exist also in *Erythrina velutina* forma *aurantiaca* (Ridl.) Kruk. and *Erythrina Grisebachii* Urb.

The crystalline erythraline and erythratine bases, their hydrobromides and hydriodides, have been described. Many microanalyses on several samples and from different species have shown that erythraline has the empirical composition, $C_{18}H_{19}NO_3$, and erythratine has the empirical composition $C_{18}H_{21}NO_4$.

Erythraline and erythramine were of comparable activity (7–8 mg./kg.) in causing a curare-like paralysis in frogs, whereas, erythratine had one-tenth of this activity.

RAHWAY, N. J. RECEIVED DECEMBER 5, 1939

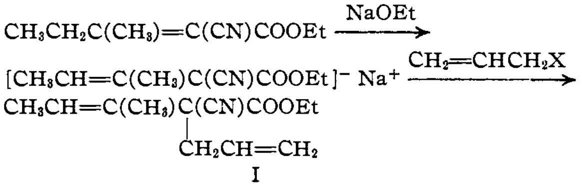
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE]

The Introduction of Substituted Vinyl Groups. V. A Rearrangement Involving the Migration of an Allyl Group in a Three-Carbon System[1]

BY ARTHUR C. COPE AND ELIZABETH M. HARDY[2]

The (dialkylvinyl)-alkylcyanoacetic esters described recently[3] were stable compounds which were not altered in any way during purification. However, in the preparation of ethyl (1-methylpropenyl)-allylcyanoacetate, which was studied but not reported in the previous work, an unstable product was formed, which changed into a stable substance of higher boiling point after several distillations in vacuum. The structures of these compounds and the nature of the rearrangement have now been determined, and are reported in this paper.

The substance formed initially when the sodium derivative prepared from ethyl (1-methylpropylidene)-cyanoacetate was treated with allyl halides proved to be sufficiently stable to be isolated in a pure state if it was distilled at a pressure of 1 mm. Analysis and molecular refraction were in agreement with the structure of the normal alkylation product, ethyl (1-methylpropenyl)-allylcyanoacetate, I.

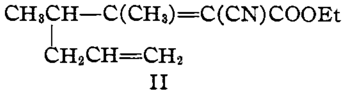


$$\mathrm{CH_3CH_2C(CH_3){=}C(CN)COOEt \xrightarrow{NaOEt} [CH_3CH{=}C(CH_3)C(CN)COOEt]^-\ Na^+ \xrightarrow{CH_2{=}CHCH_2X} CH_3CH{=}C(CH_3)\underset{\displaystyle CH_2CH{=}CH_2}{\underset{|}{C}}(CN)COOEt}$$

I

Structure I was established by quantitative reduction of the compound, which gave ethyl *s*-butyl-propylcyanoacetate, and condensation of the latter with urea, which produced 5-*s*-butyl-5-propyl-barbituric acid.

The ester I was completely rearranged on heating for four hours at 150–160°, or twenty minutes at 260°, into an isomeric substance of approximately 10° higher boiling point (at 16 mm.). The rearrangement product also had a higher index of refraction ($n^{25}D$ 1.4780 compared to 1.4609), and an exaltation in molecular refraction of +1.53. All of these properties indicate the presence of conjugated double bonds. Quantitative reduction proved the presence of two olefinic linkages, and the reduction product was proved to be a substituted cyanoacetic ester by condensation with urea, which gave a barbituric acid derivative. The high melting point of the latter (219.5–220.5°) suggested that it was a monoalkyl barbituric acid. The most probable way in which I could rearrange into a substance which would give a monoalkyl cyanoacetic ester on reduction involves a shift of the allyl group from the alpha to the gamma position, accompanied by a shift of the double bond from the β, γ to the α, β position, giving II.



$$\mathrm{CH_3\underset{\displaystyle CH_2CH{=}CH_2}{\underset{|}{CH}}{-}C(CH_3){=}C(CN)COOEt}$$

