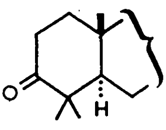
181. *Long-range Effects in Alicyclic Systems. Part II.* The Rates of Condensation of Some Triterpenoid Ketones with Benzaldehyde.*

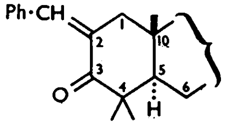
By D. H. R. BARTON, A. J. HEAD, and P. J. MAY.

The rates of base-catalysed condensation of a series of triterpenoid 3-ketones with benzaldehyde have been determined. When lanost-8-enone is taken as a standard ring A and part of ring B are kept constant, variations in rate over a factor of 43 can be demonstrated. It has been shown that neither electrostatic nor bond-induction effects will explain the rate anomalies observed. A new effect has, therefore, been postulated and described as "conformational transmission." An account of some of the results and a definition of the new effect were published [1] in preliminary form.

IT is the purpose of this series of investigations to explore the nature of the interaction of functional groups within saturated alicyclic systems. The present paper is concerned with the rate of condensation of benzaldehyde with triterpenoid 3-ketones, all of which have partial structure (I), to give benzylidene derivatives (II). This reaction was selected for the following reasons. (i) The rate of condensation catalysed by 0·1N-base at 25·0° for the standard ketone lanost-8-enone (III) proceeds at a convenient speed which can be determined by following the appearance of the band at 292 mμ characteristic of the system



(I)



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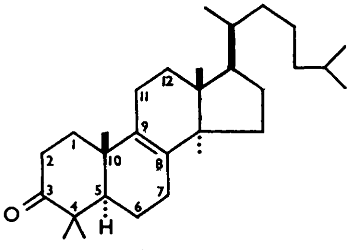

(III)

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* Part I, *J.*, 1956, 932.

[1] Barton, *Experientia*, 1955, Suppl. II, 121 (summary of a Section lecture, Internat. Congr. Pure Appl. Chem., Zürich, July, 1955).

(II). (ii) A large variety of different ketones of defined constitution, configuration, and rigid conformation can be obtained easily. (iii) The kinetics of such condensations have been investigated [2,3,4,5] and it is established that the rate is of the first order with respect to aldehyde and ketone and almost certainly [2,3] also with respect to base. Since the actual kinetic orders for the reactants are not important for our present purpose, all reactions were run in 99% v/v aqueous ethanol at the same concentration (0·1N) of potassium hydroxide at 25·0°. A known excess of benzaldehyde (about 10 : 1 molar) was employed so that the actual reaction kinetics (with respect to the appearance of the 292 mμ band) were of the first order. Preliminary experiments indicated also the expected first-order relation in benzaldehyde. Since, however, all discussion is concerned with rates relative to lanost-8-enone (III), our purpose only required that all variables, except the structure of the ketone, be kept constant. In order to ensure complete reliability the rate of reaction of the ketone (III) was always determined at the same time as the rate of reaction of the ketone under investigation: results (see Table) are summarised as percentages of the lanost-8-enone rate. This does not imply that there were large variations in the latter; it does, however, illustrate the precautions that we have tried to take in order to ensure that the differences in rate are indeed significant. The error in our measurements is not easy to determine but we are convinced that it is at least less than ±5% (relative, not absolute). All ketones examined were, of course, specially purified.

Compound	No. of runs	Average rate : % of lanost-8-enone rate	Limiting values
Masticadienonic acid (V; R = H)	2	8	6·3—9·8
Methyl masticadienonate (V; R = Me)	2	8	8·1—8·4
Lanost-7-enone (VI)	2	17	16·4—16·9
Lanosta-7 : 9(11)-dienone (VII)	3	44	43·1—45·3
Lanostanone (VIII)	2	55	54·7—56·1
α-Amyrene-3 : 11-dione (XV)	2	75	72·8—77·5
β-Amyrene-3 : 11-dione (XVI)	3	75	71·4—76·6
β-Amyra-12 : 18-diene-3 : 11-dione (XVII)	3	75	70·1—77·5
Oleanone (IX)	2	88	85·8—90·0
Noroleana-16 : 18-dienone (X)	4	91	85·2—96·1
Lupenone (XXIV; R = $CMe{:}CH_2$)	2	95	94·3—95·0
Oleanonic acid (IV; R = H)	2	97	95·9—98·5
Lupanone (XXIV; R = Pr^i)	2	98	97·6—98·1
Lanost-8-enone (III)	—	100	—
α-Amyrone (XXV)	3	100	98·2—103·3
*allo*Betulone (XXVII)	2	100	99·3—100·7
β-Amyrone (XXVI)	4	108	103·3—111
Methyl moronate (XXVIII)	2	108	107—109
Methyl 3 : 19-dioxo-olean-13(18)-enoate (XVIII)	2	111	107—114
Methyl oleanonate (IV; R = Me)	3	113	112—114
α-Amyra-9(11) : 12-dienone (XI)	2	115	115—115
Noroleana-12 : 17-dienone (XII)	2	116	115—118
α-Onoceradienedione (XIII)	2	117	117—118
Dehydro-β-amyrone (XIV; R = Me)	3	124	117—132
Methyl *iso*dehydro-oleanonate (XXIII)	5	128	125—132
Methyl dehydro-oleanonate (XIV; R = CO_2Me)	2	129	129—130
β-Amyrane-3 : 12-dione (XIX)	2	170	166—174
α-Amyr-9(11)-ene-3 : 12-dione (XX)	3	266	263—269
β-Amyr-9(11)-ene-3 : 12-dione (XXI)	2	288	282—294
β-Amyra-9(11) : 13(18)-diene-3 : 12 : 19-trione (XXII)	2	344	344—344

