and distilled to give 3.18 g. of methyleucarvol, b.p. 58° (0.9 mm.), $n^{20}D$ 1.5070.

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.47; H, 10.91. Found: C, 79.14; H, 11.63.

1,1,3,4-Tetramethylcycloheptatriene.—This material, previously prepared by Rupe[10] by the reaction of methylmagnesium bromide on eucarvone without isolation of the intermediate alcohol, was obtained by dehydration of methyl eucarvol using the procedure given above, b.p. 61° (10 mm.), $n^{20}D$ 1.5072, λ_{max} 275 mμ (log ε 3.68).

γ,δ-Dihydroeucarvone.—This substance was prepared from eucarvone by a modification of the previously described methods.[11,12] A solution of 8.00 g. (0.053 mole) of eucarvone in 160 ml. of ethanol was shaken with 0.40 g. of Lindlar palladium–lead catalyst and hydrogen overnight. The theoretical amount of hydrogen for reduction of one double bond was taken up in about 3 hours and the uptake had stopped after the overnight period at about 1.2 equivalents of hydrogen. Filtration, evaporation and distillation afforded 6.8 g. (85%) of γ,δ-dihydroeucarvone, b.p. 83° (10 mm.), $n^{20}D$ 1.4808, λ_{max} 239.5 mμ (log ε 3.9), ν_{max} 1673 cm.$^{-1}$.

Δ³-2,2,6,6-Tetramethylcyclohepten-1-one (Methyldihydroeucarvone).—In an apparatus flushed with nitrogen, sodium amide (1.0 g., 0.0256 mole), dioxane (41 ml.) and γ,δ-dihydroeucarvone (3.0 g., 0.02 mole) were combined and heated to reflux with stirring. After three hours the theoretical amount of ammonia had been evolved and the brown solution was cooled and treated with 3.64 g. (0.0256 mole) of methyl iodide at room temperature for 2 hours. The mixture was then neutralized with glacial acetic acid, concentrated and treated with ether-saturated salt solution. The ether extract was dried, concentrated and distilled to give 1.6 g. of methyldihydroeucarvone, b.p. 79–80° (15 mm.), $n^{22}D$ 1.4609, ν_{max} 1710 cm.$^{-1}$, no high intensity ultraviolet absorption, yellow color with tetranitromethane.

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.47; H, 10.91. Found: C, 79.69; H, 11.24.

URBANA, ILLINOIS

(10) H. Rupe and W. Kerkovius, *Ber.*, **44**, 2702 (1911).
(11) O. Wallach, *Ann.*, **403**, 73 (1914).
(12) Y. Naves and P. Ardizio, *Helv. Chim. Acta*, **32**, 329 (1949).

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

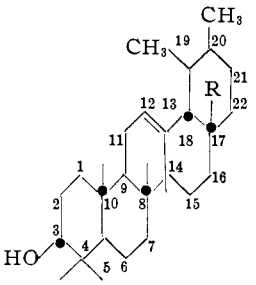
The Stereochemistry of the α-Amyrins

BY ELIAS J. COREY AND JOSEPH J. URSPRUNG

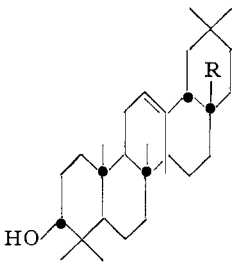
RECEIVED AUGUST 16, 1955

Evidence is presented for stereoformula I for α-amyrin and consideration is given to other proposals recently made.

In a previous communication[1] we proposed stereoformula I for α-amyrin, the parent member of the important ursane or α-amyrin family of pentacyclic triterpenes. This formula was derived by starting



I, α-amyrin, R = CH_3
II, ursolic acid, R = COOH



III, β-amyrin, R = CH_3
IV, oleanolic acid, R = COOH

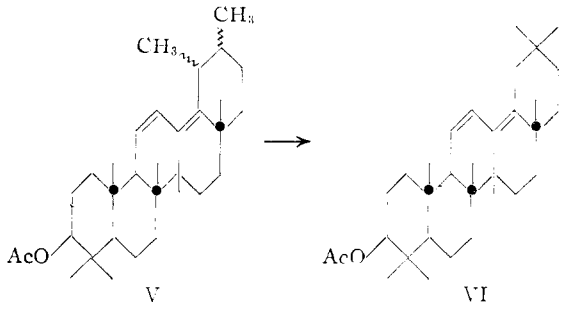
out with the previously established configurations for C_3, C_5, C_8 and C_{10} and adding assigned configurations for C_9, C_{14}, C_{17}, C_{19} and C_{20}, in that order, as deduced from chemical evidence. This evidence is reviewed herein and that portion which was presented only briefly in the preliminary note on this subject is described in more detail together with the pertinent experimental data.

The α-orientation of the hydrogen at C_9, which results in a *trans-anti-trans* arrangement for the A, B and C rings of α-amyrin, follows from the facts (1) that this center is not epimerizable when adjacent to the 11-keto function and (2) that the hydrogen at C_9 is axial to ring C. The axial orientation of the 9-hydrogen relative to ring C is indicated by the well known ease with which 11α-(axial)-bromo-12-ketones undergo dehydrobromination to give Δ^{10}-12-ketones.[2] Identical behavior is observed in the β-amyrin series (III, IV)[3] in which the 9-hydrogen is also α-oriented.

