

*Pyrone Series. Part II.\* 4 : 5 : 6-Triaryl-2-pyrones.*

By GABRA SOLIMAN and IBRAHIM EL-SAYED EL-KHOLY.

[Reprint Order No. 6009.]

Condensation of deoxybenzoin with ethyl phenylpropiolate leads to *cis*- and *trans*- $\beta$ -desylcinnamic esters of which the former subsequently cyclise to triaryl-2-pyrones (IV). *cis*- $\beta$ -Desylcinnamic acids (V) and substituted vinylacetic acids (VI) are obtained by alkaline fission of the pyrones. Conversely, the esters of these acids give the pyrones under the influence of basic reagents. *trans*- $\beta$ -Desylcinnamic esters (III) undergo an acid-catalysed change to the esters of substituted vinylacetic acids.

*cis*- $\beta$ -Desylcinnamic acids are readily decarboxylated to the ketones (IXb) when heated.

THE mechanisms proposed for the syntheses of aryl-2-pyrones from acetylenic esters (Ruhemann, *J.*, 1910, 457) or acetylenic ketones (Kohler, *J. Amer. Chem. Soc.*, 1922, **44**, 379; Sistaré, Vila, and Escala, *Anales Fis. Quim.*, 1952, **48**, B, 593) involve elimination of alcohol from the intermediate Michael addition products. Hitherto, our knowledge regarding the nature of such intermediate keto-esters has been rather scanty. Recently, however, Walker (*J. Amer. Chem. Soc.*, 1954, **76**, 309) prepared two Michael adducts from 2 : 3-dimethoxyphenylpropiolic acid derivatives and acetylacetone, though he failed to isolate analogous adducts with ethyl acetoacetate. Though we believe that the failure to obtain such intermediate unsaturated keto-esters is due to inadequate control of the condensation, there is a complication that the esters should exist in *cis*- and *trans*-forms, of which the former are liable to cyclise.

We found that condensation of deoxybenzoin with ethyl phenylpropiolate in presence of sodium ethoxide proceeds to completion, and 4 : 5 : 6-triphenyl-2-pyrone was accompanied by a compound  $C_{25}H_{22}O_3$  whose properties showed it to be ethyl *trans*- $\beta$ -desylcinnamate (III; R = H). On the other hand, alkaline fission of 4 : 5 : 6-triphenyl-2-pyrone yielded a mixture of *cis*- $\beta$ -desylcinnamic acid (V; R = H) and 5-oxo-3 : 4 : 5-triphenylpent-3-enoic acid (VI; R = H), whose esters were readily converted into the pyrone by sodium ethoxide or traces of alcoholic alkali. Moreover, the methyl pentenoate (VIII; R = H) was prepared by the action of traces of hydrochloric acid on ethyl *trans*- $\beta$ -desylcinnamate in methanol.

The behaviour of the methyl pentenoate (VIII; R = H) towards basic reagents suggests that it is not merely a methanolysis product. Further, its non-identity with methyl *cis*- $\beta$ -desylcinnamate excludes its formation by an acid-catalysed *trans*-*cis*-change. Thus, it is the outcome of a shift in the position of the double bond. The presence of the group O:C·CH·C:C:O in  $\beta$ -desylcinnamic acid accounts for the mobility of the double bond and explains the ease of pyrone formation from *cis*- $\beta$ -desylcinnamic esters as well as from the methyl pentenoate (VIII; R = H). The existence of the acid (VI; R = H) among the hydrolysis products of the pyrone is attributable to the same reason.

Irrespective of the configuration of the pent-3-enoate (VIII; R = H), a base-catalysed change in the position of the double bond should lead to a mixture of *cis*- and *trans*- $\beta$ -desylcinnamic esters of which the latter does not cyclise. Under carefully controlled conditions, however, we have been unable to find such a *trans*-ester alongside the pyrone.