II

Formula II was established by cleavage of the compound with concentrated aqueous ammonia[4] to *unsym*-methyl allyl acetone and cyanoacetamide, and verified by synthesis from methyl allyl acetone and ethyl cyanoacetate.

$$\mathrm{II \xrightarrow{NH_4OH} CH_2{=}CHCH_2CH(CH_3)COCH_3 + CH_2(CN)CONH_2}$$

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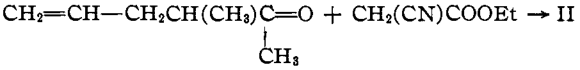
[1] Presented at the Eighth National Organic Chemistry Symposium, St. Louis, Mo., December 29, 1939.

[2] Abstracted from the M.A. Thesis submitted to Bryn Mawr College by Elizabeth M. Hardy in May, 1939.

[3] Cope and Hancock, THIS JOURNAL, **60**, 2903 (1938).

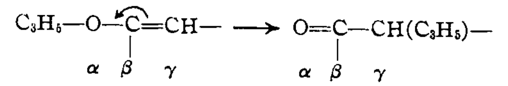
[4] Analogous to the cleavage of ethyl isopropylidenemalonate to acetone and malonamide by ammonia reported by Kötz, *J. prakt. Chem.*, [2] **75**, 479 (1907).



$$CH_2{=}CH{-}CH_2CH(CH_3)\underset{\displaystyle CH_3}{C}{=}O + CH_2(CN)COOEt \rightarrow II$$

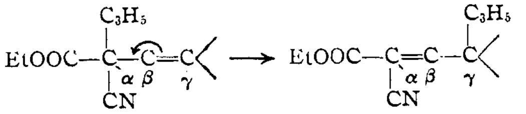
This appears to be the first case in which an allyl group has been observed to undergo a thermally induced α, γ shift in a three-carbon system. It seems probable, however, that this new rearrangement is similar in type to the Claisen rearrangement of allyl enol,[5,6] phenol[7,5,8] and vinyl[8b,9] ethers, and that it is motivated by similar forces.

In the Claisen rearrangement of ethers, an allyl group undergoes an α, γ shift from the electron attracting element oxygen to a carbon atom, and a carbonyl group is formed by migration of a double bond.



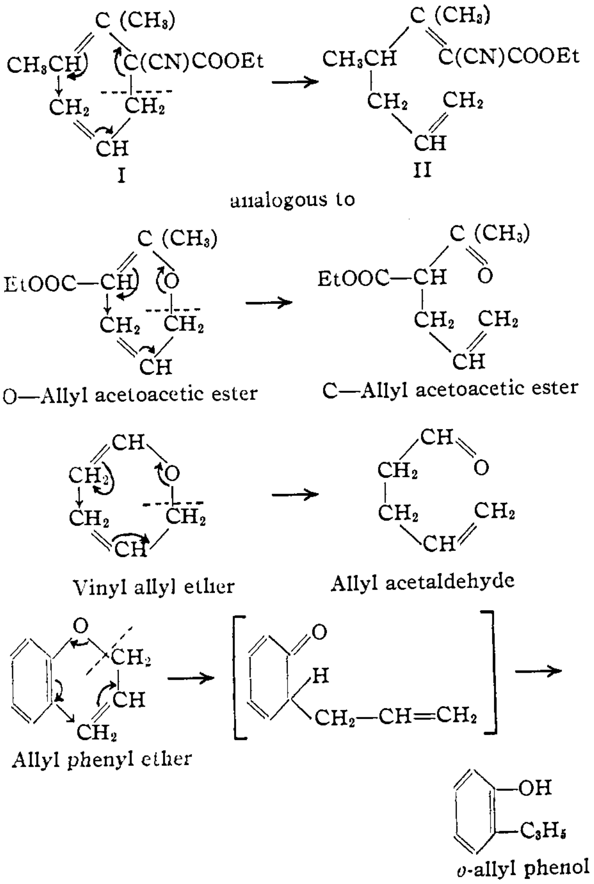
$$C_3H_5{-}\underset{\alpha}{O}{-}\underset{\beta}{C}{=}\underset{\gamma}{C}H{-} \longrightarrow \underset{\alpha}{O}{=}\underset{\beta}{C}{-}\underset{\gamma}{C}H(C_3H_5){-}$$