Since partial structure (I) is a common feature for all the ketones under consideration, steric hindrance at $C_{(2)}$ must in a classical sense be constant throughout. This is especially true because of the rigid extended conformations of these compounds. We reject, therefore, the idea that any straightforward steric effect could explain our results. The variations in rate, which range (see Table) over a factor of forty-three, could be of polar

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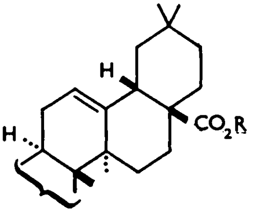
[2] Coombs and Evans, *J.*, 1940, 1295.

[3] Gettler and Hammett, *J. Amer. Chem. Soc.*, 1943, **65**, 1824.

[4] Noyce and Pryor, *ibid.*, 1955, **77**, 1397.

[5] Noyce, Pryor, and Bottini, *ibid.*, p. 1402.

origin. In the saturated type of compound here studied this means that the variation would be produced by an electrostatic effect through space or by bond induction,[6] the two effects being classified together as the inductive effect. We can reject both of these possibilities on the following grounds.



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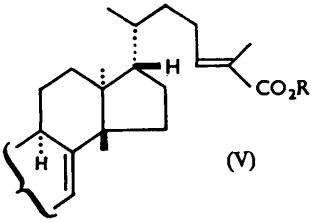

(V)

If electrostatic effects were involved, they would be greatest for unit polar charges; indeed the latter should completely dominate any dipolar interactions. In fact the rate for the anion of oleanonic acid (IV; R = H) is not very different from that for methyl oleanonate (IV; R = Me), whilst the rates for the anion of masticadienonic acid* (V; R = H) and the corresponding methyl ester (V; R = Me) are identical.

If electrostatic effects due to dipoles were of importance, the compounds containing ketone groups (other than at $C_{(3)}$) should produce much larger deviations from the lanost-8-enone rate than compounds having only ethylenic linkages. This is certainly not correct. Thus lanost-7-enone (VI), lanosta-7 : 9(11)-dienone (VII), and lanostanone (VIII) all react much more slowly, oleanone (IX) and noroleana-16 : 18-dienone (X) react significantly more slowly, whilst α-amyra-9(11) : 12-dienone (XI), noroleana-12 : 17-dienone (XII), α-onoceradienedione (XIII), and dehydro-β-amyrone (XIV; R = Me) react significantly faster than the standard lanost-8-enone. These are compounds where there are no polar linkages, except in ring A, and where the effects must be due to some special property of ethylenic linkages (see below). The compounds α- (XV) and β-amyrene-3 : 11-dione (XVI), and β-amyra-12 : 18-diene-3 : 11-dione (XVII), have rates which are slower than normal, whilst methyl 3 : 19-dioxo-olean-13(18)-enoate (XVIII) reacts faster. All 12-ketones, β-amyrane-3 : 12-dione (XIX), α- (XX) and β-amyr-9(11)-ene-3 : 12-diones (XXI), and β-amyra-9(11) : 13(18)-diene-3 : 12 : 19-trione (XXII), react considerably faster. There is, however, no obviously greater capacity shown by the compounds with polar linkages over those without in producing rate anomalies. An instructive comparison is provided by dehydro-β-amyrone (XIV; R = Me) and methyl dehydro-oleanonate (XIV; R = CO_2Me), the extra dipole in the latter having no effect on the abnormal rate constant. If it is granted that the methoxycarbonyl group of (XIV; R = CO_2Me) has nothing to do with the enhanced rate, then this must be due to the diene system as it is in (XIV; R = Me). The diene system of *iso*dehydro-oleanonate (XXIII) also, therefore, produces an abnormal rate effect. This conclusion is, however, only justified when one recognises that lupenone (XXIV; R = $CMe{:}CH_2$), lupanone (XXIV; R = Pr^i), α- (XXV) and β-amyrone (XXVI), *allo*betulone (XXVII), and methyl moronate (XXVIII) have substantially normal rate constants. From these structures one can see that, in the absence of some disturbing unsaturation, such as a diene system, the partial system (XXIX) confers the same rate constant on a compound as does the system of lanost-8-enone (III).

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* The stereochemistry of masticadienonic acid at $C_{(9)}$ was not defined in our earlier papers,[7,8] but its relation to the corresponding centre of butyrospermol was implied. Now that the latter has been convincingly shown [9] to be α-oriented at $C_{(9)}$, the corresponding configurational symbol can be introduced into the formula for masticadienonic acid.