The configurations at C_{14} and C_{17} in the α-amyrins were determined by two interlocking lines of evidence and are the same as at the corresponding centers in the β-amyrin (oleanane) series (III, IV).[4,5] First the acid $\rightleftarrows$ γ-lactone equilibrium constants for ursolic (II) and oleanolic (IV) acids are 0.33 and 0.11, respectively, indicating that the energy differences between γ-lactone and free acid due to strain and steric interactions are about the same in both cases. Eight structures, differing in configuration at C_{14}, C_{17} and C_{18}, are possible for ursolic acid and are noted in Table I. Second, acid–γ-lactone optical rotation differences for ursolic and oleanolic acid and the corresponding γ-lactones are essentially identical (Table II). After ruling out the possibilities in which there is a large amount of strain in the γ-lactone relative to the acid and the possibilities which are not in agreement with optical rotation differences, only one possibility remains for the configurations at C_{14} and C_{17}, that with the substituents at C_{14} and C_{17} α- and β-oriented, respectively, as in the β-amyrin series. This conclusion has subsequently been

(1) E. J. Corey and J. J. Ursprung, *Chemistry and Industry*, 1387 (1954).
(2) D. E. Seymour, K. S. Sharples and F. S. Spring, *J. Chem. Soc.*, 1075 (1939).
(3) (a) C. W. Picard, K. S. Sharples and F. S. Spring, *ibid.*, 1045 (1939); (b) R. Budziarek, J. D. Johnston, W. Manson and F. S. Spring, *ibid.*, 3019 (1951).
(4) D. H. R. Barton and N. J. Holness, *ibid.*, 78 (1952).
(5) A. M. Abd El Rahim and C. H. Carlisle, *Chemistry and Industry*, 279 (1954).

confirmed,[6,7] by the direct conversion of the α-amyrin derivative ursa-11,13(18)-dienyl acetate (V) to the β-amyrin derivative olean-11,13(18)-dienyl acetate (VI).



V VI

TABLE I

Isomer	Orientation of substituent at C_{14}	C_{17}	C_{18}	Remarks on the structure of the γ-lactone
1	α	β	α	All rings chair; no serious interactions
2	α	β	β	
3	α	α	β	All rings chair; strong interaction between CH_3 at C_9 and H at C_{18}
4	α	α	α	All rings chair; strong interaction between CH_3 at C_9 and H, CH_3 at C_{19}
5	β	α	β	Ring C boat
6	β	α	α	
7	β	β	α	Ring C or ring D boat
8	β	β	β	

TABLE II

Compound	$[\alpha]_D$	Δ_1[a]	Δ_2[b]
Oleanolic lactone	+19°	−56°	−50°
18-Iso-oleanolic lactone	+23°	−27°	−21°
Ursolic lactone	+ 4°	−57.5°	−58°

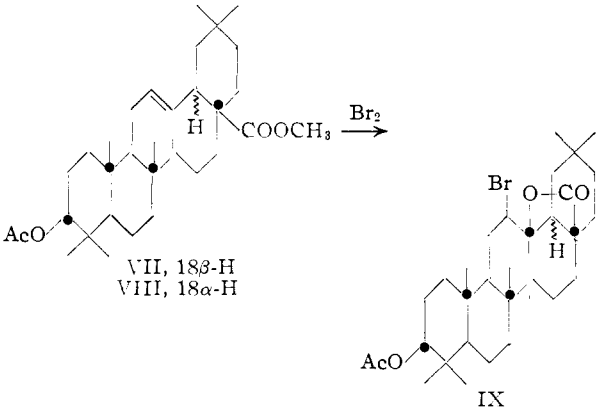
[a] $\Delta_1 = [\alpha]_D$ for lactone $- [\alpha]_D$ for corresponding free acids (acetate). [b] $\Delta_2 = [\alpha]_D$ for lactone $- [\alpha]_D$ for corresponding methyl ester acetate.

The remaining stereochemical problem, the configurations at C_{18}, C_{19} and C_{20}, has still not been settled by a direct experimental proof. However, all the evidence which is available at present strongly indicates that the solution expressed by formula I is the correct one.

The direct elucidation of the configurations at C_{19} and C_{20} is not a simple matter, because of the difficulty so far encountered of carrying out stereochemically meaningful reactions in ring E of the α-amyrins. However, many of the reactions in the accessible C and D rings of the α-amyrins are strongly affected by the configurations at C_{19} and C_{20}, as is obvious from the discussion to follow, and can be used as indirect evidence for these configurations once the configuration of C_{18} is known.

The interpretation of the chemistry of the α-amyrins in terms of the orientation of the hydrogen at C_{18} was possible only after a knowledge had been gained of the configurations at C_{14} and C_{17} and, indeed, was greatly simplified as a result of the finding that these configurations are identical in the α- and β-amyrin series. It was therefore possible by a comparison of the chemical properties of derivatives of oleanolic acid (D/E *cis*), 18-iso-oleanolic acid (D/E *trans*) and ursolic acid (D/E = ?) to show that the D/E ring fusion in the α-amyrins is *cis* (18β-hydrogen) as in oleanolic acid and not *trans* as in 18-iso-oleanolic acid.

