ratories, Inc., Waukegan, Ill.; 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose from Aldrich Chemical Co., Inc., Milwaukee, Wis.; *m*-dinitrobenzene from Fisher Scientific Co., Fair Lawn, N.J. Hexamethylphosphoramide (HMPA) was a product of Aldrich Chemical Co. and was stored before use over molecular sieves, 8–12 mesh, activated, type 4A.

1,2:5,6-Di-*O*-isopropylidene-3-*O*-(*m*-nitrophenyl)-D-Glucofuranose (1). Into a three-necked, 250-mL round-bottom flask equipped with N_2 inlet and outlet and magnetic bar stirring were charged HMPA (75 mL) and 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose (28.6 g, 110 mmol). Next NaH (50% in oil), 5.5 g (115 mmol), was added over a 1-h period in 1.0–1.5-g portions. When the evolution of H_2 was nearly complete, *m*-dinitrobenzene (16.8 g, 100 mmol) was added at once. An exothermic reaction ensued but soon subsided and the reaction mixture was allowed to cool and stir at room temperature overnight. Next, the reaction mixture was slowly poured into 1.5 L of vigorously stirred water. Subsequently, most of the water layer was decanted and then the crude product collected by filtration. The solid was dissolved in CCl_4 (250 mL), then washed well with H_2O. The CCl_4 layer was evaporated to residue, then eluted from an alumina column with initially CCl_4 and finally $CHCl_3$. Those fractions resulting in a light yellow oil were crystallized by dissolution in cyclohexane, then addition of 30–60 °C petroleum ether (PE) with scratching. The light yellow solid was filtered, washed with PE, and dried in a forced air oven at 100 °C to obtain the title compound, **1**, 31.1 g (82%): mp 119–122 °C; α^{23}_D −38° (*c* 1.0, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.3–1.6 [m, 12 H, $(CH_3)_2C$], 4.0–4.9 [m, 6 H, H-(2–6)], 5.97 (d, 1 H, H-1, $J_{1,2}$ = 4 Hz), 7.2–8.0 (m, 4 H, aromatic); IR 1520, 1370, 1340 cm^{-1} (–NO_2).

Anal. Calcd for $C_{18}H_{23}NO_8$: C, 56.69; H, 6.08; N, 3.67. Found: C, 56.89; H, 6.41; N, 3.44.

1,2:3,4-Di-*O*-isopropylidene-6-*O*-(*m*-nitrophenyl)-D-galactopyranose (3). Using the same procedure as for **1**, HMPA (70 mL), 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose (25.0 g, 96 mmol), NaH (50% in oil, 4.8 g, 100 mmol), and *m*-dinitrobenzene (14.5 g, 86 mmol) were combined to react, with stirring under N_2. The initial evolution of heat soon subsided and the reaction mixture was stirred for 44 h at room temperature before workup. The reaction mixture was partitioned between 1 L of H_2O and 300 mL of CCl_4. The CCl_4 layer was then washed well with H_2O before concentrating for elution from an alumina column with CCl_4 and then $CHCl_3$. Those fractions which gave a light yellow oil were crystallized from cyclohexane/PE at room temperature with scratching to obtain the title compound **3**, 20.3 g (62%): mp 109–111 °C; α^{23}_D −106° (*c* 1.0, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.4–1.6 [m, 12 H, $(CH_3)_2C$], 4.2–4.9 [m, 6 H, H-(2–6)], 5.63 (d, 1 H, H-1, $J_{1,2}$ = 5 Hz), 7.3–8.0 (m, 4 H, aromatic); IR 1540, 1370, 1340 cm^{-1} (–NO_2).

Anal. Calcd for $C_{18}H_{23}NO_8$: C, 56.69; H, 6.08; N, 3.67. Found: C, 57.07; H, 6.14; N, 3.67.

3-*O*-(*m*-Nitrophenyl)-D-glucopyranose (2). The following ingredients were combined and heated at reflux overnight: *p*-dioxane (20 mL), H_2O (15 mL), concentrated H_2SO_4 (4 drops), compound **1** (7.6 g, 20 mmol). TLC showed the absence of protected sugar derivative **1**. The reaction mixture was evaporated to residue, dissolved in minimum hot H_2O, and cooled with stirring overnight to crystallize. The off-white solid was collected by filtration, then recrystallized from MeOH/Et_2O/PE. The nearly white solid was filtered, washed with PE, and dried in a forced air oven at 100 °C to obtain pure title compound **2**, 3.0 g (50%): mp 142–144 °C; α^{23}_D 40° (*c* 1.0, MeOH); ^{1}H NMR (Me_2SO) showed the absence of isopropylidene groups.

Anal. Calcd for $C_{12}H_{15}NO_8$: C, 47.91; H, 5.01; N, 4.64. Found: C, 48.37; H, 5.40; N, 4.67.

6-*O*-(*m*-Nitrophenyl)-D-galactopyranose (4). Using precisely the same procedure as for **2**, compound **3** (7.6 g, 20 mmol) was deprotected to give a crude product which was dissolved in boiling MeOH by the addition of minimum H_2O. The addition of Et_2O and cooling overnight at ice temperature gave nearly white, crystalline title compound **4**, 1.6 g (26%): mp 203–206 °C; α^{23}_D 33° [*c* 1.0, THF/H_2O (1:1 v/v)]; ^{1}H NMR (Me_2SO) showed the absence of isopropylidene groups.

Anal. Calcd for $C_{12}H_{15}NO_8$: C, 47.91; H, 5.01; N, 4.64. Found: C, 47.91; H, 5.17; N, 4.57.

Acknowledgment. This work was supported by USPHS Grant GM 22911.