In the present case, an allyl group undergoes an α, γ shift from a carbon atom which is electron attracting by virtue of attachement to CN and COOEt groups to one which is less electron attracting. In the process the double bond which shifts becomes attached to the electron attracting carbon atom and conjugated with the CN and COOEt groups.



$$EtOOC{-}\overset{\displaystyle C_3H_5}{\underset{\displaystyle CN}{C}}{-}\underset{\alpha\ \beta}{C}{=}\underset{\gamma}{C}< \longrightarrow EtOOC{-}\underset{\displaystyle CN}{C}{=}\underset{\alpha\ \beta}{C}{-}\overset{\displaystyle C_3H_5}{\underset{\gamma}{C}}<$$

As in the thermal rearrangement of enol, phenol and vinyl ethers, the isomerization is dependent upon the presence of the allyl group. Three (1-methylpropenyl) alkylcyanoacetic esters, $CH_3CH{=}C(CH_3)C(R)(CN)COOEt$, in which R was methyl, propyl and butyl, were completely stable at much higher temperatures than are required to rearrange the allyl compound. Consequently a cyclic mechanism is regarded as probable.



I

II

analogous to

O—Allyl acetoacetic ester

C—Allyl acetoacetic ester

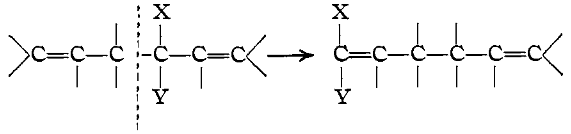
Vinyl allyl ether

Allyl acetaldehyde

Allyl phenyl ether

o-allyl phenol

If the mechanism postulated for the present rearrangement is correct, the isomerization is intramolecular and the allyl group is turned around during the shift. These points are being studied, as is the possibility that this type of rearrangement is general for appropriately substituted three carbon systems attached to allyl or substituted allyl groups.



$$>C{=}C{-}C\ \vdots\ \overset{\displaystyle X}{\underset{\displaystyle Y}{C}}{-}C{=}C< \longrightarrow \overset{\displaystyle X}{\underset{\displaystyle Y}{C}}{=}C{-}C{-}C{-}C{=}C<$$

Experimental Part

Ethyl (1-Methylpropenyl)-allylcyanoacetate (Formula I).—One-half mole of ethyl (1-methylpropylidene)-cyanoacetate[10] was converted to the sodium enolate in absolute ethyl alcohol and alkylated with allyl bromide by the general procedure described previously.[3] The reaction mixture was refluxed until it became neutral (forty-five minutes), cooled, diluted with water and extracted with benzene in the usual manner. The residue obtained on concentration of the benzene extract was distilled at a low pressure and superheating was avoided in order to minimize rearrangement. The first distillation gave 67 g. of crude ester, b. p. 90–143° (1 mm.), and 29 g. of tarry residue. The distillate was purified by shaking with 200

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(5) Summary by Claisen and Tietze, *Ber.*, **58**, 275 (1925).

(6) Lauer and Kilburn, THIS JOURNAL, **59**, 2586 (1937).

(7) Claisen, *Ber.*, **45**, 3157 (1912).

(8) References to important recent studies are made by: (a) Mumm and Möller, *ibid.*, **70**, 2215 (1937); (b) Hurd and Pollack, *J. Org. Chem.*, **3**, 550 (1939); (c) Lauer and Ungnade, THIS JOURNAL, **61**, 3047 (1939).

(9) Hurd and Pollack, *ibid.*, **60**, 1905 (1938).