Whereas methyl acetyloleanolate (VII) and methyl acetyl-18-iso-oleanolate (VIII) react instantaneously with bromine to form 12α-bromo-γ-lactones (IX), methyl acetylursolate does not react appreciably even after 24 hours. Granted that formation of the bromolactones in the oleanolic



VII, 18β-H
VIII, 18α-H

IX

and 18-isoöleanolic series proceeds by rearward displacement of the 17β-carbomethoxyl function on a 12α,13α-bromonium ion, it is clear that the resistance of methyl acetylursolate to form a bromolactone is due to its reluctance to yield a 12α,13α-bromonium ion, since it also possesses the required 17β-carbomethoxyl function. These data can be interpreted in terms of stereochemistry by reference to space formulas X (D/E *trans*) and XI (D/E *cis*) from which it is apparent that the α-side

X XI

of the $\Delta^{12,13}$-double bond is less strongly shielded, even when $R_1 = R_2 = CH_3$ and $R_3 = R_4 = H$, for the D/E *trans* than for the D/E *cis* structure. The very large degree of shielding observed for the α-side of the $\Delta^{12,13}$-double bond in the α-amyrins is consistent only with a *cis* D/E fusion, and furthermore necessitates the conclusion that considerable shielding is provided by the methyl group at C_{19}.

The lower reactivity toward perbenzoic acid of the $\Delta^{12,13}$-double bond in α-amyrin as compared with β-amyrin, which has long been known,[8] also indicates that the D/E ring fusion is *cis* in the α-amyrins. Comparison of the rate of oxidation of

(6) G. G. Allen, J. M. Beaton, J. I. Shaw, F. S. Spring, R. Stevenson, J. L. Stewart and W. S. Strachan, *Chemistry and Industry*, 281 (1955).

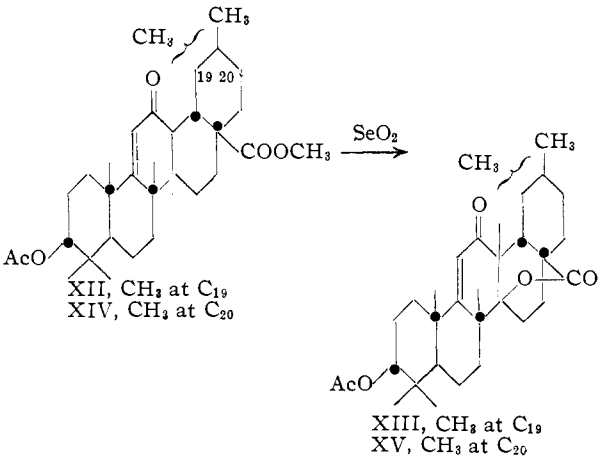
(7) The proposal that the α- and β-amyrin series differ in configuration at C_{17}: (a) O. Jeger, *Angew. Chem.*, 196 (1951), which was widely accepted before our preliminary note [see *Ann. Rep.*, **48**, 198 (1951)] and which has been made again recently; (b) J. L. Beton and T. G. Halsall, *Chemistry and Industry*, 1560 (1954), is therefore no longer tenable.

(8) L. Ruzicka, H. Silbermann and M. Furter, *Helv. Chim. Acta*, **15**, 482 (1932), report that β-amyrin is 98% oxidized by perbenzoic acid after 48 hours, whereas under the same conditions α-amyrin is only *ca.* 15% oxidized.

methyl acetyl-18-isoöleanolate, methyl acetyloleanolate and methyl acetylursolate verifies this conclusion, since the time required for 90% oxidation under comparable conditions was found to be 1 day, *ca.* 10 days, >20 days, respectively, the D/E *trans* structure being the most reactive as expected. Although the α-oxide is probably the primary product in the case of the β-amyrins (an oxide can be isolated in each case), there is no indication of the stereochemistry of the oxide, which first forms from the α-amyrins since the 12-ketone is the only isolable oxidation product.

Further data supporting the conclusion that the D/E fusion is *cis* in the α-amyrins was obtained by a comparative study of the 12-ketones in the β,18-iso-β- and α-amyrin series. Olean-12-onyl acetate and ursan-12-onyl acetate both gave enol acetates in high yield upon heating with acetic anhydride–sodium acetate for 40 hours. However, both 18-isoölean-12-onyl acetate or methyl acetyl-18-iso-12-ketodihydroöleanolate were recovered completely unchanged after similar treatment even after 80 hours. The similarity of the α- and β-amyrin derivatives and their difference from the 18-iso series argues for the *cis* D/E fusion in the α-amyrins.

Dreiding, *et al.*,[9] have found that reaction of either methyl acetyl-12-ketodihydroursolate (XII) or the corresponding Δ^9-unsaturated derivative with selenium dioxide produces a rearranged δ-lactone XIII in which the methyl group originally at C_{14} has migrated to C_{13}. This reaction would appear to be dependent on stereochemistry at C_{18} and so