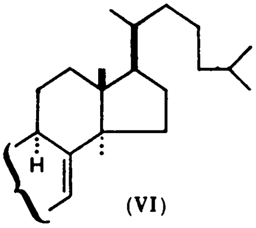
[6] Roberts and Moreland, *J. Amer. Chem. Soc.*, 1953, **75**, 2167.

[7] Barton and Seoane, *J.*, 1956, 4150.

[8] Seoane, *ibid.*, p. 4158.

[9] Lawrie, Hamilton, Spring, and Watson, *J. Org. Chem.*, 1956, **21**, 491.

There remains for consideration that part of the inductive effect which we can classify as bond induction. In compounds (XV) and (XVI) the rate is depressed. Therefore, if bond induction were important, one would conclude that the transmission of the slight positive charge on the 11-carbon atom had a retarding effect on the rate. Yet compounds (XXI)and (XXII), where the positive charge (at the β-position) is greater *and* closer to $C_{(2)}$ has exactly the opposite effect on the rate. Also compound (XIX) has the same enhanced rate as compounds (XXI) and (XXII) and yet has its positively charged carbon atom two carbon atoms more remote from $C_{(2)}$. Transmission through two extra saturated carbon atoms should of course, greatly reduce any bond-transmission effect. Compound (XVIII), where the fractional positive charge is only one carbon atom more remote, has a rate which is only slightly greater than the standard and not comparable with that for (XIX). On this evidence bond induction can be dismissed as an explanation for our anomalies.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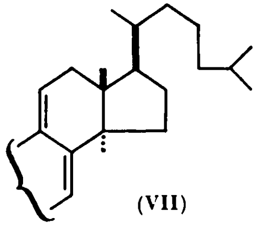
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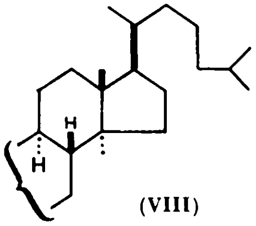
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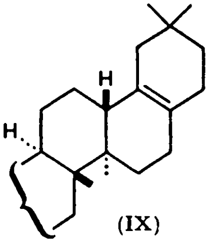
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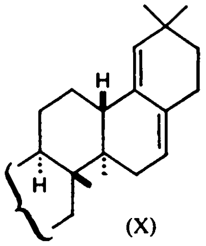
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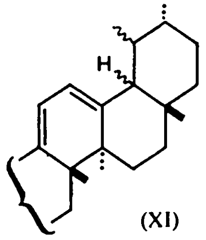
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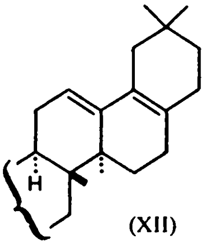
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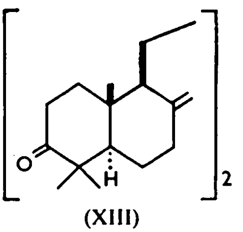
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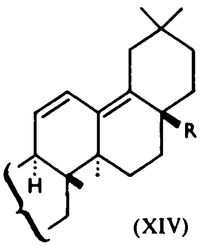
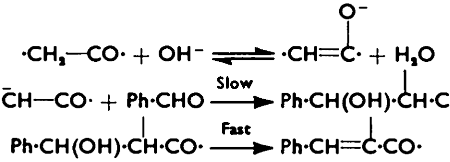

(XIV)

One may also consider if hyperconjugative effects could be operative, although this is not usually recognised as being of significance in saturated systems. By definition such effects must show alternation. Compounds (XI), (XIV; R = Me or CO$_2$Me), and (XXIII) all show enhanced rates with no indication of alternation. We reject then an explanation based on hyperconjugation.

We are, therefore, forced to admit a new effect which we have defined as follows.[1] The differences in rate from the standard probably arise, in main part, from conformational distortion produced by unsaturated substituents. We imagine that this distortion is transmitted through the saturated molecule by a slight flexing of valency angles and alteration of atomic co-ordinates. The distortion ultimately influences ring A and thus makes a difference from the standard reaction rate (see further below). The new effect may, therefore, be described as "*conformational transmission.*"

The mechanism of the benzaldehyde condensation, defined by its kinetic form, must surely be as follows :[10]

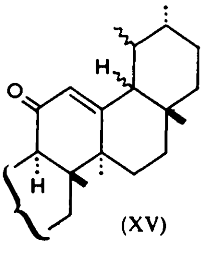


$$\cdot CH_2{-}CO\cdot + OH^- \rightleftharpoons \cdot CH{=}\overset{O^-}{\overset{|}{C}}\cdot + H_2O \quad . \; . \; . \; . \; . \; . \; . \; . \quad (i)$$

$$\cdot\bar{C}H{-}CO\cdot + Ph\cdot CHO \xrightarrow{\text{Slow}} Ph\cdot CH(OH)\cdot\overset{|}{C}H\cdot CO\cdot \quad . \; . \; . \; . \; . \; . \; . \quad (ii)$$

$$Ph\cdot CH(OH)\cdot\overset{|}{C}H\cdot CO\cdot \xrightarrow{\text{Fast}} Ph\cdot CH{=}\overset{|}{C}\cdot CO\cdot \quad . \; . \; . \; . \; . \; . \; . \; . \quad (iii)$$

The rate therefore involves the equilibrium (i) and the slow step (ii). Now, as already emphasised (see above), classical steric hindrance for step (ii) is the same for all compounds. We are inclined therefore to the view that the rate constant for step (ii) is also substantially the same for all our compounds. If this is correct, conformational transmission must influence the position of the equilibrium (i). That is, for the fast rates the equilibrium is further on the right-hand side than for the slow rates.



