SYNTHESIS OF 2-ALLYL-2-ETHYLSUCCINIC ANHYDRIDE* ** ***

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The paper describes a synthesis of 2-allyl-2-ethyl-succinic anhydride (*I*), starting from ethyl cyanoacetate, with the Wolff rearrangement of diazo ketone *XVI* as the key step. The unsuccessful attempts at the synthesis are also described. The mechanism leading to an anomalous product of the reaction between cyanohydrine *VI* and sodium ethylcyanoacetate, *viz.* ethyl 2-cyano-3-methyl-5-oxoheptanoate (*VIII*), is also discussed.

Within the framework of our synthetic programme in the field of indol alkaloids we needed 2-allyl-2-ethylsuccinic anhydride (*I*) as an intermediate. First we considered a route *via* dicyano esters *II*, accessible either by the addition of hydrogen cyanide to 3,3-disubstituted 2-cyanoacrylates (products of the Knoevenagel condensation of cyanoacetates with the corresponding carbonyl compounds[1]), or by the reaction of ketone cyanohydrines with sodium salt of ethyl cyanoacetate[2]. As the former method would have involved the ready isomerization of 1-alken-4-ones to 2-alken-4-ones[3], we chose the latter method, using masked carbonyl compounds.

The key intermediate, 2-ethyl-2-hydroxy-4-pentenenitrile (*VI*), was obtained by alkylation of protected cyanohydrines[4]. The starting compound was 2-hydroxybutyronitrile (*III*), whose reaction with ethyl vinyl ether gave a mixture of diastereoisomers of 2-(1-ethoxyethoxy)butyronitrile (*IV*). This cyano-acetal was converted into its lithium salt by the action of lithium diisopropylamide in a mixture of hexamethylphosphoramide and tetrahydrofuran at −78°C. It was alkylated with allyl bromide with the formation of a mixture of diastereoisomeric 2-(1-ethoxyethoxy)-2-ethyl-4-pentenenitriles (*V*), from which the desired cyanohydrine *VI* was liberated by acid hydrolysis in methanol in an almost quantitative yield. Its condensation with sodium ethyl cyanoacetate, expected on good grounds[2,5] to lead to cyano ester *VII*, gave rise, however, even under modified experimental conditions, to a new compound, $C_{11}H_{17}NO_3$, which we have identified as ethyl 2-cyano-3-methyl-5-oxoheptanoate (*VIII*).

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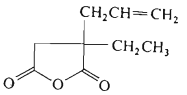
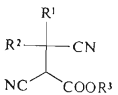
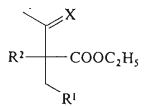


I

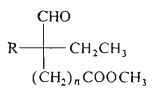


II

III, $R^1 = OH$, $R^2 = H$
IV, $R^1 = OCH(CH_3)OC_2H_5$, $R^2 = H$
V, $R^1 = OCH(CH_3)OC_2H_5$, $R^2 = CH_2CH{=}CH_2$
VI, $R^1 = OH$, $R^2 = CH_2CH{=}CH_2$
VII, $R^1 = CH(CN)COOC_2H_5$, $R^2 = CH_2CH{=}CH_2$



IXa, $R^1 = COOC_2H_5$, $R^2 = CH_2CH{=}CH_2$, X = O
IXb, $R^1 = COOC_2H_5$, $R^2 = H$, X = O
IXc, $R^1 = CH_3$, $R^2 = CH_2CH{=}CH_2$, X = *p*-$CH_3C_6H_4SO_2NHN$



Xa, R = H, n = 1
Xb, R = $CH_2CH{=}CH_2$, n = 1
XIa, R = H, n = 2
XIb, R = $CH_2CH{=}CH_2$, n = 2