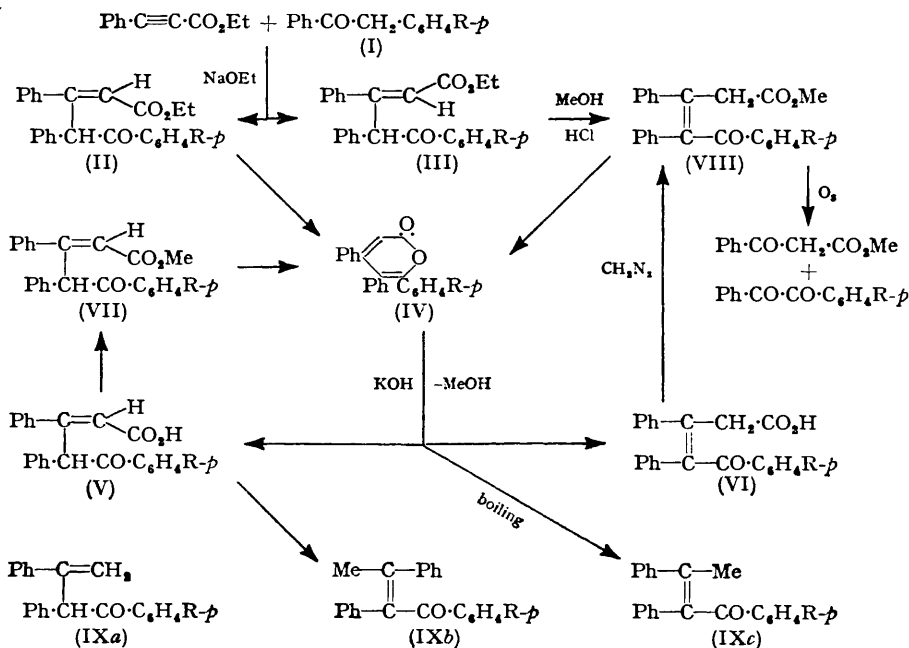
Unlike methyl  $\beta$ -benzoyl- $\alpha$ -phenylcrotonate (Kohler and Barrett, *J. Amer. Chem. Soc.*, 1924, **46**, 747), methyl *cis*- $\beta$ -desylcinnamate and methyl 5-oxo-3 : 4 : 5-triphenylpent-3-enoate are equally stable towards acidic reagents. So differentiation between the two isomers is possible only by physical methods or ozonolysis.

On account of the presence of an enolising centre next to the asymmetric carbon atom in  $\beta$ -desylcinnamic esters, they are liable to racemisation by alkali. Nevertheless, ethyl *trans*- $\beta$ -desylcinnamate and methyl *cis*- $\beta$ -desylcinnamate are dextrorotatory whereas

\* Part I, *J.*, 1954, 1755.

methyl 5-oxo-3 : 4 : 5-triphenylpent-3-enoate is optically inactive. Apparently, the activity of the former esters is due to partial resolution during purification.

Ozonolysis of methyl 5-oxo-3 : 4 : 5-triphenylpent-3-enoate (VIII; R = H) led to benzil and benzoylacetic ester which was detected by the ferric chloride reaction and by hydrolysis to acetophenone. On the other hand, methyl *cis*- $\beta$ -desylcinnamate gave on ozonolysis oxalic acid, benzil, and benzoic acid, but dibenzoylphenylmethane (Marshall, *J.*, 1915, 520) could not be detected among the resinous products which predominated.



The mechanism proposed for the synthesis of 4 : 5 : 6-triphenyl-2-pyrone is equally applicable to 6-*p*-methoxyphenyl-4 : 5-diphenyl-2-pyrone (IV; R = OMe) and 5 : 6-di-*p*-methoxyphenyl-4-phenyl-2-pyrone. They were obtained alongside ethyl *trans*- $\beta$ -4-methoxydesylcinnamate (III; R = OMe) and ethyl *trans*- $\beta$ -4 : 4'-dimethoxydesylcinnamate, respectively, from 4-methoxydeoxybenzoin and 4 : 4'-dimethoxydeoxybenzoin.

Analogously to ethyl *trans*- $\beta$ -desylcinnamate, the *trans*-ester (III; R = OMe) is converted into the ester (VIII; R = OMe) on methanolysis. And alkaline fission of the pyrone (IV; R = OMe) led to a mixture of *cis*- $\beta$ -4-methoxydesylcinnamic acid (V; R = OMe) and the acid (VI; R = OMe). Conversely, the pyrone was obtained from the esters of these two acids by basic reagents.

Condensation of *meso*-*C*-methyldeoxybenzoin with ethyl phenylpropionate gave an oil from which a crystalline ester C<sub>26</sub>H<sub>24</sub>O<sub>3</sub> was obtained and shown to be a Michael adduct. However, *meso*-*C*-phenyldeoxybenzoin failed to react.