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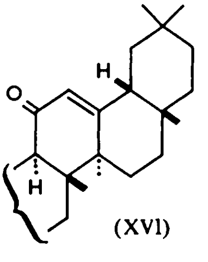

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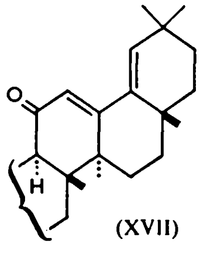

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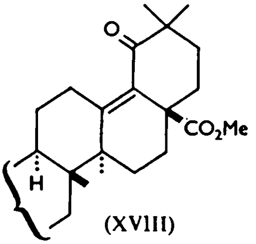

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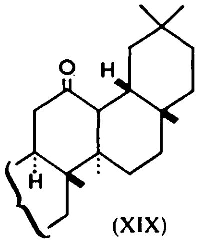

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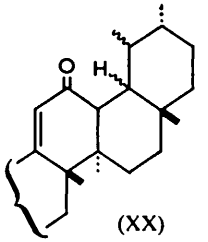

(XX)

The principal factor influencing this equilibrium (i) might well be the 1 : 3-interaction between the axial methyl groups at $C_{(4)}$ and $C_{(10)}$. Thus the markedly slower rate for lanostanone (VIII) than for compounds such as (XXIV; R = $\text{CMe}{:}\text{CH}_2$ or Pr^i) or (XXVI) must be ascribed to the absence of an axial 8-methyl group. The three axial methyl groups at $C_{(4)}$, $C_{(10)}$, and $C_{(8)}$ must interact with each other in the 1 : 3-manner in the other compounds cited.

We feel that further theoretical discussion at this point is premature. A new and subtle conformational effect has however in our view been clearly demonstrated. We are now engaged in measurements on compounds which will define the nature of the effect more closely. In the meantime it will be of interest to see if such subtle conformational factors can be detected by other methods, for example by study of optical dispersion.[11]

The benzylidene compounds formed by condensation at $C_{(2)}$ are somewhat light sensitive. Adequate precautions were taken, therefore, to exclude light. Irradiation with ultraviolet light isomerised the initial benzylidene compounds of $\lambda_{\max.}$ 292 mμ to a

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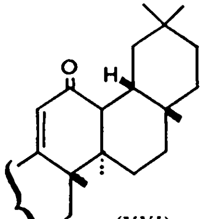
[10] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell and Sons, Ltd., London, 1953, p. 683.

[11] See Djerassi and Closson, *J. Amer. Chem. Soc.*, 1956, **78**, 3761 and later papers.

different series of compounds with $\lambda_{max.}$ 276 mμ. Details are given in the Experimental section; the phenomenon is, of course, well known.[12]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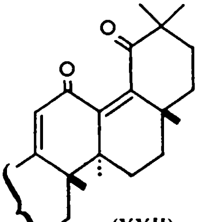
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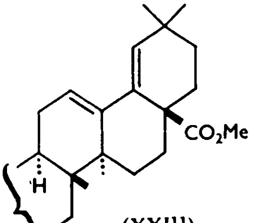
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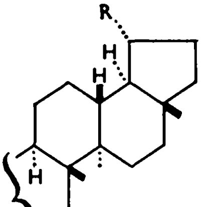
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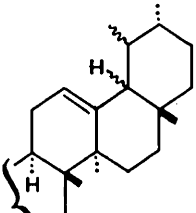
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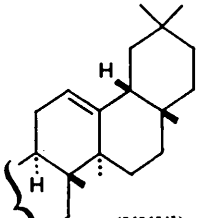
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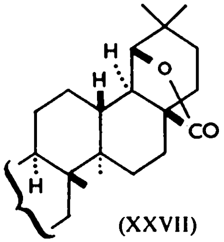
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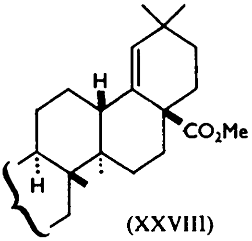
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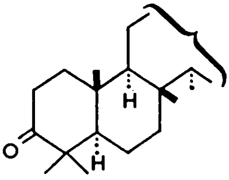
(XXIX)

EXPERIMENTAL

For general experimental details see earlier work.[13] Rotations were taken in $CHCl_3$ solution. Ultraviolet absorption spectra were determined with a Unicam S.P. 500 spectrophotometer. Absolute ethanol was used except for the kinetic runs (see below). Light petroleum refers to the fraction of b. p. 40—60°. Rate measurements were made at 25·0° in a thermostat ($\pm$0·03°), flasks being tightly covered with tin-foil. All ketones were thoroughly dried *in vacuo* before being weighed for rate measurements.