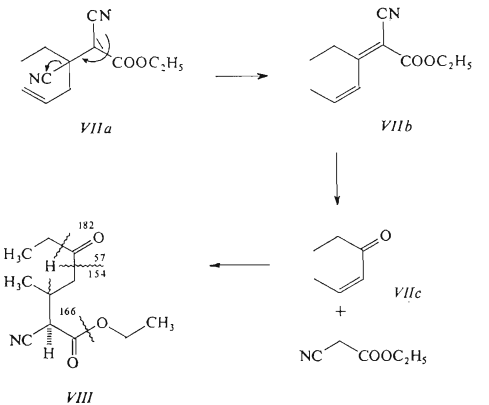
The elemental composition, determined by mass spectrometry (M^+ at *m/z* 211 $C_{11}H_{17}NO_3$), excludes the presence of a second nitrile group in the molecule. Strong absorption bands at 1750 and 1721 cm^{-1} in the IR spectrum suggested that in addition to an ester group the molecule contains a saturated keto group in the chain. However, the absorption bands of a double bond were not present in the spectrum. In agreement with this, the ^{1}H-NMR spectrum lacked the signals characteristic of olefinic protons of the allyl system. Detailed analysis of the spectrum revealed the presence of ethyl groups (in a ketonic and an ester function), but primarily it revealed the grouping —CH(CH_3)—CH(CN)—CO—, which manifests itself by an AB quartet with a centre at 3·80 ppm, the interaction constant being 4·5 Hz. The mass-spectrometric fragmentation, indicated in formula *VIII*, afforded the missing data. The keto ester *VIII* is a mixture of two diastereoisomers, as was demonstrated by both gas chromatography and ^{1}H-NMR spectrometry.

The probable mechanism of formation of the keto ester *VIII* (Scheme 1) assumes that elimination of the quaternary cyano group from the dicyano ester *VIIa* and migration of the double bond lead to the conjugated diene *VIIb*. The well-known lability of compounds of this type in strongly alkaline media[6] leads, *via* the retro-Knoevenagel reaction, to 2-hexen-4-one (*VIIc*), which in the final step is converted

by the alkali-catalysed addition of ethyl cyanoacetate into ethyl 2-cyano-3-methyl--5-oxoheptanoate (*VIII*). The alternative mechanism, consisting in the primary decomposition of the cyanohydrine *VI* to 1-hexen-4-one and the following isomerization of the latter to 2-hexen-4-one (*VIIc*), seems less likely, since conduction of the reaction in the inverse way, developed for unstable cyanohydrines of aldehydes[2] (addition of a solution of sodium ethoxide to a mixture of cyanoacetate and the cyanohydrine *VI*) led to the same product *VIII*.

In further attempts at synthesis of the anhydride *I* we tried to use diethyl 2-acetyl--2-allyl succinate (*IXa*), prepared by allylation of diethyl 2-acetylsuccinate (*IXb*). Its thioketal, however, needed for the contemplated reductive elimination of the keto group, could not be obtained, perhaps for steric hindrance, though various conditions were tried (gaseous hydrogen chloride at room temperature or an elevated temperature, boron trifluoride etherate, zinc chloride). Attempts to remove the keto group in *IXa via* the tosyl hydrazone were given up, since even with the simplest model compound, *viz.* tosyl hydrazone of ethyl 2-allyl-2-ethyl-3-oxobutanoate (*IXc*), we were unable to remove this group by reductive elimination (sodium cyanoborohydride in a mixture of sulpholane and dimethylformamide)[7].

Attempts to use enamines have also ended in failure. Thus reaction of diisobutyl enamine[8] of butyraldehyde with methyl bromoacetate afforded methyl 3-formylpentanoate (*XIa*), but diisobutyl or pyrrolidine enamine of this aldehyde-ester failed to be alkylated with allyl bromide to the desired methyl 3-ethyl-3-formyl-

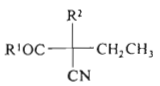


SCHEME 1

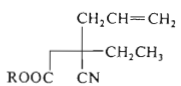
-5-hexanoate (*Xb*), although the model pyrrolidine enamine of methyl 4-formylhexanoate (*XIa*) under analogous conditions[9] gave methyl 4-ethyl-4-formyl-6-heptenoate (*XIb*) in a yield of nearly 60%. The probable cause of the failure was the lability[10] of aldehyde-esters of succinic acid and a difference in steric hindrance between the aldehyde-ester enamines *Xa* and *XIa*.

Finally, we turned to the homologization Arndt–Eistert reaction, although difficulties were expected. These really cropped up in the attempted homologization of ethyl hydrogen-allylethylmalonate[11], where the Wolff rearrangement, catalysed by silver ions, gave a complex mixture of non-identified compounds. That the double bond in γ-position to the diazoketo group was not one of the complicating factors became evident when we applied successfully the Knabe method[12] to the series of cyanoacetic acid.

