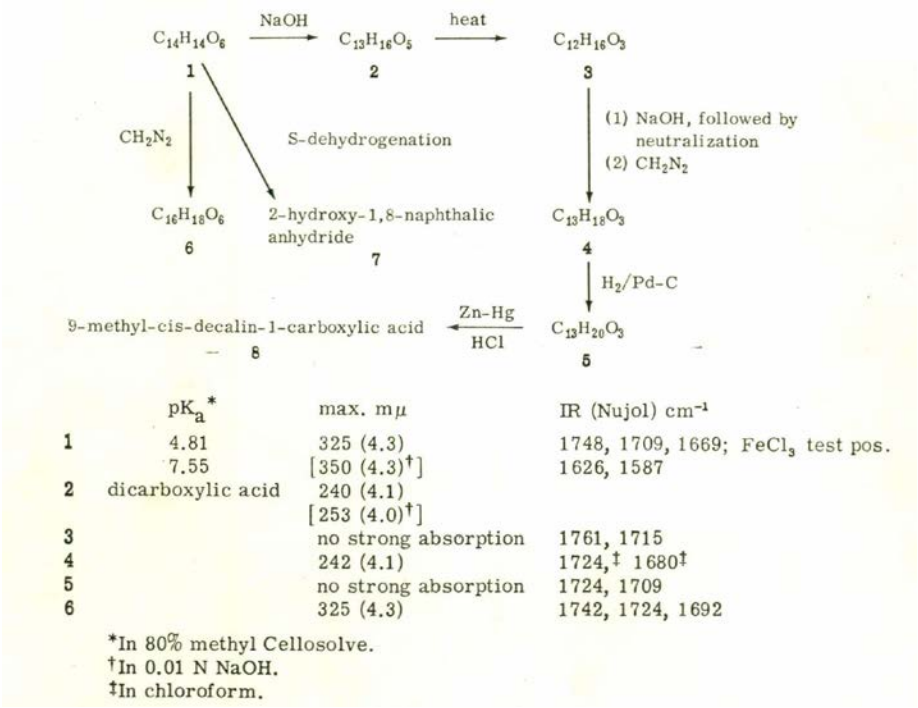
Problema de examen.

La solución de este problema implica aplicar los cálculos para predecir la longitud de onda de mayor absorción en la región ultravioleta y utilizar las tablas de interpretación para la región infrarroja, así como de tus conocimientos de química orgánica, mas podrás comprobar todas las estructuras propuestas basándote en el comportamiento espectral. El enunciado del problema es:

Deduce las estructuras para los compuestos del 1 al 8.

El significado de la operación marcada como *S-dehydrogenation* es deshidrogenación de la porción saturada. El compuesto 1 se llama ácido decevínico (decevinic acid) y tiene la estructura marcada como 1 en el artículo de referencia, tomado del *Chemical Abstracts* que se anexa en las páginas dos y tres. Se te recomienda especial atención con las etapas marcadas sobre cada flecha de reacción y además los datos que encontrarás debajo de las reacciones, que corresponden a los datos espectrales del compuesto marcado con el número correspondiente a cada etapa.

Plantea el resultado en la secuencia de reacciones con la estructura correspondiente. Te asombrarás de lo que hicieron en este trabajo los investigadores.



	pK_a*	max. mμ	IR (Nujol) cm^{-1}
1	4.81	325 (4.3)	1748, 1709, 1669; $FeCl_3$ test pos.
	7.55	[350 (4.3)†]	1626, 1587
2	dicarboxylic acid	240 (4.1)	
		[253 (4.0)†]	
3		no strong absorption	1761, 1715
4		242 (4.1)	1724,‡ 1680‡
5		no strong absorption	1724, 1709
6		325 (4.3)	1742, 1724, 1692

*In 80% methyl Cellosolve.
†In 0.01 N NaOH.
‡In chloroform.