XII, CH_3 at C_{19}
XIV, CH_3 at C_{20}

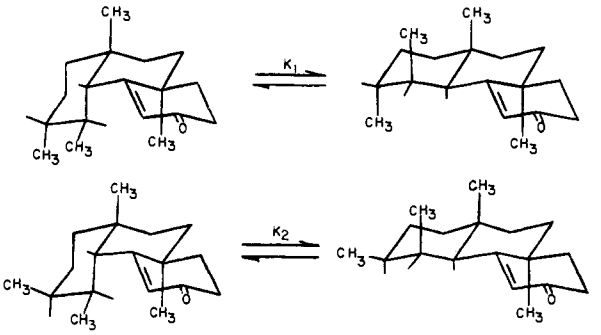
XIII, CH_3 at C_{19}
XV, CH_3 at C_{20}

selenium dioxide oxidation was carried out on methyl acetyl-12-ketodihydroöleanolate, its Δ^9-unsaturated derivative and methyl acetyl-12-ketodihydro-18-isoöleanolate. In the case of methyl acetyl-12-ketodihydroöleanolate and its Δ^9-derivative a δ-lactone (XV) analogous to XIII was produced.[10] In contrast to these results, methyl acetyl-12-ketodihydro-18-isoöleanolate reacted only sluggishly with selenium dioxide and yielded no detectable δ-lactone or 11,12-enolone.

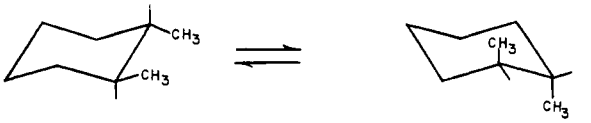
The similarity of the δ-lactones XIII and XV is indicated by their infrared spectra which exhibit identical absorption (in CCl_4) in the double bond region at 1755 cm.$^{-1}$ (lactone C=O), 1737 cm.$^{-1}$ (acetate C=O), 1675 cm.$^{-1}$ (12-keto group) and 1612 cm.$^{-1}$ (C=C), and by the almost identical change in optical rotation during lactone formation, [M_D lactone − M_D Δ^9-12-ketone] being equal to −794 and −820° for XIII and XV, respectively.

Although the D/E fusion must be *cis* in the α-amyrins on the basis of the above evidence, this arrangement is more stable than the 18-iso, D/E *trans* structure. As was first reported by Barton and Holness[4] methyl acetyl-11-ketoursolate cannot be isomerized by means of acids or bases in contrast to methyl acetyl-11-ketoöleanolate in which the D/E *cis* structure is the less stable one. A further indication of the greater stability of the D/E *cis* fusion in the α-amyrins is the fact that urs-13-(18)-enyl acetate is isomerized to α-amyrin acetate and not to the 18-iso epimer. This unusual situation wherein a *cis*-decalin type is more stable than a *trans*-decalin structure makes possible the assignment of configuration to C_{19} and C_{20}, since there is only one orientation of the two methyl groups at C_{19} and C_{20} which is consistent with this finding. This orientation, 19β-(equatorial)-methyl and 20α-(equatorial)-methyl, is such that the *cis*-locked E ring is anchored by the two methyl groups which are equatorial in the D/E *cis* structure, but which would both be forced into the unfavorable axial orientation in the D/E *trans* structure.

Considering first the configuration at C_{19}, if the methyl group were α-oriented (axial), the D/E *cis* structure would be destabilized so severely by interaction with the angular methyl group at C_{14} that the *trans* D/E fusion would certainly be the more stable. Granted that the 19-methyl group is β-oriented, the possible situations with regard to C_{20} are summarized by the equilibria (1) and (2) for which approximate equilibrium constants may be



arrived at from the data on the *trans*-1,2-dimethylcyclohexanes.[11] Assuming that the interaction between the C_{19} methine group and the methyl



$K \cong 0.05$

group at C_{14} in the D/E *cis* structures is of the same magnitude as that between the methyl groups at C_{17} and C_{19} in the D/E *trans* structures, the orienta-

(9) J. Dreiding, O. Jeger and L. Ruzicka, *Helv. Chim. Acta*, **33**, 1325 (1950).

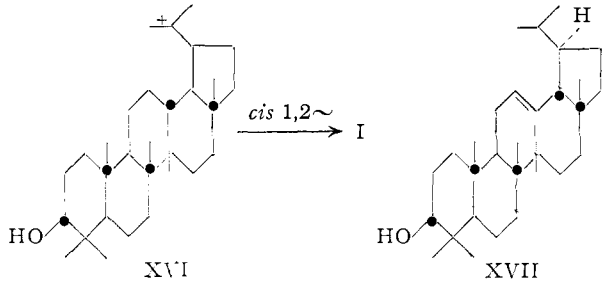
(10) The yield of δ-lactone from methyl acetyl-12-ketodihydrooleanolate is not as high as from the Δ^9-derivative because of the competing formation of the 11,12-enolone.

(11) A. K. Roebuck and B. L. Evering, THIS JOURNAL, **75**, 1631 (1953).

tion of the methyl group at C_{20} can be seen to play a decisive role. This methyl must be α-oriented since the value of K_1 (20α-methyl) would be of the order of 0.05–0.1 whereas the value of K_2 (20β-methyl) would be of the order of 10–20.