The starting compound was ethyl cyanoacetate, which was converted by reductive alkylation[13] (81·3%) into ethyl 2-cyanobutanoate (*XII*). This was alkylated to ethyl 2-ethyl-2-cyano-4-pentenoate (*XIII*), which was hydrolysed by potassium hydroxide in ethanol (1·3 equivalents) to 2-ethyl-2-cyano-4-pentenoic acid (*XIV*). Its treatment with thionyl chloride gave the corresponding chloride *XV*, whose reaction with an excess of diazomethane in ether gave rise to the diazoketone *XVI*. This, without having been purified, was subjected to the Wolff rearrangement. Treatment with silver oxide in boiling ethanol[14], or reaction with silver benzoate in methanol containing triethylamine[15], afforded ethyl or methyl ester of 3-ethyl-3-cyano-5-hexenoic acid (*XVII*) in practically the same yield (68%).



XII, $R^1 = OC_2H_5$, $R^2 = H$
XIII, $R^1 = OC_2H_5$, $R^2 = CH_2CH{=}CH_2$
XIV, $R^1 = OH$, $R^2 = CH_2CH{=}CH_2$
XV, $R^1 = Cl$, $R^2 = CH_2CH{=}CH_2$
XVI, $R^1 = CHN_2$, $R^2 = CH_2CH{=}CH_2$



XVIIa, $R = C_2H_5$
XVIIb, $R = CH_3$

The generally prefered acid hydrolysis of substituted cyanopropionates, either by hydrochloric acid[16] or a mixture of sulphuric acid, water and acetic acid[17], failed in this case, because of the labile allyl system. By contrast, alkaline hydrolysis[6] of the cyanopropionates *XVII*, by heating them in 25% aqueous potassium hydroxide for 30 h, followed by the action of acetyl chloride on the non-isolated succinic acid, gave 2-allyl-2-ethylsuccinic anhydride (*I*), b.p. 130·5–132°C/1410 Pa, in a high yield. The structure of the compound was corroborated by mass spectrometry (molecular ion m/z 168) and infrared spectroscopy (ν(C=O) 1835 and 1788 cm^{-1} in tetra-

chloromethane); the ^{1}H-NMR spectrum contained a clear-cut system of the allyl group signals (5·7, 1 H, 1 H, m; 5·21, 1 H, d. with str., J = 11·0 Hz; 5·16, 1 H, d. with str., J = 17·0 Hz). The overall yield of anhydride *I* based on the cyanobutanoate *XII* was 44·5%.

EXPERIMENTAL

The boiling points and melting points (Boetius microblock) are not corrected. Analytical samples were dried for 6 h at room temperature and a pressure of 1·4 Pa. Purity of the compounds was tested by gas chromatography with and apparatus CHROM III IKZ (ČSSR). ^{1}H-NMR spectra were measured on an 80 MHz apparatus BS 487 (Tesla, ČSSR). The chemical shifts are given in the δ-scale (ppm), with the use of tetramethylsilane as internal standard (d. with str. = doublet with a structure). The infrared spectra were determined on an apparatus UR 10 (Zeiss, Jena, G.D.R.). The ultraviolet spectra were recorded on a spectrophotometer Specord Uvis (Zeiss, Jena, G.D.R.) in methanolic solutions. The mass spectra were measured on a high-resolution double focusing mass spectrometer MS 902 (AEI, Great Britain), the energy of ionizing electrons being 70 eV.

2-(1-Ethoxyethoxy)butyronitrile (*IV*)

To 210·0 g (2·47 mol) of 2-hydroxybutyronitrile[18] (*III*) (b.p. 84·5—86°C/1 470 Pa), pre-heated to 50°C, was added dropwise under stirring 180·3 g (2·50 mol) of ethyl vinyl ether at such a rate that the temperature kept at 60°C. The mixture was then stirred for 1·5 h at 100°C. Distillation and redistillation *in vacuo* yielded 291·0 g (75·1%) of a liquid boiling at 72·5—76°C/1 220 Pa. GLC (62°C) showed that it was a mixture of two diastereoisomers (purity 96%): R_t = 8·5 min (61%) and R_t 11·4 min (39%). IR spectrum in CCl_4: 2265 cm^{-1} (C≡N). ^{1}H-NMR spectrum in $CDCl_3$: 4·92 and 4·84 (a total of 1 H, 2 × q, J = 5·5 Hz; —O—CH(CH$_3$)—O—); 4·43 and 4·26 (a total of 1 H, 2 × t, J = 6·5 Hz; —CH$_2$—CH(CN)—O—); 3·60 (2 H, m; CH$_3$—CH$_2$—O—). Mass spectrum: *m/z* 157 (M^+, $C_8H_{15}NO_2$).