F. Amézquita L.

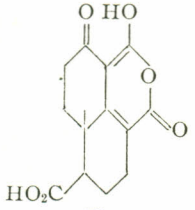
these reactions. In the plant, few alkaloids survive as II but are metabolized further to I and related compds. *N*-Oxide intermediates are postulated in the formation of berberine, cryptopine, benzophenanthridine and benzylisoquinoline alkaloids, sempervirine, cinchonamine, vomicine, some mitragyna alkaloids, and gelsemine (III). Two alternative schemes are suggested for the biogenesis of the oxindole part of III (cf. Gibson and Robinson, *C.A.* 45, 7128*h*; Goutarel, *et al. C.A.* 46, 2554*a*; and Witkop, *et al. C.A.* 47, 565*g*, and *ibid.* 48, 7032*g*). It is suggested that nornicotine is formed via the *N*-oxide of nicotine. The α-amino alcohol grouping found in senecio, tropane, and other alkaloids may arise from an enamine. A mechanism for the conversion by the plant of amino acids to aldehydes is proposed. Thelma E. Habgood

Synthesis in the benzoquinolizine group. XXIII. Synthesis of *dl*-*C*-bisnoremetine. Shigehiko Sugasawa and Koji Oka (Univ. Tokyo). *Pharm. Bull.* (Japan) 2, 85–8(1954); cf. *C.A.* 49, 8255*g*.—A mixt. of 1.4 g. *N*-3, 4-dimethoxyphenethyl-2(1*H*)-pyridone-4-carboxylic acid, 12 g. $(COCl)_2$, and 2 drops pyridine allowed to stand at 30° for 72 hrs., warmed with 25 ml. $CHCl_3$ for 20 min., and evapd. *in vacuo* at room temp. gave the corresponding acid chloride-HCl (I), used without purification. I (4.7 g.) dissolved in 30 ml. $CHCl_3$ contg. 1 to 2 ml. pyridine, was dropped into a cold C_6H_6 soln. of CH_2N_2 (from 20 g. nitrosomethylurea), the excess CH_2N_2 decompd. with aq. HOAc, the mixt. filtered, the C_6H_6 layer washed with H_2O, dried, evapd. below 30°, the residue dissolved in C_6H_6, purified by alumina column, and the C_6H_6 evapd. below 30° gave 2.3 g. *N*-3,4-dimethoxyphenethyl-2(1*H*)-pyridon-4-yl diazomethyl ketone (II), m. 116° (decompn.). A mixt. of 1 g. II and 5 g. 3,4-$(MeO)_2C_6H_3$-$(CH_2)_2NH_2$ was warmed in 40 ml. abs. EtOH, 5 ml. 10% aq. alc. $AgNO_3$ was added in 4 portions, the mixt. refluxed 1 hr., the alc. evapd., the sirup dissolved in 5% HCl, washed with C_6H_6, compd. taken up in $CHCl_3$, washed with $NaHCO_3$, $CHCl_3$ evapd., the sirup dissolved in 3 ml. AcOEt and cooled to give the *N*-3,4-dimethoxyphenethylamide of *N*-3,4-dimethoxyphenethyl-2(1*H*)-pyridone-4-acetic acid (III), m. 136–8° (from AcOEt). III (0.5 g.) absorbed 2 moles H over Raney Ni to give 0.45 g. of the corresponding piperidyl compd. (IV), m. 130–1° (from AcOEt). IV (0.34 g.) was boiled with 5 ml. $POCl_3$ for 1.5 hrs., cooled, petr. ether added, the sirup sepd., washed with petr. ether, dissolved in HCl, purified with C, and KI added to give 4′,5′-dimethoxy-8-(6″,7″-dimethoxy-3″,4″-dihydro-1″-isoquinolylmethyl)-3,4,6,7,8,9-hexahydrobenzo[2′,1′:1,2]quinolizinium iodide, converted to the corresponding chloride (V), an unstable salt, forming a picrolonate. V absorbed 2 moles H over Pt, the product dissolved in water, NH_4OH added, the liberated base dissolved in AcOEt, and solvent evapd. leaving *dl*-*C*-bisnoremetine, a sirupy base; dipicrolonate, yellow pillars from 80% AcOH; dipicrate, darkens 148–53°, m. 213–14° (decompn.). These cryst. salts represent 1 of the 4 racemic forms. *N*-Benzyl-2,4-dioxopiperidine phenylhydrazone, m. 155–8° (from EtOH), undistillable at 0.05 mm., readily formed a bimol. condensation product, m. 162–4°, and a trimol. condensation product, m. 196–8.5°. W. T. S.