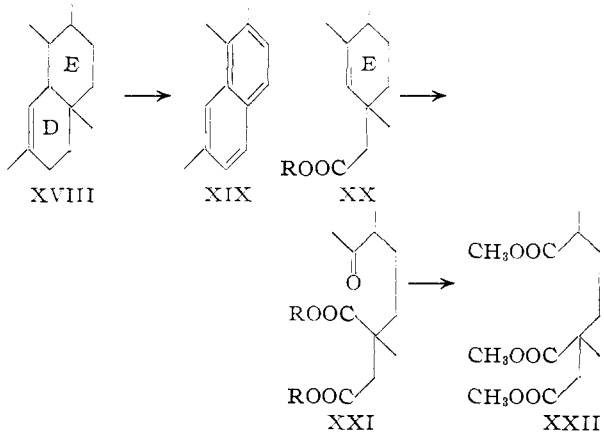
Formula I for the α-amyrins is capable of explaining the striking differences between the behavior of the α- and β-amyrins despite the identity of the configurations at all common asymmetric centers. The inertness of the 12(13)-double bond in the α-amyrins, for example, is the result of the hindrance caused by the 19β-methyl group. The instability of the 13(18)-double bond as compared with the 12(13)-double bond in the α-amyrins, as contrasted with the β-amyrins,[12] and the reluctance of the α-amyrins to undergo reactions which create a 13(18)-double bond may be explained, in part, by the fact that the methyl groups at C_{19} and C_{20} upon introduction of 13(18)-unsaturation would be forced into the axial orientation.

The formation of structure I from the postulated intermediate lupanyl cation[13] (XVI) is biogenetically reasonable since the required 1,2-shifts of carbon and hydrogen lead to the configurations given



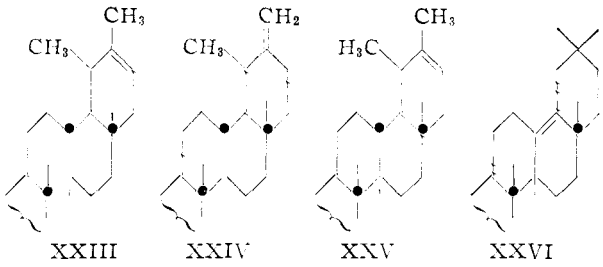
in I. A sequence of 1,2-shifts starting from the lupanyl cation also leads to the correct stereochemistry for β-amyrin[4] as well as for the further transformation product friedelin.[14]

An alternative formulation (XVII) has recently been given for α-amyrin by Spring and co-workers[6] in which the E ring is *five*-membered and bears an isopropyl substituent. This structure is in apparent disagreement with the results of several degradative



studies on the α-amyrins which indicate that ring E is *six*-membered and carries methyl groups at C_{19} and C_{20}, *e.g.*, the formation of the degradation products XVIII–XXII.[6a]

Furthermore, it is unnecessary to adopt the *five*-membered E ring to explain the conversion of ursa-11,13(18)-dienyl acetate to olean-11,13(18-)dienyl acetate[6] since this conversion is only to be expected on the basis of a *six*-membered E ring as in I. Jones and his co-workers[15] have already demonstrated that ψ-taraxastene (XXIII), taraxastene (XXIV) and lupene I (XXV) are each converted by treatment with sulfuric acid in acetic acid to olean-13(18)-ene (XXVI). This rearrangement involves the transformation of a 19,20-dimethyl-E ring structure to the 20,20-dimethyl-$\Delta^{13,18}$-system and is completely analogous to that which is required if I is indeed the structure of α-amyrin.



If the α-amyrins possessed a *five*-membered E ring, ursolic lactone (*trans*-pentalane ring system) would be much more strained than oleanolic lactone (*trans*-hydrindane ring system) and, in fact, to the extent that lactone formation should be negligible at equilibrium, again contrary to observations. It seems reasonable, therefore, to conclude that structure XVII is improbable for the α-amyrins,[16] and that I remains as preferable.

Although most of the 18-isoöleanolic acid derivatives required for this work had been prepared previously by Kitasato[17] and by Barton and Holness,[4] we found that the yields obtained the procedures described were poor. Improved procedures for these transformations have now been developed which are given in detail in the Experimental section. It was found that sodium dichromate in acetic acid is a much superior reagent to chromic acid for the oxidation of methyl acetyloleanolate to the 11-keto derivative, the yields with the former reagent being 80%, approximately twice that obtained with chromic acid.[18] The isomerization of methyl acetyl-11-ketoöleanate to the 18-iso-compound with hydrogen bromide proceeded in variable, but usually low, yield until the standardized procedure described in the Experimental section was employed. The reason for the capricious nature of this reaction is still not known. Catalytic hydrogenolysis of the 18-iso-11-ketone to methyl

(12) G. S. Davy, T. G. Halsall and E. R. H. Jones, *J. Chem. Soc.*, 458 (1951).

(13) L. Ruzicka, A. Eschenmoser and H. Heusser, *Experientia*, **9**, 357 (1953).

(14) E. J. Corey and J. J. Ursprung, THIS JOURNAL, **77**, 3668, 3669 (1955).

(15) T. R. Ames, J. L. Beton, A. Bowers, T. G. Halsall and E. R. H. Jones, *J. Chem. Soc.*, 1905 (1954).

(16) The same conclusion has been reached in a paper which appeared after the submission of the present manuscript, A. Meisels, R. Ruegg, O. Jeger and L. Ruzicka, *Helv. Chim. Acta*, **38**, 1298 (1955).

(17) Z. Kitasato, *Acta Phytochim.*, **8**, 1 (1934).