2-(1-Ethoxyethoxy)-2-ethyl-4-pentenenitrile (*V*)

To a stirred solution of diisopropylamine (160 g, 1·58 mol) in tetrahydrofuran (850 ml) was added dropwise under nitrogen a 2·1M solution of n-butyl lithium (775 ml, 1·58 mol) in hexane in the course of 1 h. After stirring for another 0·5 h and cooling the mixture to −78°C a mixture of the nitrile *IV* (234·1 g, 1·49 mol) and hexamethylphosphoramide (325·0 g) was added dropwise during 45 min. After stirring for 1·5 h a solution of allyl bromide (259·5 g, 2·14 mol) in tetrahydrofuran (600 ml) was added dropwise in the course of 1 h. The mixture was stirred for 2·5 h at −78°C, warmed during 1 h to 15°C, left standing overnight at room temperature and decomposed with water (900 ml). The organic layer was evaporated and distilled *in vacuo*; the aqueous phase was extracted with benzene (600 ml, 2 × 350 ml). The residue and the organic extracts were combined, washed with water (500 ml, 2 × 300 ml) and brine (350 ml) and dried. The solvent was removed *in vacuo*. Repeated vacuum distillation of the residue through a column afforded an oily product (130·4 g, 44·4%), boiling at 95·5—97°C/1 330 Pa. According to GLC (87°C) it was a mixture of two diastereoisomers (purity 94%), with R_t = 24·5 min (41%) and R_t = 28·2 min (59%). IR spectrum in $CHCl_3$: 2270 (C≡N), 1651 cm^{-1} (C=C). ^{1}H-NMR spectrum in $CDCl_3$: all signals were multiplets. Mass spectrum: *m/z* 197 (M^+, $C_{11}H_{19}NO_2$).

2-Ethyl-2-hydroxy-4-pentenenitrile (*VI*)

A mixture of the nitrile *V* (119·5 g, 0·61 mol), 5% sulphuric acid (125 ml) and methanol (760 ml) was stirred at room temperature for 15 min and concentrated *in vacuo*. The residue was partitioned between benzene (200 ml, 2 × 60 ml) and water (100 ml). After drying the benzene extracts and evaporation of the benzene, distillation of the residue *in vacuo* gave an oil (73·6 g, 96·8%), boiling at 93·5–95°C/1 350 Pa. IR spectrum in $CHCl_3$: 3 400 (OH), 2 260 (C≡N), 1 645 cm^{-1} (C=C). ^{1}H-NMR spectrum in $CDCl_3$: 5·31 (1 H, d with str., J = 10·0 Hz; *cis*-H—CH=CH—CH_2—); 5·28 (1 H, d with str., J = 16·0 Hz; *trans*-H—CH=CH—CH_2—); 3·25 (1 H, bs; H—O—C(CN)—); 1·85 (2 H, q, J = 7·0 Hz; CH_3—CH_2—C(CN)—); 1·12 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C(CN)—). Mass spectrum: no molecular ion or a ion characteristic of nitriles ($(M+1)^+$ or $(M-1)^+$) was detected. The highest ion, m/z 98 ($C_6H_{10}O$), corresponded to a loss of hydrogen cyanide, probably by a cyclic mechanism.

Ethyl 2-Cyano-3-methyl-5-oxoheptanoate (*VIII*)

a) To a suspension of sodium salt of ethyl cyanoacetate, prepared from ethyl cyanoacetate (3·165 g, 28·0 mmol) and sodium (0·64 g, 27·8 mmol) in ethanol (12 ml), was added dropwise, under stirring and cooling to 10°C, the nitrile *VI* (3·51 g, 28·1 mmol) in the course of 15 min. The stirring was continued for 30 min and the mixture was left standing in a refrigerator for 40 h. It was then brought to pH 4–5 with 10% hydrochloric acid and concentrated *in vacuo*. The combined ethereal extracts (30 ml, 2 × 15 ml) of the concentrate were washed with two 10 ml portions of 5% sodium hydrogen carbonate and 20 ml of water, dried with anhydrous calcium chloride and freed from the ether by evaporation. Distillation of the residue gave an oil (2·85 g, 46·3%) boiling at 155–159°C/1 200 Pa. According to GLC it was a mixture of two diastereoisomers in a ratio of *c.* 4 : 5 (purity 93%). IR spectrum in $CHCl_3$: 2 280 (C≡N), 1 750 (O—C=O), 1 721 cm^{-1} (C=O). ^{1}H-NMR spectrum in $CDCl_3$: 4·30 and 4·27 (a total of 2 H, 2 × q, J = = 7·0 Hz; —COO—CH_2—CH_3); 3·94 and 3·66 (a total of 1 H, 2 × d, J = 4·5 Hz; —CH(CH_3)—CH—CN); 2·48 (2 H, q, J = 7·0 Hz; CH_3—CH_2—CO—); 1·36 (3 H, t, J = 7·0 Hz; —COO—CH_2—CH_3); 1·09 (3 H, t, J = 7·0 Hz; CH_3—CH_2—CO—). Mass spectrum: (m/z) 211 (M^+, $C_{11}H_{17}NO_3$), 182 ($M-C_2H_5$), 166 ($M-C_2H_5O$), 154 ($M-C_3H_5O$), 57 (100%, C_3H_5O).