Alcohols were oxidised to ketones by the following method.[14] A 10% (w/v) suspension of " AnalaR " chromium trioxide in " AnalaR " pyridine was prepared by cautious addition of the trioxide to the pyridine with cooling. To this was added a 10% (w/v) solution of the alcohol in " AnalaR " pyridine. About six times the theoretical amount of chromium trioxide was employed. For working up, the mixture was diluted with water, the excess of oxidant destroyed by sulphur dioxide, and the ketone extracted in the usual way.

Materials.—(i) *Ethanol.* A large reservoir of ethanol was prepared by diluting absolute ethanol with water to 99% by volume. This solvent was used for all kinetic measurements. The addition minimises possible errors due to variable traces of water.

(ii) *Benzaldehyde.* The aldehyde was washed with 10% aqueous sodium carbonate solution, dried ($CaCl_2$), and fractionated under reduced pressure in oxygen-free nitrogen. The pure aldehyde was stored in sealed ampoules under oxygen-free nitrogen. For each determination a fresh ampoule of benzaldehyde was employed.

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[12] See, *e.g.*, Lutz and Jordan, *J. Amer. Chem. Soc.*, 1950, **72**, 4090; Kuhn, Lutz, and Bauer, *ibid.*, p. 5058; Black and Lutz, *ibid.*, 1955, **77**, 5134.

[13] Barnes, Barton, Fawcett, and Thomas, *J.*, 1952, 2339.

[14] Poos, Arth, Beyler, and Sarett, *J. Amer. Chem. Soc.*, 1953, **75**, 422.

(iii) *Standard alkali.* The following procedure was found to be satisfactory for the storage of alcoholic potassium hydroxide. Approx. 0·15N-alcoholic potassium hydroxide was prepared by dissolving the requisite amount of the " AnalaR " reagent in freshly boiled-out 99% ethanol. The solution was filtered through sintered glass into a storage vessel in which the reagent could be kept under oxygen-free nitrogen and from which it could be delivered by applying an external pressure of the same gas. In spite of these precautions to exclude carbon dioxide during the filling of the storage vessel, a little potassium carbonate was always deposited during the first two days' storage; this did not, however, pass over with the alkali delivered from the storage vessel through the sintered-glass disc. The alkali was stored in the dark. It was standardised against potassium hydrogen phthalate in the usual way. For a rate determination exactly 0·1N-reagent was prepared by measuring the requisite volume of freshly boiled-out 99% ethanol into a volumetric flask and diluting it to the mark with alkali from the storage vessel. A fresh supply of standard alkali was prepared for every day's kinetic measurements. From Caldin and Long's results [15] it would not be expected that the addition of 1—2% of water to the 99% ethanolic solution would affect the concentration of ethoxide ion appreciably. This was confirmed by rate measurements, although any possible adventitious contamination with water is very much less than 1%.

(iv) *Benzylidene derivatives.* The following procedure was employed. The ketone (1 mol.) in 0·1M-potassium hydroxide in ethanol or dioxan–ethanol was treated with redistilled benzaldehyde (10 mols.) in a stoppered flask overnight at room temperature. The mixture was worked up in the usual way, the ethereal extract being washed, first, with saturated sodium metabisulphite to remove the excess of benzaldehyde. Removal of the solvent and recrystallisation of the residue, care being taken to avoid undue exposure to light, gave the required benzylidene derivatives.

The light-induced isomerisation of the normal benzylidene compounds was effected as follows. The benzylidene derivative in ethanol was irradiated with ultraviolet light. At suitable intervals aliquot parts were withdrawn and the absorption at 276 and 292 mμ measured. When the 276 mμ band no longer changed in intensity the alcohol was removed *in vacuo* and the residue recrystallised from the appropriate solvent. The " *iso*benzylidene " compounds were, in general, more insoluble and more easily crystallised than the normal derivatives.

(v) *Ketones.* Ketones required for this study were carefully purified to constant m. p. and rotation. These physical constants were, in general, in good agreement with those recorded in the literature. We report only on those preparations where special comment is required or where new compounds are involved.

Lanost-7-*enone*.—This was prepared by oxidation of lanost-7-en-3β-ol with pyridine–chromium trioxide. Chromatographed and then recrystallised from chloroform–methanol it had m. p. (plates) 144—146°, $[\alpha]_D$ −15° (*c* 2·04), and gave only a very weakly positive Zimmermann test. Lawrie, Hamilton, Spring, and Watson [9] record m. p. 146—147°, $[\alpha]_D$ −20° (*c* 2·8).

Lanosta-7 : 9(11)-*dienone*.—The derived *benzylidene* compound (needles from methanol) had m. p. 107—109°, $[\alpha]_D$ +9° (*c* 1·74), $\lambda_{max.}$ 236, 244, 252, 291 (ε 18,500, 20,800, 16,100, and 16,600 respectively) (Found: C, 86·25; H, 9·85. $C_{37}H_{52}O$ requires C, 86·65; H, 10·2%). Isomerisation with light gave the *isobenzylidene* compound (fine needles from methanol), m. p. 120—121°, $[\alpha]_D$ −72°, $\lambda_{max.}$ 236, 244, 252, 271 (ε 24,000, 24,500, 18,200, and 8,900 respectively) (Found: C, 86·85; H, 9·8%). Lanosta-7 : 9(11)-dienone itself had ε 18 at 292 mμ.