(18) Several cases have been encountered in our laboratory in which sodium dichromate–acetic acid is superior to chromic acid–acetic acid for the oxidation of a methylene group alpha to a double bond to a carbonyl group (ref. 14).

acetyl-11-keto-18-isoöleanolate proceeded smoothly to give methyl acetyl-18-isoöleanolate when highly active platinum oxide catalyst (Baker and Co. activity 535) was used, but not at all with any of the ordinary commercial catalysts (*e.g.*, Baker and Co. activity 350, Bishop and Co.).[19] The conversion of methyl acetyl-18-isoöleanolate to methyl acetyl-12-keto-dihydro-18,18-isoöleanolate was accomplished by oxidation with perbenzoic acid to the 12,13α-oxide and subsequent rearrangement with boron trifluoride etherate to the 12-ketone.

Experimental[20]

Equilibration of Oleanoic Acid Acetate with Anhydrous Acid.—Dry hydrogen chloride gas was passed into a solution of 1.95 g. of oleanolic acid acetate, m.p. 258–260°, $[\alpha]_D$ +75°, in 50 ml. of alcohol-free chloroform for one-half hour. The acid-saturated solution was allowed to stand at room temperature for two days, then evaporated to dryness and the residue crystallized once from methanol to give 1.9 g. of a mixture of acid and lactone as indicated by the infrared spectrum. The mixture was adsorbed on a column of alumina and eluted with ether–chloroform (1:1) collecting 10-ml. fractions. Fifteen fractions were collected and the solvent changed to chloroform. Fractions 1–8 were evaporated and the solid was crystallized from methanol to give 455 mg. (24%) of oleanolic lactone acetate, m.p. 292–295°; carbonyl absorption (carbon tetrachloride) 1775, 1737 cm.$^{-1}$; $[\alpha]_D$ +19° (*c* 1.83).[21] Fractions 8–22 were evaporated and the solid crystallized from methanol to give 1.42 g. of oleanolic acid acetate, m.p. 259–260°; $[\alpha]_D$ +75°.[21]

Equilibration of Ursolic Acid Acetate with Anhydrous Acid.—Equilibration of ursolic acid acetate, m.p. 288–290°, $[\alpha]_D$ +73°, with dry hydrogen chloride was carried out in the same manner as was used for oleanolic acid acetate. A mixture of acid and lactone was obtained quantitatively from 1.6 g. of the ursolic acid acetate. The mixture was chromatographed on basic alumina. Carbon tetrachloride eluted ursolic lactone acetate, which crystallized from methanol at prisms (170 mg., 11%) of m.p. 283–285°; infrared maximum (carbon disulfide) 1772, 1734 cm.$^{-1}$; $[\alpha]_D$ +4.6° (*c* 1.88).[21] Acetic acid eluted ursolic acid acetate, which crystallized from methanol as fine white needles (1.4 g.) of m.p. 288–290°; $[\alpha]_D$ +73°.

Equilibration of Ursolic Lactone Acetate with Anhydrous Acid.—Dry hydrogen chloride gas was passed into a solution of 95 mg. of ursolic lactone acetate in 20 ml. of alcohol-free chloroform for one-half hour. The acid-saturated solution was allowed to stand at room temperature for five days, then evaporated to dryness. An infrared spectrum of a sample of the product showed that an acid had been formed. The material was chromatographed on alumina. Methylene chloride eluted 10 mg. of ursolic lactone acetate, m.p. 283–285°, which showed no melting point depression when admixed with a sample of ursolic lactone acetate prepared by equilibration of ursolic acid acetate. Acetic acid eluted 60 mg. of ursolic acid acetate, m.p. 289–292°. No melting point depression was observed when it was admixed with an authentic sample of ursolic acid acetate. As was the case when ursolic acid acetate was equilibrated with acid, the lactone constituted 11% of the equilibrium mixture.

Methyl Acetyl-11-ketoöleanolate.—A solution of 20.0 g. of methyl acetyloleanolate and 20.0 g. of sodium dichromate dihydrate in 300 ml. of acetic acid was heated at 100–102° for 6.25 hours. Ethanol (10 ml.) was added to the hot solution to decompose the excess dichromate and the resulting green solution was diluted with hot water to *ca.* 850 ml. which caused crystallization. The mixture was filtered after cooling and the product was washed with 50% methanol and recrystallized from alcohol–water to yield 16.5 g. of large colorless prisms, m.p. 243.5–245°.

Methyl Acetyl-11-keto-18-isoöleanoate.—To a solution of 12.0 g. of methyl acetyl-11-ketoöleanolate in 150 ml. of *anhydrous* acetic acid at 85° under nitrogen was added 25 ml. of a 40% solution of hydrogen bromide in anhydrous acetic acid. The solution was heated at 85–86° for 12 minutes and then diluted slowly with hot water to precipitate the product. The cooled mixture was filtered and the solid product was washed with water and recrystallized from acetic acid–water to give 8.2 g. of the 18-iso compound, m.p. 306–307°, infrared absorption 1740, 1670, 1640 cm.$^{-1}$.

Methyl Acetyl-12,13α-oxido-18-isoöleanolate.—Catalytic reduction of methyl acetyl-11-keto-18-isoöleanolate was carried out in acetic acid solution with high activity platinum oxide catalyst and afforded *ca.* 85% of methyl acetyl-18-isoöleanolate.[4] This was epoxidized with a threefold excess of perbenzoic acid in chloroform for 24 hours and the product was purified by recrystallization from methylene chloride–methanol, m.p. 269–271°, $[\alpha]^{25}_D$ +66°, carbonyl absorption 1740 cm.$^{-1}$ (acetate).