b) A suspension of sodium salt of ethyl cyanoacetate, prepared from ethyl cyanoacetate (66·0 g, 0·58 mol), sodium (12·87 g, 0·56 mol) and ethanol (300 ml), was slowly added at room temperature to a stirred solution of the nitrile *VI* (73·0 g, 0·58 mol) in ethanol (70 ml). After 2 days' standing at room temperature the mixture was diluted with water (300 ml) and neutralized under cooling with 10% hydrochloric acid (to pH 5). After evaporation of the ethanol *in vacuo* it was extracted with 3 portions of ether (250 ml, 2 × 100 ml). The combined extracts were washed with 60 ml of water, 5% sodium carbonate (100 ml, 3 × 50 ml) and brine (2 × 60 ml), dried with anhydrous calcium chloride and concentrated *in vacuo*. Repeated distillation of the residue over a column (length 10 cm) gave an oil (45·9 g, 35·8%), showed by GLC to be identical with that obtained by procedure *a*.

Diethyl 2-Acetyl-2-allylsuccinate (*IXa*)

To a stirred suspension of sodium hydride (16·85 g, 0·70 mol) in a mixture of dimethylformamide (60 ml) and benzene (1 200 ml), was added diethyl acetylsuccinate[19] (*IXb*) (150·0 g, 0·69 mol) in the course of 30 min. The stirring was continued for another 30 min, then allyl bromide (84·8 g,

0·70 mol) was added dropwise in the course of 25 min and the mixture was refluxed for 2 h. The cooled mixture was poured into 2% sulphuric acid (400 ml). After the phase separation and extraction of the aqueous phase with benzene the combined benzene extracts were washed with water and brine. The solution was dried with magnesium sulphate, the solvent was evaporated and the residue was distilled *in vacuo*; yield 144·5 g (81·4%) of a liquid boiling at 102 to 106°C/14 Pa, purity 96% (GLC). IR spectrum in CCl_4: 1730 and 1710 (C=O), 1640 cm^{-1} (C=C). ^{1}H-NMR spectrum in $CDCl_3$: 5·14 (1 H, d with str., J = 10·0 Hz; *cis*-**H**—CH=CH—CH_2—); 5·11 (1 H, d with str., J = 16·0 Hz; *trans*-**H**—CH=CH—CH_2—); 4·24 and 4·11 (2 × 2 H, 2 × q, J = 7·0 Hz; —COO—CH_2—CH_3); 2·94 (2 H, s; —C(—CH_2—COO—)—); 2·76 (2 H, d with str., J = 6·5 Hz; CH_2=CH—CH_2—C(—)—); 2·30 (3 H, s; CH_3—CO—); 1·31 and 1·26 (2 × 3 H, 2 × t, J = 7·0 Hz; —COO—CH_2—CH_3). Mass spectrum: m/z 256 (M^+, $C_{13}H_{20}O_5$).

p-Toluenesulphonyl Hydrazone of Ethyl 2-Allyl-2-ethyl-3-oxobutanoate (*IXc*)