α-*Amyr*-12-*ene*-3 : 11-*dione*.—The derived *benzylidene* compound (needles from methanol) had m. p. 212—215°, $[\alpha]_D$ +51° (*c* 1·73), $\lambda_{max.}$ 232, 255, and 293 mμ (ε 12,400, 17,000, and 18,300 respectively) (Found: C, 84·35; H, 9·15. $C_{37}H_{50}O_2$ requires C, 84·35; H, 9·55%). This compound was also obtained by acid-catalysed condensation as follows. α-Amyr-12-ene-3 : 11-dione (160 mg.) in ethanolic hydrogen chloride (40 ml.; 34% w/w) was treated with redistilled benzaldehyde (0·57 ml.) at room temperature overnight. Working up in the usual way gave material identical with that described above. The parent ketone had ε <50 at 293 mμ.

β-*Amyr*-12-*ene*-3 : 11-*dione*.—The derived *benzylidene* compound (from methanol) had m. p. about 152° (decomp.), $[\alpha]_D$ +59° (*c* 2·05), $\lambda_{max.}$ 231, 255, and 294 mμ (ε 11,400, 16,300, and 18,100 respectively) after drying (Found: C, 82·0; H, 9·55. $C_{37}H_{50}O_2,CH_4O$ requires C, 81·65; H, 9·75%). The parent ketone had ε <50 at 294 mμ.

[15] Caldin and Long, *J.*, 1954, 3737.

β-Amyra-12 : 18-diene-3 : 11-dione.—3β-Hydroxy-β-amyra-12 : 18-dien-11-one [16] was oxidised at room temperature with pyridine–chromium trioxide overnight. Filtration of the product in benzene through alumina (Brockmann grade 2) and crystallisation from methanol afforded *β-amyra-12 : 18-diene-3 : 11-dione*, m. p. 214—216°, $[\alpha]_D$ +405° (*c* 1·12), $\lambda_{max.}$ 285 mμ (ε 12,700) (Found: C, 82·4; H, 9·9. $C_{30}H_{44}O_2$ requires C, 82·5; H, 10·15%). The ketone had absorption at 292 mμ (ε 11,400) which value was used in all runs for correcting the apparent ε value at 292 mμ.

Noroleana-16 : 18-dienone.—Oleanone (630 mg.) (prepared from morolic acid by Barton and Brooks's method [17]) in methylene dichloride (10 ml.) was treated with 0·62N-monoperphthalic acid (20 ml.) in ether, and the solution made up to 50 ml. with ether. After 17 hr. (1·04 mol. uptake of oxidant) the product was isolated, then taken up in methanol (100 ml.) and aqueous 2N-sulphuric acid (15 ml.) and refluxed for 30 min. Filtration of the product through alumina in benzene–light petroleum gave *noroleana-16 : 18-dienone* (from chloroform–methanol), m. p. 164—166°, $[\alpha]_D$ −14° (*c* 2·27), $\lambda_{max.}$ 240 mμ (ε 18,100) (Found: C, 85·4; H, 10·55. $C_{29}H_{44}O$ requires C, 85·25; H, 10·85%). This compound had ε <50 at 292 mμ.

Lanost-8-enone.—The derived *benzylidene* compound (needles from methanol) had m. p. 104—106°, $[\alpha]_D$ −22° (*c* 1·75), −19° (*c* 2·07), $\lambda_{max.}$ 292 mμ (ε 18,120: mean determination) (Found: C, 86·15; H, 10·55. $C_{37}H_{54}O$ requires C, 86·3; H, 10·55%). Isomerisation by light afforded the iso*benzylidene* compound (from methanol), m. p. 110—111°, $[\alpha]_D$ +42° (*c* 1·87), $\lambda_{max.}$ 276 mμ (ε 8900) (Found: C, 86·2; H, 10·4%). The parent ketone had ε 36 at 292 mμ.

α-Amyra-9(11) : 12-dienone.—Oxidation of α-amyra-9(11) : 12-dienol with pyridine–chromium trioxide gave α-amyra-9(11) : 12-dienone (from methanol), m. p. 145—148°, $[\alpha]_D$ +414° (*c* 2·14 in pyridine), $\lambda_{max.}$ 281 mμ (ε 9600). The value of ε at λ 292 mμ was 8000. Widely different m. p.s are given in the literature for this compound but the rotations are in good agreement.[18, 19]

Noroleana-12 : 17-dienone.—Noroleana-16 : 18-dienone (see above) was isomerised with hydrogen chloride in chloroform according to Barton and Brooks's general method,[17] to give *noroleana-12 : 17-dienone*, m. p. 115—118°, $[\alpha]_D$ +118° (*c* 1·33), $\lambda_{max.}$ 236 and 243 mμ (ε 19,300 and 20,900 respectively) (Found: C, 84·85; H, 11·00. $C_{29}H_{44}O$ requires C, 85·25; H, 10·85%). The ketone had ε 170 at 292 mμ.