A neutral compound has been obtained by pyrolysis of *cis*- $\beta$ -desylcinnamic and 5-oxo-3 : 4 : 5-triphenylpent-3-enoic acid. Among the three structural formulæ which are consistent with its analysis, the formula (IXb; R = H) is assigned to it by elimination of the two other possibilities : it is not identical with Ruhemann's ketone (*loc. cit.*) whose structure (IXc; R = H) was established by oxidation to acetophenone and benzoic acid; and a substance of the structure (IXa; R = H) should give an oxime and formaldehyde on ozonolysis, whereas the new ketone is inert towards carbonyl reagents and gave on ozonolysis acetophenone and benzil. Thus it is stereoisomeric with Ruhemann's ketone, and being the higher-melting form would be the *trans*-isomer (IXb). Again, formation of

this ketone appears to involve a shift in the position of the double bond during decarboxylation. Likewise, the ketone (IXb; R = OMe) was obtained by heating *cis*- $\beta$ -4-methoxy-desylcinnamic acid.

The crystalline compounds obtained by heating the thermolabile *trans*-desyl esters (III; R = H and OMe) are being studied in order to gain additional information regarding their configuration.

#### EXPERIMENTAL

Light petroleum used had b. p. 60—80°, unless otherwise stated.

*Condensation of Deoxybenzoin with Ethyl Phenylpropiolate.*—Deoxybenzoin (5.6 g., 1 mol.) and ethyl phenylpropiolate (5 g., 1 mole) were successively added to an ice-cold ethereal suspension of sodium ethoxide (1.95 g., 1 mol.), and the mixture was kept in the ice-chest for 2 days. It was then poured into water and the precipitated 4 : 5 : 6-triphenyl-2-pyrone (4 g.) was separated from the ethereal and the alkaline layers. The ethereal solution yielded an oily residue (1.6 g.) from which 0.5 g. of the pyrone were recovered. The alkaline layer was acidified and extracted with ether, and the solution was shaken with sodium hydrogen carbonate which was then acidified and extracted with ether. 4 : 5 : 6-Triphenyl-2-pyrone crystallised from acetic acid in pale yellowish prismatic needles, m. p. 246° (Found : C, 85.1; H, 5.2. Calc. for C<sub>23</sub>H<sub>16</sub>O<sub>3</sub> : C, 85.2; H, 5.0%).

*Ethyl trans- $\beta$ -desylcinnamate* was isolated from the viscous residue (3.5 g.) recovered from the non-acidic ethereal extract. It solidified on cooling, crystallised from methanol, and recrystallised from benzene–light petroleum in needles, m. p. 127° (decomp.) (Found : C, 80.8; H, 6.1; OEt, 11.4. C<sub>25</sub>H<sub>22</sub>O<sub>3</sub> requires C, 81.1; H, 6.0; OEt, 12.2%), and had  $[\alpha]_D^{20} + 10.9^\circ$  (*c*, 2.21 in C<sub>6</sub>H<sub>6</sub>). It gave a negative test with ferric chloride and a yellow colour with aqueous potassium hydroxide.

The acidic ethereal solution gave on evaporation a mixture of acids (1.4 g.) from which benzoic acid was removed by boiling water. When the water-insoluble residue was digested with *cyclohexane*, the insoluble portion crystallised from benzene in needles, m. p. 190° (decomp.), identical with *cis*- $\beta$ -desylcinnamic acid.

When condensation was carried out at room temperature, the yields of the pyrone and the desyl ester were 2.5 g. and 4.6 g., respectively.

*Degradation of 4 : 5 : 6-Triphenyl-2-pyrone.*—The pyrone (3 g.) was refluxed with 10% methyl-alcoholic potassium hydroxide (40 ml.) for 6 hr., and after removal of the solvent, the residue was diluted with water and extracted with ether. The ethereal solution yielded a residue (0.7 g.) from which 1-oxo-1 : 2 : 3-triphenylbut-2-ene, m. p. 90°, was obtained. The alkaline solution gave on acidification and extraction with ether an acidic mixture (2 g.) from which benzoic acid was removed by boiling water. The residue gave  $\beta$ -benzylcinnamic acid which crystallised from benzene–light petroleum in needles, m. p. 169° (cf. Ruhemann, *loc. cit.*; Spring, *J.*, 1934, 1333). *Methyl  $\beta$ -benzylcinnamate*, prepared by diazomethane, crystallised from light petroleum (b. p. 30—50°) in aggregates of needles, m. p. 56° (Found : C, 81.1; H, 6.1; OMe, 12.4. C<sub>17</sub>H<sub>14</sub>O<sub>3</sub> requires C, 80.9; H, 6.4; OMe, 12.3%).