To a suspension of *p*-toluenesulphonyl hydrazide (2·8 g, 15·0 mmol) in 25 ml of benzene was added ethyl 2-allyl-2-ethyl-3-oxobutanoate[20] (3·0 g, 15·1 mmol). After 2 hours' refluxing followed by 2 days' standing at room temperature the mixture was filtered and distilled *in vacuo*; yield 5·48 g (98·7%) of an oily product, which crystallized on standing; m.p. 98·5—101°C (benzene–light petroleum). IR spectrum in CCl_4: 3240 (NH), 1730 (C=O), 1650 (C=N), 1605 (C=C), 820 cm^{-1} (*para*-disubstituted benzene), ^{1}H-NMR spectrum in $CDCl_3$: 7·97 (1 H, bs; =N—**NH**—SO_2—); 7·85 (2 H, d, J = 8·0 Hz; 2 *ortho*-**H** arom.); 7·30 (2 H, d, J = 8·0 Hz; 2 *meta*-**H** arom.); 4·08 (2 H, q, J = 7·0 Hz; —COO—CH_2—CH_3); 2·43 (3 H, s, CH_3—C(=N—)—) 1·68 (3 H, s; CH_3—C_6H_4—); 1·18 (3 H, t, J = 7·0 Hz; —COO—CH_2—CH_3); 0·55 (3 H, t J = 7·5 Hz; CH_3—CH_2—C(—)—). Mass spectrum: m/z 366 (M^+, $C_{18}H_{26}N_2O_4S$).

Methyl 3-Formylpentanoate (*Xa*)

A mixture of butyraldehyde (14·4 g, 0·20 mol) and diisobutylamine (26·1 g, 0·20 mol) in benzene (160 ml) was refluxed under a water separator for 8 h. Then, at 40°C, a solution of methyl bromoacetate (41·3 g, 0·27 mol) in acetonitrile (100 ml) was added and the mixture was kept at this temperature for 2 h, then heated to the boiling point for 15 h. After an addition of 12·3 ml of glacial acetic acid in 40 ml of water the mixture was kept at the boiling temperature for another 1 3/4 h. After cooling, the organic phase was separated and the aqueous phase was extracted with 100 ml of benzene. The combined organic phases were washed with 30 ml of 1% hydrochloric acid, two 50 ml portions of water and two 50 ml portions of brine, dried with anhydrous magnesium sulphate and concentrated *in vacuo*. Two-fold distillation *in vacuo* yielded an oily product (18·6 g, 64·7%), boiling at 88—92°C/1330 Pa; purity 94% (GLC). ^{1}H-NMR spectrum in $CDCl_3$: 9·70 (1 H, t, J = 1·5 Hz; —CH(—)—CH=O); 3·74 (3 H, s; —COO—CH_3); 0·95 (3 H, t, J = 7·5 Hz; —CH_2—CH_3).

Methyl 4-Ethyl-4-formyl-6-heptenoate (*XIb*)

This was obtained from methyl 4-formylhexanoate[21] (*XIa*) by a reported procedure[9] in a yield of 59·2%, b.p. 105—107°C/27 Pa (reported[9] b.p. 92—96°C/27 Pa). ^{1}H-NMR spectrum in $CDCl_3$: 9·62 (1 H, d, J = 2·0 Hz; —CH(—)—CH=O); 3·70 (3 H, s; —COO—CH_3); 0·95 (3 H, t, J = = 7·0 Hz; CH_3—CH_2—).

Ethyl 2-Cyano-2-ethyl 4-pentenoate (*XIII*)

To an ethanolic solution of sodium ethoxide, prepared by dissolving sodium (54·2 g, 2·36 mol) in ethanol (930 ml), was added dropwise ethyl 2-cyanobutanoate (*XII*) (330·5 g, 2·34 mol) in the course of 20 min. (This was prepared by a described procedure[13] in a yield of 81·3% and purity 97% (GLC); b.p. 91–93°C/1 350 Pa, reported[13], b.p. 84–85°C/930 Pa). After 15 minutes' stirring at 50°C allyl bromide (296·5 g, 2·45 mol) was added dropwise in the course of 40 min and the mixture was boiled for 30 min (pH 7). The ethanol was distilled off and the residue was partitioned between benzene (500 ml) and water (450 ml). The aqueous phase was extracted with three 150 ml portions of benzene. The combined organic layers were washed with two 150 ml portions of water, once with 100 ml of brine dried with anhydrous sodium sulphate and evaporated *in vacuo*. Distillation of the residue gave an oily product (393·0 g, 92·7%) boiling at 107–109·2°C/1 340 Pa, purity 98% (GLC); reported[22] b.p. 120°C/2940 Pa. IR spectrum in CCl_4: 2241 (C≡N), 1731 (C=O), 1640 cm^{-1} (C=C). ^{1}H-NMR spectrum in $CDCl_3$: 5·28 (1 H, d with str., J = 11·0 Hz; *cis*-**H**—CH=CH—CH_2—); 5·24 (1 H, d with str., J = 17·0 Hz; *trans*-**H**—CH=CH—CH_2—); 4·29 (2 H, q, J = 7·0 Hz; —COO—CH_2—CH_3); 1·33 (3 H, t, J = 7·0 Hz; —COO—CH_2—CH_3); 1·08 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C—). Mass spectrum: m/z 181 (M^+, $C_{10}H_{15}.NO_2$).