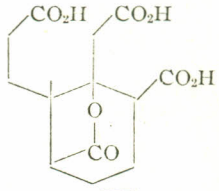
Synthesis of some derivatives of alkaloids. I. K. Babor, I. Ježo, and D. Rybár (Slovenská akad. vied, tech. org. látok, Bratislava, Czech.). *Chem. Zvesti* 8, 14–17 (1954).—A synthesis of ψ-cryptopalmatine from papaverine through tetrahydropapaverine, norcoralydine, norcoralydine-MeI, anhydrotetrahydromethyl-ψ-palmitine, and its oxide is described. II. K. Babor, L. Dúbravková, I. Ježo, and P. Šefčovič. *Ibid.* 53–62.—A synthesis of 1-(6′-bromoveratryl)norhydrohydrastinine is described. By reaction of β-piperonylpropionyl azide with 6-bromohomoveratric acid, *N*-β-piperonylethyl-3,4-dimethoxy-6-bromophenylacetamide is formed, which with $POCl_3$ gives 1-(6′-bromoveratryl)-6,7-methylenedioxy-3,4-dihydroisoquinoline and finally by hydrogenation 1-(6′-bromoveratryl)norhydrohydrastinine is formed. 3,4-Dimethoxy-6-bromophenylacetaldehyde and homopiperonylamine give corresponding Schiff base, which, in dild. HCl, gives 1-(6′-bromoveratryl)-norhydrohydrastinine. III. I. Ježo and A. Rybár. *Ibid.* 201–6.—Two methods for prepn. of tetrahydroberberine (I) are described. (1) By treatment of homoprotocatechuic acid dibenzyl ether with homopiperonylamine; *N*-(3,4-methylenedioxyphenethyl) - 3,4 - dibenzyloxyphenylacetamide is formed and dehydrated to 1-(3,4-dibenzyloxybenzyl)-6,7-methylenedioxy-3,4-dihydroisoquinoline. This is catalytically hydrogenated to 1-(3,4-dihydroxybenzyl)-norhydrohydrastinine and finely, after condensation with CH_2O and methylation, I is formed. (2) In the 2nd method the reaction with dibenzyl ether is omitted. IV. L. Dúbravková, I. Ježo, P. Šefčovič, and Z. Votický. *Ibid.* 255–60.—The synthesis of ψ-corydaldine and *N*-homoveratryl-3-methylglutarimide from 3-methylglutaric acid, β-(3,4-dimethoxyphenyl)propionazide, and homoveratrylamine is described and the oxidation products of these compds. are identified. V. L. Dúbravková, I. Ježo, P. Šefčovič and Z. Votický. *Ibid.* 576–9.—The synthesis of 1-methoxy-7,8-dihydroberberine-MeI (I), m. 267–8°, from narcotine through 1-(2-methyl-6,7-methylenedioxy-8-methoxy-1,2,3,4-tetrahydro)isoquinolyl(2-hydroxymethyl-3,4-dimethoxyphenyl)carbinol and its ditosyl deriv. is described. Jan Micka

Alstonia alkaloids. IV. Structure of alstoniline—observations on structure of alstonine. Stephen L. Wythe (Columbia Univ.). *Univ. Microfilms* (Ann Arbor, Mich.), *Publ.* No. 8872, 78 pp. (microfilm, $1.00; paper enlargement, $7.80); *Dissertation Abstr.* 15, 1317(1955). A. W. W.

Veratrum alkaloids. V. The constitution of decevinic acid. F. Gautschi, O. Jeger, V. Prelog, and R. B. Woodward (Harvard Univ.). *Helv. Chim. Acta* 37, 2280–94 (1954)(in German); cf. *C.A.* 48, 8234*i*; 49, 1068*h*, 1745*h*.—Decevinic acid (I), obtained by Craig and Jacobs (*C.A.* 34, 6262[5]) as degradation product of cevine, was further degraded to (+)-9-methyl-*cis*-decalin-1-carboxylic acid (II). The constitution of II was proved by conversion to (+)-9-methyl-*cis*-1-decalone. This degradation and the interpretation of the results of earlier studies and the phys. properties and derivs. of I lead to formula I for decevinic acid and to formula III for the oxidation product of cevine from which I is formed by pyrolysis. I and III are important for the investigation

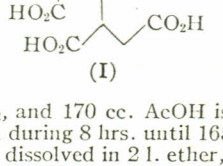


(I)

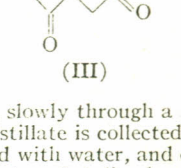


(III)

of the constitution of rings A, B, and C of cevine. VI. **The constitution of the hexanetetracarboxylic acid from cevine and germine.** O. Jeger, R. Mirza, V. Prelog, Ch. Vogel, and R. B. Woodward. *Ibid.* 2295–2301.—One of the oxidation products of cevine is an hexanetetracarboxylic acid $C_{10}H_{14}O_4$, for which the formula I was proposed. I gives with Ac_2O a dianhydride (II) which was converted into the keto anhydride (III) by pyrolysis. *dl*-III was synthesized by 2 methods, showing that the structure proposed for I is correct. A mixt. of 110 g. Et levulinate, 80 g. $NCCH_2CO_2Et$, 20 g.