*Oxidation of the Ketone (IXc; R = H).*—A solution of 1-oxo-1 : 2 : 3-triphenylbut-2-ene (0.4 g.) in glacial acetic acid (15 ml.) was mixed with a solution of chromic oxide (0.4 g.) in acetic acid (5 ml.) and a few drops of water. The mixture was warmed on the water-bath for 1 hr. and then kept at room temperature overnight. It was poured into water and extracted with ether, and the ethereal solution was shaken with sodium hydrogen carbonate solution which yielded benzoic acid (0.2 g.). The neutral fraction gave on steam-distillation acetophenone which was identified as the 2 : 4-dinitrophenylhydrazone, m. p. 248°.

*Ring Fission.*—4 : 5 : 6-Triphenyl-2-pyrone (4 g.) was warmed with 5% methyl-alcoholic potassium hydroxide (60 ml.) until it dissolved completely. The orange solution was diluted with water, extracted with ether, and acidified and the sticky precipitate extracted with ether. The acidic product (4 g.), recovered from the ethereal solution, was refluxed with *cyclohexane*, and the insoluble portion was subjected to fractional crystallisation from benzene, and the fraction, m. p. 180°, which separated first contained *cis*- $\beta$ -desylcinnamic acid, needles (from benzene), m. p. 190° (decomp.) (Found : C, 80.9; H, 5.3. C<sub>23</sub>H<sub>18</sub>O<sub>3</sub> requires C, 80.7; H, 5.3%). *Methyl cis- $\beta$ -desylcinnamate*, prepared by diazomethane, crystallised from methanol or benzene–light petroleum in prisms, m. p. 130°,  $[\alpha]_D^{20} + 14.8^\circ$  (*c*, 2.03 in C<sub>6</sub>H<sub>6</sub>) (Found : C, 80.7; H, 5.7; OMe, 9.1. C<sub>24</sub>H<sub>20</sub>O<sub>3</sub> requires C, 80.9; H, 5.7; OMe, 8.7%), giving a negative

test with ferric chloride, a yellowish-orange colour with aqueous potassium hydroxide, and recovered unchanged after being heated with hydroxylamine. *Ethyl cis-β-desylcinnamate*, obtained when a suspension of silver *cis-β-desylcinnamate* (1 g.) in benzene was refluxed with ethyl iodide (5 g.) for 2 hr., crystallised from light petroleum in cubes, 93° (Found : C, 81.1; H, 6.0; OEt, 11.4.  $C_{23}H_{22}O_3$  requires C, 81.1; H, 6.0; OEt, 12.2%). Both esters were also prepared catalytically and were recovered unchanged after being heated with traces of hydrochloric acid in alcohol. They were readily converted into the pyrone on treatment with 1 mol. of sodium ethoxide in ether, or when their alcoholic solutions were mixed with a few drops of 5% alcoholic potassium hydroxide.

*5-Oxo-3 : 4 : 5-triphenylpent-3-enoic acid* was obtained from the benzene liquors left after separation of *cis-β-desylcinnamic acid*. It recrystallised from benzene in fine needles, m. p. 149° (decomp.) (Found : C, 80.8; H, 5.5.  $C_{23}H_{18}O_3$  requires C, 80.7; H, 5.3%). Its *methyl ester*, prepared by the action of diazomethane and crystallised from benzene-light petroleum, gave two forms of crystals; the few prismatic crystals of *methyl cis-β-desylcinnamate* were mechanically separated from the desired ester, which then crystallised from methanol in rhombs, m. p. 107° (Found : C, 81.1; H, 5.7; OMe, 8.6.  $C_{24}H_{20}O_3$  requires C, 80.9; H, 5.7; OMe, 8.7%). Its solution in benzene showed no rotation. This ester was also prepared when ethyl *trans-β-desylcinnamate* (1 g.) in methanol (30 ml.) containing 3 drops of concentrated hydrochloric acid was refluxed for 30 min., during which 0.1 g. of the pyrone separated. The solution was diluted with water and extracted with ether, and the ethereal solution shaken with sodium hydrogen carbonate. The ester recovered from the ethereal solution crystallised from methanol in rhombs, m. p. and mixed m. p. 107° (Found : C, 80.9; H, 5.7; OMe, 8.7%). This ester was quantitatively converted into the pyrone by the action of sodium ethoxide in ether or traces of alcoholic potassium hydroxide.