2-Ethyl-2-cyano-4-pentenoic Acid (*XIV*)

A mixture of the ester *XIII* (49·0 g, 0·27 mol), potassium hydroxide (19·7 g, 0·35 mol) and ethanol (220 ml) was boiled for 6·5 h, filtered and distilled *in vacuo*. The residue was taken into 130 ml of water, and after concentration to 4/5 of the volume 50 g of ice was added. The cooled solution was brought to pH 2 with 10% hydrochloric acid and extracted with a mixture of benzene and ether (1 : 1, 150 and 2 × 100 ml). The organic layer was washed with two 50 ml portions of water and 75 ml of brine, dried with anhydrous magnesium sulphate and concentrated. Distillation of the residue *in vacuo* gave an oily product (36·8 g, 89·0%) boiling at 99–102°C/40 Pa, purity 98% (GLC). IR spectrum in CCl_4: 2241 (C≡N), 1718 (C=O), 1640 cm^{-1} (C=C). ^{1}H-NMR spectrum in $CDCl_3$: 10·76 (1 H, bs; —COO**H**); 5·28 (1 H, d with str., J = 11·0 Hz; *cis*-**H**—CH=CH—CH_2—); 5·24 (1 H, d with str., J = 17·0 Hz; *trans*-**H**—CH=CH—CH_2—); 1·13 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C—). Mass spectrum: m/z 153 (M^+, $C_8H_{11}NO_2$).

2-Ethyl-2-cyano-4-pentenoyl Chloride (*XV*)

A mixture of the acid *XIV* (34·8 g, 0·23 mol), thionyl chloride (33·8 g, 0·28 mol) and benzene (150 ml) was refluxed for 14 h, cooled and concentrated under reduced pressure. The residue was distilled *in vacuo*; yield 35·0 g (89·9%) of a liquid boiling at 88·5°C/1 260 Pa, purity 97% (GLC). IR spectrum in CCl_4: 2240 (C≡N), 1770 (C=O), 1640 cm^{-1} (C=C). ^{1}H-NMR spectrum in $CDCl_3$: 5·37 (1 H, d with str., J = 11·0 Hz; *cis*-**H**—CH=CH—CH_2—); 5·32 (1 H, d with str., J = 17·0 Hz; *trans*-**H**—CH=CH—CH_2—); 1·18 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C—). Mass spectrum: m/z 171 (M^+, $C_8H_{10}ClNO$).

1-Diazo-3-ethyl-3-cyano-5-hexen-2-one (*XVI*)

A solution of the chloride *XV* (31·7 g, 0·18 mol) in ether (100 ml) was added dropwise under stirring and cooling to −8°C to a solution of diazomethane (25·6 g, 0·61 mol) in ether (850 ml) during 45 min. The stirring and cooling was continued for 1 h, then the mixture was left standing

overnight at room temperature and evaporated *in vacuo*; yield 34·6 g (105·5%) of a yellow oil. UV spectrum in acetonitrile: λ_{max} (log ε) 275 nm (3·880), 251 nm (3·783). IR spectrum in CCl_4: 2231 (C≡N), 1638 cm^{-1} (conj. C=O). ^{1}H-NMR spectrum in $CDCl_3$: 5·98 (1 H, s; N_2=C**H**—CO—); 5·26 (1 H, d with str., J = 11·0 Hz; *cis*-**H**—CH=CH—CH_2—); 5·21 (1 H, d with str., J = 17·0 Hz; *trans*-**H**—CH=CH—CH_2—); 1·07 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C—). Mass spectrum: m/z 177 (M^+, $C_9H_{11}N_3O$).