α-Onoceradienedione.—The derived *dibenzylidene* compound (needles from methanol) had m. p. 213—216°, $[\alpha]_D$ −37° (*c* 1·76 or 1·78), $\lambda_{max.}$ 225 and 292 mμ (ε 2 × 7600 and 2 × 17,900 respectively) (Found: C, 86·15; H, 8·6. $C_{44}H_{54}O_2$ requires C, 85·95; H, 8·85%). Isomerisation with light gave the iso*dibenzylidene* compound, fine needles (from chloroform–methanol), m. p. 223—224°, $[\alpha]_D$ −225° (*c* 1·51), $\lambda_{max.}$ 221 and 274 mμ (ε 2 × 14,100 and 2 × 8700 respectively) (Found: C, 85·75; H, 8·85%).

β-Amyra-11 : 13(18)-dienone.—Prepared by oxidation of the corresponding alcohol with pyridine–chromium trioxide, this ketone (from chloroform–methanol) had m. p. 241—242°, $[\alpha]_D$ −54° (*c* 1·75), $\lambda_{max.}$ 242, 250, and 260 mμ (ε 26,900, 30,400, and 19,600 respectively) (Found: C, 84·85; H, 11·25. Calc. for $C_{30}H_{46}O$: C, 85·25; H, 10·95%). Shaw, Spring, and Stevenson [19] record m. p. 236—240°, $[\alpha]_D$ −49°. The ketone had ε 42 at 292 mμ.

Methyl iso*Dehydro-oleanonate.*—Methyl *iso*dehydro-oleanolate [17] was oxidised with pyridine–chromium trioxide to give *methyl* iso*dehydro-oleanonate*, needles (from aqueous methanol), m. p. 153—154°, $[\alpha]_D$ +237°, $\lambda_{max.}$ 232 mμ (ε 7500) (Found: C, 79·9; H, 9·7. $C_{31}H_{46}O_3$ requires C, 79·8; H, 9·95%). The ketone had ε 60 at 292 mμ.

Methyl Dehydro-oleanonate.—Methyl dehydro-oleanolate, prepared from morolic acid by Barton and Brooks's method,[17] was oxidised with pyridine–chromium trioxide, to give *methyl dehydro-oleanonate* (from methanol), m. p. 186—187°, $[\alpha]_D$ −130° (*c* 1·44), $\lambda_{max.}$ 243, 251, and 260 mμ (ε 26,100, 29,500, and 18,500 respectively) (Found: C, 79·95; H, 9·7. $C_{31}H_{46}O_3$ requires C, 79·8; H, 9·95%). The ketone had ε 31 at 292 mμ.

α-Amyr-9(11)-ene-3 : 12-dione.—3β-Hydroxy-α-amyr-9(11)-ene-12-one [20] was oxidised with pyridine–chromium trioxide at room temperature overnight, to furnish *α-amyr-9(11)-ene-3 : 12-dione*, m. p. (from methanol) 192—194°, $[\alpha]_D$ +91° (*c* 1·80), $\lambda_{max.}$ 248 mμ (ε 11,000) (Found: C, 82·3; H, 10·25. $C_{30}H_{46}O_2$ requires C, 82·15; H, 10·55%). The ketone had ε 86 at 292 mμ.

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[16] Picard and Spring, *J.*, 1941, 35.
[17] Barton and Brooks, *J.*, 1951, 257.
[18] Jacobs and Fleck, *J. Biol. Chem.*, 1930, **88**, 137.
[19] Shaw, Spring, and Stevenson, *J.*, 1956, 465.
[20] Seymour, Sharples, and Spring, *J.*, 1939, 1075.

β-*Amyr*-9(11)-*ene*-3 : 12-*dione*.—3β-Hydroxy-β-amyr-9(11)-ene-12-one [21] was oxidised with pyridine–chromium trioxide at room temperature for 7 hr., to give β-*amyr*-9(11)-*ene*-3 : 12-*dione*, needles (from methanol), m. p. 205—206°, $[\alpha]_D$ +52° (*c* 1·34), $\lambda_{max.}$ 248 mμ (ε 9500) (Found : C, 82·2; H, 10·45. $C_{30}H_{44}O_2$ requires C, 82·15; H, 10·55%).

β-*Amyra*-9(11) : 13(18)-*diene*-3 : 12 : 19-*trione*.—The corresponding alcohol [22] was oxidised with pyridine–chromium trioxide for 4 hr. at room temperature, to furnish β-*amyra*-9(11) : 13(18)-*diene*-3 : 12 : 19-*trione*, m. p. (from aqueous methanol) 289—291° (decomp.), $[\alpha]_D$ −96° (*c* 1·58), $\lambda_{max.}$ 277 mμ (ε 11,600) (Found : C, 80·35; H, 9·25. $C_{30}H_{42}O_3$ requires C, 79·95; H, 9·4%). The ketone had ε 9900 at 292 mμ.