*Ozonolysis of Methyl cis-β-Desylcinnamate*.—A chloroform solution of the ester (0.5 g.) was treated with ozonised oxygen and, after removal of the solvent, the ozonide was decomposed and distilled with steam. The distillate was extracted with ether, and the extract, which gave a negative ferric chloride test, was shaken with sodium hydrogen carbonate, yielding benzoic acid (0.1 g.). The neutral ethereal solution yielded 0.1 g. of benzil. The non-volatile resinous residue (0.2 g.), which was separated by extraction with ether, contained the unchanged ester, but dibenzoylphenylmethane could not be isolated. When the aqueous solution was neutralised with ammonia, concentrated, and mixed with calcium chloride, the precipitate obtained gave a positive aniline-blue test for oxalic acid (Vogel, "Qualitative Chemical Analysis," Longmans, Green and Co., London, 1948, p. 311).

*Ozonolysis of Methyl 5-Oxo-3 : 4 : 5-triphenylpent-3-enoate*.—The ozonide obtained from this ester (0.5 g.) was decomposed and steam-distilled and the distillate extracted with ether. The ethereal solution was then shaken with sodium hydrogen carbonate, whereby traces of benzoic acid were obtained. The oily residue (0.45 g.) recovered from the ethereal solution yielded benzil (0.25 g.), m. p. and mixed m. p. 95°, on treatment with cold light petroleum. The oil recovered from the light petroleum solution gave a plum colour with ferric chloride and yielded on alkaline hydrolysis and steam-distillation acetophenone which was identified as its 2 : 4-dinitrophenylhydrazone, m. p. 248°.

*trans-1-Oxo-1 : 2 : 3-triphenylbut-2-ene* (IXb; R = H).—*cis-β-Desylcinnamic acid* (0.5 g.) was heated just above its m. p. and kept at that temperature until carbon dioxide ceased to be evolved. The glassy residue dissolved in boiling light petroleum, leaving traces of the pyrone, and, on cooling, the ketone (0.3 g.) separated. It recrystallised in clusters of prisms, m. p. 105°, depressed on admixture with the isomer (IXc; R = H) (Found : C, 88.2; H, 6.3.  $C_{22}H_{18}O$  requires C, 88.6; H, 6.1%). This ketone, which was also obtained by heating the acid (VI; R = H) above its m. p., did not react with hydroxylamine.

A chloroform solution of the ketone (0.5 g.) was exposed to ozonised oxygen at  $-10^\circ$ , and after evaporation of the solvent the ozonide was decomposed and distilled with steam. The distillate containing a yellow solid and oily droplets was extracted with ether, and the residue (0.45 g.) recovered from the ethereal solution yielded benzil on treatment with cold light petroleum. The petroleum mother-liquor afforded an oil which was converted into a 2 : 4-dinitrophenylhydrazone. It was freed from benzil 2 : 4-dinitrophenylhydrazone by boiling alcohol, and the residue crystallised from acetic acid in red needles, m. p. 248°, identical with acetophenone 2 : 4-dinitrophenylhydrazone. When this ketone was oxidised with chromic oxide as for its isomer (IXc; R = H), acetophenone and benzoic acid were obtained.

*6-p-Methoxyphenyl-4 : 5-diphenyl-2-pyrone*.—4-Methoxydeoxybenzoin (6.5 g.) and ethyl phenylpropionate (5 g.) were condensed at 0° and the product worked up as before. The pyrone

(3.3 g.) crystallised from benzene in yellowish plates, m. p. 200° (Found: C, 81.5; H, 5.25; OMe, 8.8.  $C_{24}H_{18}O_3$  requires C, 81.3; H, 5.1; OMe, 8.8%).

*Ethyl trans-β-4-Methoxydesylcinnamate.*—This ester (4.4 g.) crystallised from benzene–light petroleum in needles, m. p. 151° (decomp.) (Found: C, 78.3; H, 6.0.  $C_{26}H_{24}O_4$  requires C, 78.0; H, 6.0%). It gave a negative test with ferric chloride and a yellow colour with aqueous potassium hydroxide. The acidic product of the reaction gave *p*-anisic and *cis*-β-4-methoxydesylcinnamic acids on fractional crystallisation from benzene.