Ethyl 3-Ethyl-3-cyano-5-hexenoate (*XVIIa*)

To a solution of the crude diazo ketone *XVI* (11·0 g, 58·8 mmol) in ethanol (110 ml) was added *c.* 1/4 of a suspension of silver oxide (5 g, 21·6 mmol) in ethanol (30 ml) under stirring at 60°C; on heating the mixture to the boiling temperature nitrogen began to evolve vigorously. The rest of the suspension was added to the boiling mixture in the course of 5 h. The mixture was then briefly boiled with charcoal, filtered and concentrated *in vacuo*. The residue was distilled over a column; yield 7·77 g (67·7%) of an oily product boiling at 124·5—127°C/1 340 Pa, purity 96% (GLC). IR spectrum in CCl_4: 2232 (C≡N), 1728 (C=O), 1640 cm^{-1} (C=C). ^{1}H-NMR spectrum in $CDCl_3$: 5·28 (1 H, d with str., J = 11·0 Hz; *cis*-**H**—CH=CH—CH_2—); 5·24 (1 H, d with str., J = 17·0 Hz; *trans*-**H**—CH=CH—CH_2—); 4·21 (2 H, q, J = 7·0 Hz; —COO—CH_2—CH_3); 2·60 (2 H, s; —C—CH_2—COO—); 2·52 (2 H, d with str., J = 7·0 Hz; CH_2=CH—CH_2—C—); 1·31 (3 H, t, J = 7·0 Hz; —COO—CH_2—CH_3); 1·11 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C—). Mass spectrum: m/z 195 (M^+, $C_{11}H_{17}NO_2$).

Methyl 3-Ethyl-3-cyano-5-hexenoate (*XVIIb*)

To a solution of the diazo-ketone *XVI* (23·3 g, 124·8 mmol) in methanol (240 ml) was gradually added, during 1 h, a solution of silver benzoate (4·1 g, 19·3 mmol) in triethylamine (32 ml). The stirring was continued for 30 min at room temperature, then the mixture was briefly boiled with charcoal, filtered and evaporated. The residue was taken between 190 ml of a benzene–ether mixture (3 : 2) and 50 ml of a 7% solution of potassium hydrogen carbonate; the separated aqueous phase was extracted with 50 ml of ether. The combined organic layers were washed with two 20 ml portions of water and 50 ml of brine, dried with anhydrous magnesium sulphate and distilled to remove the solvents. Distillation of the residue gave a yellowish liquid boiling at 121 to 123·5°C/1 340 Pa, purity 96% (GLC); yield 15·5 g (68·4%). IR spectrum in CCl_4: 2232(C≡N), 1731 (C=O), 1640 cm^{-1} (C=C). ^{1}H-NMR spectrum in $CDCl_3$: 5·25 (1 H, d with str., J = 10·5 Hz; *cis*-**H**—CH=CH—CH_2—); 5·19 (1 H, d with str., J = 17·5 Hz; *trans*-H—CH=CH—CH_2—); 3·72 (3 H, s; —COO—CH_3); 2·62 (2 H, s; —C—CH_2—COO—); 2·50 (2 H, d with str., J = 6·5 Hz; CH_2=CH—CH_2—C—); 1·10 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C—). Mass spectrum: m/z 181 (M^+, $C_{10}H_{15}NO_2$).

2-Allyl-2-ethylsuccinic Anhydride (*I*)

a) A mixture of the ester *XVIIa* (27·0 g, 138·3 mmol) and a 25% solution of potassium hydroxide (350 ml) was heated to the boiling temperature for 32 h, cooled, filtered and extracted with ether (50 ml). The cooled aqueous phase was brought to pH 2 with concentrated hydrochloric acid and extracted with ether (300 ml, 3 × 100 ml). Evaporation of the dried organic phase gave an oil (27·2 g), which was treated with acetyl chloride (32·6 g, 412·9 mmol). After the spontane-

ous reaction had ceased the mixture was kept at the boiling temperature for 5 h and freed from the solvent. Distillation of the residue over a 15 cm column gave an oily product (20·5 g, 88·2%), boiling at 130·5—132°C/1410 Pa, purity 98% (GLC). IR spectrum in CCl_4: 1835 and 1788; (C=O), 1631 cm^{-1} (C=C). ^{1}H-NMR spectrum in $CDCl_3$: 5·21 (1 H, d with str., J = 11·0 Hz, *cis*-H—CH=CH—CH_2—); 5·16 (1 H, d with str., J = 17·0 Hz; *trans*-H—CH=CH—CH_2—); 2·95 and 2·60 (2 × 1 H, 2 × d,, J = 16·5 Hz; —C—CH_2—CO—); 0·99 (3 H, t, J = 7·0 Hz; CH_3—CH_2—C—). Mass spectrum: m/z 168 (M^+, $C_9H_{12}O_3$).

b) The same procedure starting from the ester *XVIIb* gave the anhydride *I* in a yield of 89·3%, purity 98% (GLC).

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