(10) Prepared by condensing methyl ethyl ketone with ethyl cyanoacetate in the presence of piperidine acetate or ammonium acetate and acetic acid and removing the water formed by distilling benzene from the mixture. See Cope, THIS JOURNAL, **59**, 2327 (1937). The ester has been described by Scheiber and Meisel, *Ber.*, **48**, 259 (1915).

cc. of 20% sodium bisulfite solution for twelve hours and redistilling through a Widmer column. The yield of pure ester was 37 g. (34%); b. p. 94.5–96° (1 mm.); $n^{25}\text{D}$ 1.4609; $d^{25}{}_{25}$ 0.9735; $M\text{D}$ calcd. 58.10, found 58.54.

Anal. Calcd. for $C_{12}H_{17}O_2N$: N, 6.76. Found: N, 6.58.

The ester also was prepared by a similar alkylation using allyl chloride, but the yield was smaller (17%).

Ethyl (1,2-Dimethyl 4-Pentenylidene)-cyanoacetate (Formula II).—When the alkylation product prepared by the method described in the preceding section was purified by distillation at pressures of 15 to 20 mm., partial rearrangement occurred. A typical product had b. p. 141–148° (16 mm.); $n^{25}\text{D}$ 1.4683. This material was refractionated at 16 mm. several times in an effort to obtain a pure product, but each distillation resulted in a rise in both the boiling point and refractive index of each fraction. The various fractions were finally combined and refluxed for periods of one to five hours at pressures of 18 to 60 mm., and refractionated through a Widmer column after each period of refluxing until there was no further rise in refractive index or boiling point. The properties of the pure rearranged ester (Formula II) obtained in this way were: b. p. 147–148° (16 mm.); $n^{25}\text{D}$ 1.4780; $d^{25}{}_{25}$ 0.9816; $M\text{D}$ calcd. 58.10; found 59.63, exaltation +1.53.

Anal. Calcd. for $C_{12}H_{17}O_2N$: N, 6.76. Found: N, 6.50.

The rearrangement was practically complete after the ester I was refluxed for four hours at 18 mm., at which pressure the temperature of the refluxing liquid was 150–160°. There was little if any decomposition during the period of heating, and the yield of the rearrangement product (25–30%) differed from that of the normal alkylation product only by the amount to be expected because of the manipulative losses resulting from several distillations.

The rearrangement can be carried out more rapidly by refluxing the ester at atmospheric pressure (b. p. approximately 260°). A 12-g. sample of pure ethyl (1-methylpropenyl)-allylcyanoacetate (Formula I) was refluxed for twenty minutes at atmospheric pressure and then distilled in vacuum. The yield of the rearrangement product (Formula II, properties described above) was 8 g. Some high boiling material was formed at this temperature.

Thermal Stability of Other Ethyl (1-Methylpropenyl)-alkylcyanoacetates.—A 10-g. sample of ethyl (1-methylpropenyl)-propylcyanoacetate was refluxed for two hours at atmospheric pressure. There was only slight darkening of the liquid during heating, and on distillation in vacuum 9 g. of the pure ester was recovered, unchanged in boiling point and refractive index. Samples of ethyl (1-methylpropenyl)-ethylcyanoacetate and ethyl (1-methylpropenyl)-butylcyanoacetate[3] were also refluxed for two hours at atmospheric pressure. On distillation following the period of heating 80 to 90% of each of the pure esters was recovered.

Proof of the Structure of Ethyl (1-Methylpropenyl)-allylcyanoacetate (Formula I).—Several samples of the ester were hydrogenated in alcohol solution at room temperature, using a palladinized charcoal catalyst.[11] Complete reduction, which required two moles of hydrogen, was obtained only by several additions of catalyst, or preferably by purification of the partially reduced ester by distillation after the catalyst had become deactivated. The reduced ester (5.8 g. from the reduction of 7.1 g. of I) had b. p. 138–140° (25 mm.) and $n^{25}\text{D}$ 1.4358, in agreement with the properties of a known sample of ethyl (*s*-butyl)-propylcyanoacetate (see below).

