated that this was predominantly a single product. Attempted purification by preparative g.l.c. (15 ft 10% SE30 column; 210°) yielded 6-methyldeca-*trans*-3,*trans*-5,9-trien-2-one and the *trans*-3,*cis*-5-isomer in approximately equal quantities. The isomers were not readily distinguished by their i.r. spectra $\nu_{max.}$ (neat) 1665br, 1630, 1590, 1450, 1370, 1260br, 990, 925, and 765 cm^{-1}. The *trans*-5-isomer showed δ 1·93br (3H, s, $W_{\frac{1}{2}}$ 2·5 Hz, 6-Me), 2·17 (3H, s, 1-H_3), 2·25 (4H, 's', 7- and 8-H_2), 4·85—5·15 (2H, m, 10-H_2), 5·45—6·15 (3H, m, 3-, 5-, and 9-H), and 7·31 (1H, dd, *S* 15·5 and 11, 4-H). The *cis*-5-isomer showed corresponding signals at δ 1·89, 2·15, 2·15—2·4 (4H, m, 2 main lines at 2·24 and 2·31), 4·8—5·2, 5·45—6·15, and 7·26.

An attempt was made to correlate the isomers with the 6-methyldeca-3,5,9-trien-2-one reported by Helg *et al.*[2] The *trans*-5-isomer yielded a 2,4-dinitrophenylhydrazone (Found: C, 58·9; H, 5·8; N, 16·1. Calc. for $C_{17}H_{20}N_4O_4$: C, 59·3; H, 5·85; N, 16·3%), m.p. 161—163° (lit.,[2] 162—164°), and a semicarbazone, m.p. 160—161° (lit.,[2] 159—161°). The *cis*-5-isomer deposited a red gum when treated with 2,4-dinitrophenylhydrazine solution. The gum slowly crystallised, and after several recrystallisations afforded a derivative identical with that obtained from the *trans*-5-isomer. The semicarbazone crystallised after a week to yield a derivative identical with that obtained from the *trans*-5-isomer.

The two isomers were hydrogenated in ether over 10% palladium–charcoal to yield the same saturated ketone. The n.m.r. spectrum was consistent with that expected for 6-methyldecan-2-one; δ 0·75—1·05 (6H, m, 6-Me and 10-H_3), 1·05—1·7 (11H, m, 5 × CH_2 and 6-H), 2·04 (3H, s, 1-H_3), and 2·30 (2H, t, *S* 6, 3-H_2).

5-*Isopropylideneocta*-trans-3,7-*dien*-2-*one* (VI).—A solution of 6-methyldeca-4,5,9-trien-2-one (IV) (5 g) in xylene (50 ml) was heated under reflux for 24 h. G.l.c. of the mixture (5 ft 10% SE30 column; 120°) showed peaks at t_R 1·5 (9%), 4·1 (13%), identified as 6-methyldeca-4,5,9-trien-2-one, 6·4 (4%), and 7·8 min (75%), later identified as 5-isopropylideneocta-*trans*-3,7-dien-2-one (VI). The solvent was removed under reduced pressure, and the crude product was distilled (b.p. 89—92° at 0·6 mmHg). The ketone (VI) was purified by preparative g.l.c. on a 15 ft 10% SE30 column at 210°; $\nu_{max.}$ (neat) 1665, 1620, 1590, 1470, 1265, and 1230br cm^{-1}, δ 1·89 and 2·02 (each 3H, s, CMe_2), 2·16 (3H, s, 1-H_3), 6·02 (1H, d, *S* 15·5, 3-H), and 7·56 (1H, d, *S* 15·5, 4-H).

1-*Ethynyl*-1-*methylpent*-4-*enyl Acetate* (IX).—3-Methylhept-6-en-1-yn-3-ol (10 g) in pyridine (10 ml) and acetic anhydride (10 ml) was kept for 24 h at room temperature, then more acetic anhydride (10 ml) was added. The solution was maintained at room temperature for 3 days, then poured on crushed ice (100 g) and extracted with petroleum (b.p. 30—40°). The extract was washed with saturated aqueous sodium hydrogen carbonate, cold M-hydrochloric acid, and brine, then dried ($MgSO_4$), and distilled to yield the acetate (IX) (9·9 g, 74%), b.p. 88—91° at 27 mmHg, δ 1·66 (3H, s, 1-Me), 1·97 (3H, s, OAc), 1·8—2·4 (4H, m, 2- and 3-H_2), 2·40 (1H, s, ≡CH), 4·80—5·20 (2H, m, 3 main lines at 5·11, 5·01, and 4·83, 5-H_2), and 5·5—6·05 (1H, m, 4-H), *m/e* (70 eV) 124 (8%, $M - COCH_2$), 109(20), 106(3), 105(6), 91(41), 81(5), 79(7), 69(8), and 43(100).