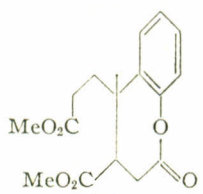
(I)



(III)

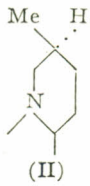
$AcNH_2$, and 170 cc. AcOH is distd. slowly through a short column during 8 hrs. until 165 cc. distillate is collected, the residue dissolved in 2 l. ether, washed with water, and dried to yield di-Et 1-cyano-2-methyl-Δ^1-butene-1,4-dicarboxylate (IV), $b_{1.5}$ 145–7°. To IV (32 g.) in 150 cc. EtOH is added with stirring 17.5 g. KCN in 100 cc. H_2O, the soln. cooled to 10°, 40 cc. dil. HCl contg. 22 cc. HCl (d. 1.15) are added slowly, the mixt. stirred for 2 hrs. and poured into 800 cc. 5% HCl. The sepd. thick oil is taken up in ether and distd. *in vacuo*, yielding 22 g. di-Et 1,2-dicyano-2-methyladipate (V), b_7 164–6°. V (26.6 g.) and 2.3 g. Na in 200 cc. pure dioxane were refluxed for 2 hrs., 20 g. $BrCH_2CO_2Et$ added, refluxing was continued 1 hr., the NaBr filtered off, and the dioxane evapd. *in vacuo* to give 13.5 g. tri-Et 2,3-dicyano-3-methyl-1,2,5-pentanetricarboxylate (VI), $b_{0.7}$ 190–5°. VI (4 g.) was refluxed 14 hrs. with 50 cc. concd. HCl, the HCl

distd. off *in vacuo*, the residue extd. with abs. ether, and the ether evapd. to give 2.95 g. amorphous acids. This product (1 g.) was heated in a Pyrex tube at 15 mm. and 260° for 30 sec., then for 4 min. at 0.1–0.3 mm. The volatile products were dissolved in $CHCl_3$, the $CHCl_3$ evapd., the residue dissolved in 10 cc. abs. ether and cooled to −40°. The racemic form of **III** sepd., was sublimed *in vacuo* and recrystd. from benzene-petr. ether, m. 97–8°. To a suspension of 6.9 g. EtONa in 80 cc. dry C_6H_6 under N is added 18 cc. of dried HCO_2Et, the mixt. stirred 0.5 hr., cooled to 0° and 10 g. 1-oxo-12-methyl-1,2,3,4,9,10,11,12-octahydrophenanthrene is added dropwise. After addn. of 70 cc. dry C_6H_6, stirring 7 hrs. at room temp. under N and standing overnight, the mixt. is poured into ice water, taken up in ether, the ether extd. with NaOH soln., the alk. exts. are acidified with concd. HCl and the sepd. crystals (0.9 g.) of 1-oxo-2-hydroxymethylene-12-methyl-1,2,3,4,9,10,11,12-octahydrophenanthrene (**VII**) taken up in ether and recrystd. from MeOH-H_2O, m. 73–4°. A soln. of 9.3 g. **VII** in 190 cc. EtOH, 260 cc. 2*N* NaOH and 75 cc. H_2O_2 (30%) is allowed to stand 3 hrs. at room temp., and after addn. of further 75 cc. H_2O_2, the mixt. refluxed 1 hr., 75 cc. H_2O_2 added, and refluxing continued 1 hr. The mixt. is allowed to cool, acidified with 2*N* H_2SO_4, extd. with ether and the ether soln. extd. with satd. $NaHCO_3$ soln. to give 7.3 g. of acidic products from the $NaHCO_3$ soln. as yellow oil, which gives after recrystn. from acetone 5 g. of β-(1-methyl-2-carboxy-1,2,3,4-tetrahydro-1-naphthyl)propionic acid (**VIII**), m. 179–80° (decompn.). The yellow oily unrecrystd. **VIII** (7.3 g.) in MeOH is treated with ethereal CH_2N_2 soln. to yield 7.3 g. Me ester (**IX**), $b_{0.2}$ 151–5°, n_D^{20} 1.527. CrO_3 soln. (40 cc., 25%) in AcOH-H_2O (8:2) is added to 5.8 g. **IX** in 90 cc. AcOH; the temp. is kept below 20°. After standing overnight, the excess CrO_3 is destroyed with MeOH, H_2O added, the oxidation product taken up in ether, the ether exts. washed with water, 2*N* Na_2CO_3, and water, the remaining oily product dissolved in petr. ether-benzene (1:1), chromatographed on Al_2O_3 (activity III) and eluted with 430 cc. petr. ether-benzene (1:1) + 180 cc. benzene, yielding 4.1 g. oil, which was refluxed in 110 abs. EtOH and 7.7 cc. AcOH with 5 g. Girard reagent T for 1.5 hrs., then poured into a soln. of 6.39 g. Na_2CO_3 in 1 l. ice water, washed with ether, acidified with H_2SO_4 to 0.5*N*, extd. with ether after 2 hrs., the ether soln. evapd., and the ketonic residue (2.75 g.) distd. at 175–185° (bath)/0.15 mm., to give after several days crystals of the Me ester of β-(1-methyl-2-carbomethoxy-4-oxo-1,2,3,4-tetrahydro-1-naphthyl)propionic acid (**IX**), m. 76–8° (from acetone-ether-petr. ether); 2,4-dinitrophenylhydrazone, m. 206–7° (from CH_2Cl_2-EtOH). **IX** (3.85 g.) is treated with 7.4 cc. of a soln. of BzO_2H in $CHCl_3$ (203 mg. O) at room temp. for 10 days in the dark, the reaction product taken up in ether, the ether exts. washed with H_2O, 2*N* Na_2CO_3, and H_2O, the ether evapd. *in vacuo* to give an oily residue which crystd., giving 0.705 g. of the lactone of **IX** (**X**), m. 132–3° (from acetone-ether), and 1.266 g. less pure material. **X** (1.128 g.)