The reduced ester described above was converted into a solid derivative by condensation with urea in the presence of alcoholic sodium ethoxide in the usual manner.[12] Hydrolysis of the intermediate iminobarbituric acid obtained from 5.8 g. of the ester gave a mixture of neutral and acidic material, from which the substituted barbituric acid was separated by extraction with dilute sodium hydroxide. The product obtained by acidification of the alkaline extract was purified by one crystallization from 50% alcohol. The yield of pure 5-propyl 5-*s*-butyl-barbituric acid,[13] m. p. 135–137°, was 0.6 g. (10%). The identity of this barbituric acid derivative was established by comparison with a known sample of 5-propyl-5-*s*-butyl-barbituric acid[14] prepared from the known ethyl (*s*-butyl)-propylcyanoacetate described below. The m. p. and mixed m. p. of the two samples were identical.

The known ethyl (*s*-butyl)-propylcyanoacetate referred to above was prepared from ethyl (1-methylpropylidene)-cyanoacetate.[10] Fifty grams of the alkylidene ester, 100 cc. of alcohol and 2 g. of palladinized charcoal catalyst were shaken with hydrogen at 15 to 30 lb. (1–2 atm.) pressure until reduction had become very slow and the theoretical amount of hydrogen had been absorbed (forty minutes). The catalyst was removed by filtration, the solvent distilled in vacuum, and the residue shaken with a 20% sodium bisulfite solution to remove any unreduced ester. The ester layer was combined with an ether extract of the sodium bisulfite solution, washed with dilute hydrochloric acid, and distilled through a Widmer column. The yield of pure ethyl (*s*-butyl)-cyanoacetate[15] was 37.5 g. (74%); b. p. 105–106° (11 mm.); $n^{25}\text{D}$ 1.4273; $d^{25}{}_{25}$ 0.9617; $M\text{D}$ calcd. 45.18, found 45.31.

Anal. Calcd. for $C_9H_{15}O_2N$: N, 8.28. Found: N, 8.28.

The ethyl (*s*-butyl)-cyanoacetate (30.3 g.) was converted into the sodium derivative by addition to a solution of sodium (4.14 g.) in 150 cc. of absolute alcohol. *n*-Propyl bromide (24.6 g.) was added and the solution refluxed for one and one-half hours. The reaction mixture was diluted with water and extracted with benzene. The benzene was distilled and the crude ester was purified by shaking with concd. ammonium hydroxide overnight to remove any remaining monoalkyl cyanoacetic ester. Distillation through a Widmer column gave 26.7 g. (73%) of ethyl (*s*-butyl)-propylcyanoacetate, b. p. 122.5–123.5° (11 mm.) $n^{25}\text{D}$ 1.4356; $d^{25}{}_{25}$ 0.9378; $M\text{D}$ calcd. 59.04, found 58.99.

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[11] Hartung, This Journal, **50**, 3372 (1928).

[12] *Cf.* Cope and Hancock, *ibid.*, **61**, 353 (1939).

[13] Shonle and Waldo, *ibid.*, **55**, 4649 (1933).

[14] The barbituric acid derivative identifies the ester obtained by reduction even though it was formed in low yield, for under the same conditions the ester of known structure also gave 5-propyl-5-*s*-butyl-barbituric acid in only 10% yield. Relatively large amounts of the same neutral by-product were formed from both samples of the ester.

[15] This ester has been described by Roger in French Patent 598,072, which records only b. p. 118° (17 mm.).

Anal. Calcd. for $C_{12}H_{21}O_2N$: N, 6.63. Found: N, 6.57.

Proof of the Structure of Ethyl (1,2-Dimethyl 4-Pentenylidene)-cyanoacetate (Formula II). Reduction.—Duplicate samples of the ester were reduced rapidly and quantitatively in alcohol solution at room temperature and pressure in the presence of palladinized charcoal, absorbing 105 and 107% of two molar equivalents of hydrogen. From the reduction of 5.8 g. of II, 3.0 g. of ethyl (1,2-dimethylpentyl)-cyanoacetate was obtained; b. p. 134–136° (12 mm.); n^{25}D 1.4389.