The acetate was also prepared by reaction of the alcohol with acetyl chloride and diethylaniline in boiling ether.

3-*Methylhepta*-1,2,6-*trienyl Acetate* (X).—A solution of anhydrous silver perchlorate in benzene was prepared by azeotropic distillation of silver perchlorate monohydrate (38 mg) with benzene, with the volume of the solution maintained at *ca.* 10 ml throughout. To this solution was added butan-2-one (500 ml) containg tetramethylguanidine (10 drops) and the acetate (IX) (8·3 g). After 0·5 h at reflux, g.l.c. of the mixture indicated no starting material, and an essentially quantitative yield of a single product. The mixture was cooled and saturated ammonium chloride solution (5 ml) was added. The mixture was diluted with ether (500 ml), washed with water, dried ($MgSO_4$), and evaporated under reduced pressure to yield 3-methylhepta-1,2,6-trienyl acetate (X) (8·4 g), δ 1·81 (3H, d, *S* 2·5, 3-Me), 2·05 (3H, s, OAc), 2·1—2·25 (4H, m, 2 main lines at 2·13 and 2·19, 4- and 5-H_2), 4·8—5·2 (2H, m, 4 main lines at 4·83, 4·87, 5·03, and 5·11, 7-H_2), 5·45—6·05 (1H, m, 6-H), and 7·1—7·35 (1H, m, 1-H).

3-*Methylhepta*-2,6-*dienal* (XI).—According to the method of Benn,[6] a solution of the acetate (X) (5 g) in 80% acetic acid (100 ml) was warmed on a steam-bath under nitrogen for 1 h and then diluted with water (500 ml). The product was extracted with ether. The ethereal solution was washed with sodium carbonate solution and dried; the ether was removed under reduced pressure, affording a brown oil (3·8 g), $\nu_{max.}$ (neat) 1710 and 1655 cm^{-1}, δ (CCl_4) 1·96 (0·9H, d, *S* 1·5, 3-Me of *cis*-isomer), 2·14 (2·1H, d, *S* 1·5, 3-Me of *trans*-isomer), 2·0—2·7 (4H, m, 4- and 5-H_2), 4·8—5·25 (2H, m, 7-H_2), 5·45—6·15 (1H, m, 6-H), 5·78br (1H, d, *S* 7·5, 2-H), 11·21 (0·3H, d, *S* 7·5, 1-H of *cis*-isomer), and 11·26 (0·7H, d, *S* 7·5, 1-H of *trans*-isomer).

2-*Isopropylidenepent*-4-*enal* (XIII).—A solution of the acetate (X) (3·0 g) in xylene (50 ml) was heated under reflux for 24 h under nitrogen. G.l.c. then showed two new peaks in approximately equal proportions, and no starting material. The xylene was removed by column chromatography on silica gel; however little separation of the two components [presumably *cis*- and *trans*-isomers

[6] W. R. Benn, *J. Org. Chem.*, 1968, **33**, 3113.

of 2-isopropenylpenta-1,4-dienyl acetate (XII)] was effected; moreover, considerable hydrolysis of the acetate mixture occurred on the column, so the fractions eluted were combined and hydrolysed with sodium hydrogen carbonate in methanol,[6] to yield a brown oil (1·2 g). The crude product was distilled to yield 2-isopropylidenepent-4-enal (XIII) (0·5 g), b.p. 80—84° at 22 mmHg (lit.,[7] 80—82° at 20 mmHg), δ 1·7 and 1·85 (each 3H, s, CMe_2), 3·08 (2H, d, *S* 5, 3-H_2), 4·7—5·1 (2H, m, 5-H_2), 5·55—6·2 (1H, m, 4-H), and 9·90 (1H, s, 1-H).

[7] A. T. Babayan, M. G. Indzhikyan, A. A. Grigoryan, and R. V. Minasyan, *Izvest. Akad. Nauk Armyan. S.S.S.R. khim. Nauk.*, 1962, **15**, 567; A. T. Babayan, M. G. Indzhikyan, A. A. Grigoryan, and L. Kh. Gamburyan, *Zhur. org. Chim.*, 1966, **2**, 2122.

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