Anal. Calcd. for $C_{33}H_{52}O_5$: C, 74.96; H, 9.91. Found: C, 75.11; H, 10.08.

Methyl Acetyl-12-ketodihydro-11-isoöleanolate.—A mixture of 300 mg. of methyl acetyl-12,13α-oxido-18-isoöleanolate and 4 drops of boron trifluoride etherate in 5 ml. of methylene chloride was maintained at room temperature for 4 hours, evaporated and crystallized from methanol. Recrystallization from methylene chloride–methanol gave 280 mg. of 12-ketone, m.p. 278–279°, $[\alpha]^{25}_D$ +61.3°,[21] infrared absorption 1740, 1710 cm.$^{-1}$.

Anal. Calcd. for $C_{33}H_{52}O_5$: C, 74.96; H, 9.91. Found: C, 74.94; H, 9.94.

The 18-iso-12-ketone was recovered unchanged after refluxing with acetic anhydride–sodium acetate even for as long as 80 hours. Bromination with free bromine in dry acetic acid containing hydrogen bromide was very slow as compared with methyl acetyl-12-keto-dihydroöleanolate or ursolate. The bromoketone which was obtained in each of two runs was apparently contaminated with the starting material as judged from the analytical data (found, Br, 12.40). It had m.p. 265–266° dec., $[\alpha]_D$ +50°, carbonyl absorption 1740, 1713 cm.$^{-1}$ (axial bromine) and was much more stable to dehydrobromination than corresponding bromoketones in the oleanolate and ursolate series.

Reaction of the 18-iso-12-ketone with selenium dioxide in selenium dioxide at reflux is also unusually slow. After a 4-hour heating period, sufficient to give δ-lactones in the oleanolate and ursolate series most of the starting material could be recovered. Prolonged refluxing gave no δ-lactone, as determined by infrared analysis of the total reaction product, no isolable 11,12-enolone, and none of the Δ^9-unsaturated derivative, as determined by infrared. Low yields of an unidentified material, m.p. 304–306° (from methylene chloride–heptane), which showed ester carbonyl absorption at 1740 cm.$^{-1}$ and very weak non-conjugated ketone absorption at 1715 cm.$^{-1}$. The material gives no coloration with tetranitromethane–chloroform or ferric chloride–ethanol shows no selective, high intensity ultraviolet absorption and decomposes rapidly on alumina and appreciably on florisil.

Anal. Found: C, 73.82–74.22; H, 9.35–9.70. (Five analyses on different samples).

Acetyl-12α-bromo-18-isoöleanolic Lactone.—To a solution of 150 mg. of methyl acetyl-18-isoöleanolate in 2 ml. of methylene chloride was added dropwise a solution of 65 mg. of bromine in 1 ml. of methylene chloride. The bromine was absorbed immediately and was in excess after the completion of the addition. Removal of the solvent and three recrystallizations from methylene chloride methanol afforded 108 mg. of bromolactone, m.p. 290–292° dec., $[\alpha]^{25}_D$ +119°,[21] carbonyl absorption 1765, 1725 cm.$^{-1}$ in chloroform.

Anal. Calcd. for $C_{32}H_{49}O_4Br$: C, 66.53; H, 8.55; Br, 13.84. Found: C, 66.60; H, 8.51; Br, 13.80.

Bromination of methyl acetyloleanolate was carried out in the same way to give acetyl-12α-bromoöleanolic lactone, m.p. 223.5–224°, $[\alpha]^{25}_D$ +70°, carbonyl absorption 1765, 1725 cm.$^{-1}$ in chloroform.[22]

Bromination of methyl acetylursolate did not proceed under the same conditions and the starting material could be recovered completely.

δ-Lactone XV from Methyl Acetyl-12-ketodihydroöleanolate and its Δ^9-Unsaturated Derivative.—This lactone was

(19) Platinum oxide catalyst prepared at 520° according to the directions recently described, V. L. Frampton, J. D. Edwards and H. R. Henze, THIS JOURNAL, **73**, 4432 (1951), also proved satisfactory.

(20) Analyses by Mr. J. Nemeth and associates. All melting points are corrected.

(21) All rotations in chloroform, *c* = *ca.* 1.

(22) See Z. Kitasato, *Acta Phytochim.*, **8**, 315 (1935).

prepared by the method used by Dreiding, *et al.*,[9] in the ursolate series and was purified by recrystallization from methylene chloride–cyclohexane, m.p. 300–301°, $[\alpha]_D$ −69.5°, infrared absorption as described above.

Anal. Calcd. for $C_{32}H_{46}O_5$: C, 75.25; H, 9.08. Found: C, 75.40; H, 9.12.