Stability of Methyl Esters to Base.—In runs involving the use of methyl esters it was important to establish that the results were not vitiated through reduction in the concentration of base by hydrolysis of the ester. Such a possibility with oleanolic acid derivatives can at once be rejected (see Ruzicka, Furter, and van der Sluys-Veer [23]). The following experiment showed that hydrolysis was not significant in the experiments with methyl masticadienonate. The ester (18·7 mg.) in ethanolic 0·1N-potassium hydroxide (10 ml.) was kept at 25° for 7 hr. The solution was just acidified with dilute hydrochloric acid and extracted with ether. The dried (Na_2SO_4) ethereal solution was evaporated to dryness and the residue analysed (Found : OMe, 5·5. Calc. for $C_{30}H_{46}O_3$: 1OMe, 6·6%).

Absorption Measurements.—In order to correct for any day-to-day variation in the behaviour of the Unicam S.P. 500 spectrophotometer an absorption standard was prepared, consisting of pure naphthalene in ethanol (96%) measured against a blank of the same solvent. The intensities of the minimum at 284 mμ and the maximum at 266 mμ were determined with the same pair of stoppered 1 cm. cells on each occasion. No variation in the position of the maximum and minimum was ever observed (check on the wavelength scale). When variations in intensity were noted, both the maximum and minimum changed simultaneously. Such changes were generally less than 1%, but occasionally larger discrepancies were noted which must be ascribed to variation in the instrument. Measurements of the naphthalene solution on a particular day were taken as a standard value. The instrument was checked against this standard before each series of kinetic runs and, if instrument variation was detected, a proportional correction was applied to all measurements.

Technique.—Kinetic runs were made as follows. 10—20 mg. of the ketone were weighed (semimicro-balance) into a 10 ml. graduated flask. About 4 ml. of freshly prepared exactly 0·1N-ethanolic potassium hydroxide (see above) were added and the ketone was dissolved (if necessary with gentle warming). An ampoule of benzaldehyde (see above) was opened and about 300 mg. (∼10 mols.) weighed into a 25 ml. volumetric flask and made up to the mark with the ethanolic 0·1N-potassium hydroxide. A portion (5 ml.) was pipetted into the ketone solution, and the mixture rapidly made up to the mark with the ethanolic potassium hydroxide, the time being noted. All solutions were kept at thermostat temperature (25·0°) until thermally equilibrated before being mixed. An identical control was prepared (without the ketone).

At suitable intervals aliquot parts (1 ml.) of both control and test solution were withdrawn and diluted at once to 10 ml. (volumetric flask) with 96% ethanol. The absorption of the test solution was measured at 292 mμ against the blank solution, 1 mm. quartz cells being used. It was established by prior experiment that this dilution technique effectively quenched the reaction during the time required to make measurements. Measurements were made at the benzylidene maximum of 292 mμ except where otherwise stated.

The stability of the control solution was examined and shown to vary only slightly with time (at zero time, at 292 mμ, ε 945, after 3 hr. ε 965, and after 70 hr. ε 1134). Clearly, however, the concentration of benzaldehyde diminishes by one molar proportion as the reaction proceeds. By measurement of the absorption spectrum of benzaldehyde at 292 mμ it was a simple matter to correct the observed intensities for this effect. The correction was, of course, in any case small.

The absorption of all compounds at 292 mμ was determined separately and, if significant, an appropriate correction to the observed ε at this wavelength was made for each kinetic observation. All calculations were referred to a maximum absorption at 292 mμ of 18,100. This value was established by careful measurements on the benzylidene derivative of lanost-8-enone

[21] Pickard, Sharples, and Spring, *J.*, 1939, 1045.

[22] Ruzicka and Jeger, *Helv. Chim. Acta*, 1941, **24**, 1236.

[23] Ruzicka, Furter, and van der Sluys-Veer, *ibid.*, 1938, **21**, 1735

and shown to apply to several analogous benzylidene compounds (see above). The observations gave first-order plots from which the appropriate values of k were calculated and corrected for any slight variation in the 10 : 1 ratio of benzaldehyde to ketone. As emphasised in the text *all* experiments were run in pairs, one flask containing the standard lanost-8-enone, the other the ketone under examination. Expressing the results as the ratio of the two rates cancels any day-to-day variation in unforeseen factors. For ethanolic 0·1N-potassium hydroxide the mean rate constant for lanost-8-enone (106 runs) was $7{\cdot}78 \times 10^{-4}$ mole^{-1} l. sec.$^{-1}$ at 25·0° with error limits (calculated from the formula $\sqrt{\{\sum\Delta^2/[n(n-1)]\}}$, where the symbols have their usual significance) of ±0·05.

In preliminary experiments it was shown that three-fold variation in the benzaldehyde concentration had little effect (see annexed Table) on the rate constant calculated as above. Since the variations in the benzaldehyde : ketone ratio were, in fact, minor, the small corrections applied (second-order kinetics being assumed) are undoubtedly justified.

Lanost-8-enone (mole l.$^{-1}$)	Benzaldehyde (mole l.$^{-1}$)	10^5k (sec.$^{-1}$)	10^4k/[Ph·CHO] (mole^{-1} l. sec.$^{-1}$)
0·00258	0·0306	2·43	7·94
0·00248	0·0521	4·36	8·36
0·00237	0·0994	8·01	8·07

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Birkbeck College, London, W.C.1.
The University, Glasgow, W.2.

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