*Fission of the Pyrone.*—The pyrone (3 g.) was dissolved in warm 5% methyl-alcoholic potassium hydroxide (60 ml.), and most of the alcohol was then distilled. The residue was diluted with water and extracted with ether, and the alkaline solution acidified and extracted with ether. *cis*-β-4-Methoxydesylcinnamic acid, m. p. 170°, recovered from the ethereal solution, crystallised from benzene in needles, m. p. 196° (decomp.) (Found: C, 77.6; H, 5.6.  $C_{24}H_{20}O_4$  requires C, 77.4; H, 5.4%). The mother-liquor afforded impure 5-oxo-5-*p*-methoxyphenyl-3:4-diphenylpent-3-enoic acid, m. p. 163° (decomp.). *Methyl cis-β-4-methoxydesylcinnamate*, prepared by diazomethane, crystallised from methanol in prisms, m. p. 140° (Found: C, 77.0; H, 5.9; OMe, 15.9.  $C_{25}H_{22}O_4$  requires C, 77.7; H, 5.7; 2OMe, 16.1%). This ester gave the pyrone on treatment with basic reagents as above.

*Methyl 5-p-Methoxyphenyl-5-oxo-3:4-diphenylpent-3-enoate.*—This was prepared when a solution of ethyl *trans*-β-4-methoxydesylcinnamate (0.5 g.) in methanol (20 ml.) containing 2–3 drops of concentrated hydrochloric acid was refluxed for 30 min. After separation of the pyrone (0.15 g.), the ester was isolated and crystallised from methanol in needles, m. p. 113° (Found: C, 77.7; H, 5.85; OMe, 16.8.  $C_{25}H_{22}O_4$  requires C, 77.7; H, 5.7; 2OMe, 16.1%). This ester was also obtained by fractional crystallisation of the product obtained by methylating the impure pent-3-enoic acid. It gave the pyrone with basic reagents.

*trans*-1-*p*-Methoxyphenyl-1-oxo-2:3-diphenylbut-2-ene (IXb; R = OMe).—This ketone was isolated from the residue left after decarboxylation of *cis*-β-4-methoxydesylcinnamic acid as before. It crystallised from light petroleum in rhombs, m. p. 100° (Found: C, 83.8; H, 6.4.  $C_{23}H_{20}O_2$  requires C, 84.1; H, 6.15%).

5:6-Di-*p*-methoxyphenyl-4-phenyl-2-pyrone.—4:4'-Dimethoxydeoxybenzoin (7.4 g.) and ethyl phenylpropionate (5 g.) were condensed at 0° and the product worked up as before. The viscous residue (4.9 g.) recovered from the ethereal solution gave the pyrone (3.1 g.) on treatment with methanol. This crystallised from methanol in yellowish cubes, m. p. 153° (Found: C, 78.0; H, 5.3; OMe, 16.2.  $C_{25}H_{20}O_4$  requires C, 78.1; H, 5.25; 2OMe, 16.2%).

*Ethyl trans-β-4:4'-dimethoxydesylcinnamate* was recovered from the alkaline solution of the product as a reddish-yellow viscous oil (6.8 g.) which solidified on treatment with methanol. It crystallised from benzene–light petroleum in needles, m. p. 150° (decomp.), which gave a yellow colour with potassium hydroxide, and was recovered unchanged from sodium ethoxide (Found: C, 75.5; H, 6.0; OMe, 14.2; OEt, 10.3.  $C_{27}H_{26}O_5$  requires C, 75.3; H, 6.1; 2OMe, 14.4; OEt, 10.5%).

*Ethyl β-(1-Benzoyl-1-phenylethyl)cinnamate.*—*meso*-C-Methyldeoxybenzoin (6 g.) and ethyl phenylpropionate (5 g.) were condensed at 0° in presence of sodium ethoxide (1.95 g.); when the product was worked up, the ethereal solution yielded a viscous oil (9 g.). After being kept in the ice-chest for 3 months, the oil deposited the ester (1.2 g.) which crystallised from methanol in cubes, m. p. 113° (Found: C, 81.4; H, 6.15.  $C_{26}H_{24}O_3$  requires C, 81.2; H, 6.3%).