The 11,12-enolone (enolic 11,12-diketone) was also isolated when the saturated 12-ketone was employed instead of its Δ^9-unsaturated derivative. It had m.p. 219–220°, gave a dark green coloration with ferric chloride–ethanol, showed infrared absorption at 3430, 1735, 1667 and 1637 cm.$^{-1}$ and corresponds in every way to the compound reported by Barton.[4]

URBANA, ILLINOIS

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF MINNESOTA]

The Diels–Alder Reaction of Anthracene with Nitroölefins. A New Route to 11-Nitro- and 11-Amino-9,10-dihydro-9,10-ethanoanthracenes[1]

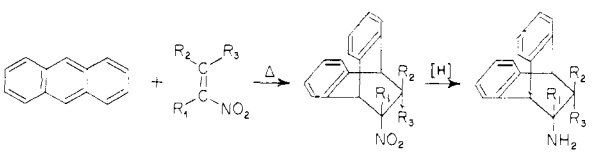
BY WAYLAND E. NOLAND, HOWARD I. FREEMAN AND M. SCOTT BAKER

RECEIVED JULY 27, 1955

The preparation of a series of seven Diels–Alder adducts of anthracene and common nitroölefins unsubstituted, 1- or 2-monosubstituted or 1,2- or 2,2-disubstituted is described; in the latter two cases the practical limits of the reaction appear to have been reached. The four adducts obtained in the best yields (19–62%) have been converted to the corresponding amines and their derivatives. The ultraviolet spectra of all the compounds compare favorably with the spectra of dihydroanthracenes reported in the literature.

Anthracene is known to undergo Diels–Alder reactions with many dienophiles[2] but until recently there were no published reports of a reaction between anthracene and a nitroölefin acting as a dienophile. Hurd and Juel[3] recently reported a reaction with anthracene at 300°, in which 1-nitronaphthalene appears to act as a nitroölefin dienophile with subsequent aromatization of the adduct by loss of nitrous acid. While this paper was being written, Klager[4] reported a 71% yield from the reaction of anthracene and nitroethylene (in excess), a reaction which we have also carried out and about which a preliminary report already has appeared.[5]

We have obtained adducts from reactions between anthracene and nitroölefins 1- or 2-monosubstituted, 1,2-disubstituted or 2,2-disubstituted. In the latter two cases the practical limits of the reaction appear to have been reached, since with β-methyl-β-nitrostyrene (1-phenyl-2-nitropropene) the yield of V was only 2%, with 2-nitro-2-butene the yield of VI was 0.5% and with 2-methyl-1-nitropropene the yield of VII was 0.6%.



I-VII Ia-IVa

Except with the β-nitrostyrenes and 2-methyl-1-nitropropene, polymerization of the nitroölefins appears to be competitive with the Diels–Alder reaction and is an important factor affecting the yield. In general, conditions for obtaining optimum yields were not determined, but with 1-nitropropene the maximum yield of 62% was obtained by adding a solution of 1-nitropropene to a refluxing solution of a fourfold proportion of anthracene in *o*-dichlorobenzene. The tertiary nitro group[6] in IV was formed from 2-nitropropene in reasonable yield, but the additional presence of a substituent on the carbon at the other end of the double bond from the nitro group sharply reduced the yield of V and VI. Refluxing a xylene solution of β-methyl-β-nitrostyrene with a 2.2-fold proportion of anthracene for 3.4 days gave no V and β-methyl-β-nitrostyrene was recovered in 97% yield. Increasing the reaction temperature by using boiling *o*-dichlorobenzene as solvent gave a 2% yield of V. An attempt to substitute an ethyl group for the methyl group in V by using β-ethyl-β-nitrostyrene (1-phenyl-2-nitro-1-butene) gave no reaction with anthracene in either boiling xylene or *o*-dichlorobenzene solutions. That the formation of a quaternary carbon is a difficult process is suggested by the low yield (0.6%) of the fluorescent adduct VII.

Chromatography is effective for separating nitroölefin adducts from their most persistent contaminant, anthracene. Elution with light petroleum (b.p. 60–68°) or solutions of ether in light petroleum removes anthracene from a column of alumina. Where the nitro group is so sterically hindered that it cannot be strongly adsorbed on alumina, as in the tertiary nitro compounds IV–VI, the compounds are eluted just after anthracene with light petroleum or solutions of ether in light petroleum. With the secondary nitro compounds I–III and VII, however, elution with methanol is necessary for complete removal from alumina.

The assignment of the *trans* configuration to II and III is based upon the following facts: (a) Both II and III were regenerated in their original con-

(1) From the M.S. theses of Howard I. Freeman (on training assignment from the U. S. Air Force Institute of Technology), December, 1953, and M. Scott Baker, June, 1955, and from work by the senior author 1953–1955. Paper presented before the Organic Division at the 128th National Meeting of the American Chemical Society, Minneapolis, Minn., Sept. 16, 1955.

(2) For numerous references see: (a) K. Alder and C. V. Wilson and J. A. Van Allan in "Newer Methods of Preparative Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1948, pp. 485–491; (b) M. C. Kloetzel and H. L. Holmes in "Organic Reactions," Vol. 4, John Wiley and Sons, Inc., New York, N. Y., 1948, Chapters 1 and 2; (c) J. A. Norton, *Chem. Revs.*, **31**, 319 (1942).

(3) C. D. Hurd and L. H. Juel, THIS JOURNAL, **77**, 601 (1955).

(4) K. Klager, *J. Org. Chem.*, **20**, 650 (1955).

(5) W. E. Noland, *Chem. Revs.*, **55**, 137 (1955).

(6) For the first report of the formation of tertiary nitro compounds by the Diels–Alder reaction see W. E. Noland and R. E. Bambury, THIS JOURNAL, **77**, 6386 (1955).