Anal. Calcd. for $C_{12}H_{21}O_2N$: N, 6.63. Found: N, 6.50.

Condensation of the ethyl (1,2-dimethylpentyl)-cyanoacetate with urea, followed by hydrolysis, gave 5-(1,2-dimethylpentyl)-barbituric acid, m. p. 219.5–220.5°.

Anal. Calcd. for $C_{11}H_{18}O_3N_2$: N, 12.38. Found: N, 12.54.

Cleavage with Ammonia.—Seven grams of the rearranged ester (II) and 50 cc. of concd. aqueous ammonia were shaken for thirty hours. The ammonia was extracted twice with ether and the extract dried over potassium carbonate. Distillation gave 2.2 g. (60%) of *unsym*-methyl allyl acetone (3-methyl-5-hexene-2-one), b. p. 137–138°, n^{25}D 1.4215. Evaporation of the ammonia solution left a crystalline residue which on recrystallization from alcohol gave 1.5 g. (54%) of cyanoacetamide, m. p. and mixed m. p. with a known sample 121–122°.

In order to be certain of the identity of the *unsym*-methyl allyl acetone produced by cleavage a known sample and solid derivatives were made. The ketone was prepared by the hydrolysis of ethyl allylmethylacetoacetate as described by Jacobi and Merling.[16] The ethyl allylmethylacetoacetate[17] was synthesized from ethyl allylacetoacetate.[18] The *unsym*-methyl allyl acetone had b. p. 137–138° (previously reported as 138–140°) and n^{25}D 1.4218. Its semicarbazone (m. p. 84–85°) and 2,4-dinitrophenylhydrazone (m. p. 41–42°) were prepared by standard methods.

Anal. of the semicarbazone. Calcd. for $C_8H_{15}ON_3$: N, 24.83. Found: N, 24.70. *Anal.* of the dinitrophenylhydrazone. Calcd. for $C_{13}H_{16}O_4N_4$: N, 19.17. Found: N, 19.35.

The semicarbazone and 2,4-dinitrophenylhydrazone prepared from the ketone isolated from the cleavage of II with ammonia were identical in m. p. and mixed m. p. with the derivatives prepared from the known ketone.

Synthesis of II from *unsym*-Methyl Allyl Acetone.—*unsym*-Methyl allyl acetone (9.3 g.), ethyl cyanoacetate (9.5 g.), ammonium acetate (0.8 g.), acetic acid (1.2 g.) and benzene (25 cc.) were refluxed under a constant water separator for one hour. The benzene solution was cooled, washed with water and distilled in vacuum. The reaction was incomplete, for 6 g. of ethyl cyanoacetate was recovered, but 5 g. (29%) of ethyl (1,2-dimethyl 4-pentenylidene)-cyanoacetate was obtained, b. p. 153–154° (23 mm.); n^{25}D 1.4781. These properties are in good agreement with those of the ester II prepared by the thermal rearrangement of I.

Summary

Ethyl (1-methylpropenyl)-allylcyanoacetate rearranges readily on heating at temperatures between 150 and 260°, giving ethyl (1,2-dimethyl 4-pentenylidene)-cyanoacetate. In the rearrangement the allyl group migrates from the α to the γ carbon atom of a three carbon system, while the double bond in the latter shifts from the β, γ to the α, β position.

It appears probable that this rearrangement involving the migration of an allyl group in a three carbon system occurs for reasons similar to those responsible for the Claisen rearrangement of enol, phenol and vinyl ethers, and that the two types of rearrangement follow similar mechanisms.

BRYN MAWR, PA. RECEIVED DECEMBER 18, 1939

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[16] Jacobi and Merling, *Ann.*, **278**, 11 (1894).

[17] James, *ibid.*, **226**, 207 (1884).

[18] Brühl, *J. prakt. Chem.*, **50**, 132 (1894).