(X)

in 15 cc. 2*N* methanolic KOH is refluxed 2 hrs., dild. with water, the MeOH evapd., the light brown residue neutralized with dil. HCl, acidified with AcOH, extd. with ether, the ether soln. washed with water, the ether evapd. *in vacuo*, the oily residue dissolved in 45 cc. AcOEt, and 5 cc. MeOH, and an ozone stream (27 mg. O_3/min.) introduced in the soln. 7 hrs. at room temp. The soln. is concd. to 20 cc., refluxed with 20 cc. HCO_2H and 5 cc. H_2O_2 (30%) 2 hrs. (5-cc. portions of H_2O_2 added after 40 and 80 min.), the mixt. evapd. *in vacuo*, the residue dissolved in 51 cc. 2*N* alc. KOH and 10 cc. water, refluxed 0.5 hr., concd. *in vacuo*, acidified with HCl, satd. with NaCl, continuously extd. with ether, the residue of the ether soln. dissolved in MeOH, and esterified with ethereal CH_2N_2 soln., yielding 427 mg. of tetra-Me 3-methyl-1,2,3,5-pentanetetracarboxylic acid (**XI**), $b_{0.05}$ 115–120°. **XI** (265 mg.) in 10 cc. 2*N* KOH soln. in EtOH-water (9:1) is heated 7 hrs. at 150° in a bomb, the EtOH evapd. *in vacuo*, the residue dild. with water, acidified with HCl, satd. with NaCl, continuously extd. with ether, the ext. (172 mg.) purified by countercurrent distribution between EtOAc and H_2O, fractions 2–7 are combined (52 mg.) and slowly heated to 280° in a bulb tube. The product of the pyrolysis is the racemic form of **III**, m. 96–99.5° (from acetone-ether). **VII. The constitution of ring F and the absolute configuration of carbon atom 25 of cevine.** O. Jeger, V. Prelog, E. Sundt, and R. B. Woodward. *Ibid.* 2302–6; Craig and Jacobs, *C.A.* **36**, 7749.—One of the products of the oxidation of cevine with chromic acid isolated by C. and J. (*loc. cit.*) is a cryst. compd., $C_6H_{11}ON$, which was assumed to be 5-methyl-2-piperidone. In order to prove this assumption, D(+)-5-methyl-2-piperidone (**I**) is synthesized and found to have the same infrared absorption spectrum and other properties (except the direction of rotation) as compd. $C_6H_{11}ON$ from cevine. This confirms that the proposed constitution of ring F (**II**) of cevine is correct and that C-25 has the L-configuration and the Me group on C-25 has the β-configuration. D(+)-citronellal



(II)

(40 g.) and 25.8 g. $NH_2OH.HCl$ in 100 cc. *N* Na_2CO_3 (pH 7–8) are shaken 12 hrs., and the mixt. extd. with ether, yielding 36.06 g. citronellal oxime (**III**), b_9 125–8°, n_D^{20} 1.472. **III** (34.5 g.) stirred 2 hrs. at 102° with 5.5 g. Raney Ni, the product dissolved in ether, the catalyst filtered, and the ether evapd. gives D(+)-citronellamide (**IV**), m. 80–81.5° (from petr. ether), $[\alpha]_D^{21}$ 9° (*c* 1.08, EtOH). **IV** (1.0 g.) in 20 cc. AcOH is ozonized at room temp. for 20 min. with a 4% O_3-O_2 mixt. (500 cc./min.), the soln. refluxed 2 hrs. with 2 cc. H_2O_2 (30%), the AcOH distd. off *in vacuo*, the residue taken up in ether, extd. with *N* Na_2CO_3, the Na_2CO_3 ext. acidified and continuously extd. with ether to give 0.6 g. D(+)-β-methyladipamic acid (**V**), m. 132–3°, $[\alpha]_D^{23}$ 13.5° (*c* 1.18, EtOH). **V** (1.0 g.) is added slowly to a NaOBr soln. at 0° (prepd. from 1.2 g. Br and 1.5 g. NaOH in 20 cc. H_2O), the mixt. heated on a water bath 1 hr., acidified with HCl, evapd. to dryness, the residue dissolved in H_2O, the soln. extd. with ether, and then brought to pH 6 by addn. of NH_3 soln. and evapd. *in vacuo* to dryness. MeOH is added to the residue, the soln. evapd. again and this procedure repeated several times with 10 cc. MeOH, which was satd. with HCl. The last residue is dissolved in 20 cc. dil. NH_3, the soln. extd. with ether, neutralized with HCl, and extd. continuously with ether 48 hrs., yielding 0.42 g. of a yellow oil, which is chromatographed in 10 cc. C_6H_6 on 14.2 g. Al_2O_3 (activity III); it is eluted first with benzene and ether (0.22 g. material obtained), then with ether-MeOH (9:1), giving 0.158 g. of an oil, which after distn. at 136–145° (bath)/9 mm. gives 0.115 g. **I**, m. 40°, $[\alpha]_D^{23}$ 84° (*c* 2.18, EtOH), hygroscopic. The infrared absorption spectra of **III**, **IV**, **V**, and of the L(−)-5-methyl-2-piperidone from cevine are recorded. Kurt Weinberg

Samandarine and related alkaloids. V. The preparation of hydrocarbons by dehydrogenation of samandiol. Clemens Schöpf, Dieter Klein, and Ernst Hofmann (Tech. Hochschule, Darmstadt, Ger.). *Chem. Ber.* **87**, 1638–60 (1954); cf. *C.A.* **45**, 1605*d*.—$LiAlH_4$ (1.9 g.) in Et_2O added to 5 g. samandarine at 15°, the mixt. refluxed 30 min., dild. with H_2O, and the Et_2O evapd. gave 4.9 g. *samandiol* (**I**) $C_{19}H_{33}NO_2$, m. 196–9° (from MeOH-H_2O); *hydrochloride*, decomp. between 280° and 320°; *picrate*, m. 243–5° (decompn.)(from MeOH). **I** recrystd. from aq. Me_2CO, m. 203° (**II**), depressing the m.p. of **I** from MeOH-H_2O. Both **I** and **II** gave the same *triacetyl deriv.*, $C_{25}H_{39}NO_5$, m. 194° (from 10% AcOH). **I** and $Pb(OAc)_4$ at 80° gave H_2CO and a *base* $C_{18}H_{29}NO$ (**III**), m. 198–9° (from EtOAc). **III** condensed with *o*-$H_2NC_6H_4CHO$ (**IV**), giving a product whose ultraviolet spectrum was identical with the α-tripiperideine-**IV** compd. and hydrogenated (Pt, 0.1*N* HCl) to $C_{18}H_{31}NO$ (**V**), m. 151–2° (from MeOH-H_2O); *hydrochloride*, m. 315–6° (decompn.)(from dil. HCl). **V** formed a *hydrate*, m. 135–6°, which could be desiccated to the form, m. 151-