Registry No.—**1**, 62263-57-4; **2**, 62263-58-5; **3**, 62263-59-6; **4**, 62263-60-9; 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose, 582-52-5; *m*-dinitrobenzene, 99-65-0; 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose, 4064-06-6.

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(10) The absence of aglycon *m*-nitrophenol was verified in the final hydrolysis solution by thin layer chromatography. Compound **2** appeared to be unaffected by hydrolysis.

Synthesis of 2*H*-Pyrido[1,2-*b*]-*as*-triazines Using Azirines Generated by Modified Neber Reactions

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In earlier studies[1,2] we have shown that pyridinium *N*-imines reacted smoothly with 2-phenylazirine to afford the corresponding 3-phenyl-1,9a-dihydro-2*H*-pyrido[1,2-*b*]-*as*-triazine derivatives and that this reaction has a high synthetic value in virtue of the wide variability of pyridinium *N*-imines. So far as isolated azirines are used, however, further extension of this reaction must be limited to a large extent by the problems in an azirine synthesis. For example, Hassner's procedure[3,4] is one of the most convenient methods for the preparation of azirine derivatives at present, but not applicable to the cases in which appropriate olefins are not available. On the other hand, if azirines without isolation can be used in the reactions with pyridinium *N*-imines, many routes to azirine may serve for the preparation of dihydropyridotriazines. Among these types of azirine formations, Neber[5,6] and related reactions[7–9] are especially important because of the ready availability of the ketonic precursors. This paper deals with the reactions of pyridinium *N*-imines with various azirines generated in situ by modified Neber reactions and the extended syntheses of the corresponding 1,9a-dihydro-2*H*-pyrido[1,2-*b*]-*as*-triazines.

We examined at first the possibility for the preparation of dihydropyridotriazines by the reactions involving oxime *O*-tosylates as an azirine precursor, but found that these reactions have only a low synthetic value for lack of reproducibility and for the instability and the low yields of oxime *O*-tosylates. These problems were, however, solved by replacing oxime *O*-tosylates with dimethylhydrazone methiodides.

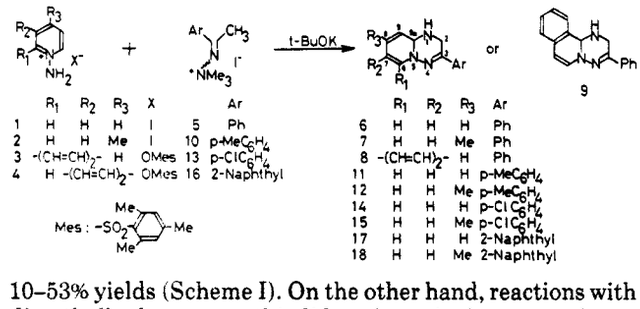
The reactions of 1-aminopyridinium salts or quinolinium *N*-imine dimer with dimethylhydrazone methiodides of several aryl alkyl ketones were carried out in tetrahydrofuran in the presence of potassium *tert*-butoxide with stirring at room temperature or on heating at the reflux temperature. For example, the reactions of the salts **1–4** with acetophenone, *p*-methyl-, *p*-chloroacetophenone, and 2-acetonaphthone dimethylhydrazone methiodides, **5**, **10**, **13**, and **16**, proceeded smoothly at room temperature to give the corresponding 3-aryldihydropyridotriazines **6–9**, **11**, **12**, **14**, **15**, **17**, and **18** in

Table I. ^{1}H NMR Spectral Data of 2*H*-Pyridotriazines

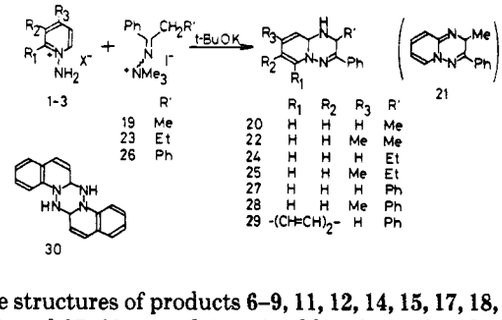
Registry no.	Compd	C_6	C_7	C_8	C_9	C_{9a}	NH	C_2H	C_2R'	Ar	
62154-45-4	**11**	6.60 (d)	4.71 (br t)	5.97 (m)	5.22 (br d)	5.41 (br s)	1.97 (br s)	3.76 (d)	4.08 (d)	7.08[a] (d)	7.46[a,b] (d)
				$J_{6,7}$ = 7.5, $J_{7,8}$ = 7.5, $J_{8,9}$ = 11.0, $J_{2,2}$ = 17.5 Hz							
62154-46-5	**12**	6.61 (d)	4.64 (dd)	1.77 (d)	5.00 (br s)	5.33 (br s)	1.90 (br s)	3.73 (d)	4.06 (d)	7.13[a] (d)	7.50[a,c] (d)
				$J_{6,7}$ = 7.5, $J_{7,9}$ = 1.5, $J_{8,9}$ = 1.0, $J_{2,2}$ = 18.0 Hz							
62154-47-6	**14**	6.56 (d)	4.73 (br t)	5.95 (m)	5.20 (br d)	5.37 (br s)	2.35 (br s)	3.67 (d)	4.01 (d)	7.23[a] (d)	7.47[a] (d)
				$J_{6,7}$ = 7.5, $J_{7,8}$ = 7.5, $J_{8,9}$ = 10.0, $J_{2,2}$ = 17.5 Hz							
62154-48-7	**15**	6.56 (d)	4.66 (dd)	1.75 (d)	5.00 (br s)	5.32 (br s)	2.00 (br s)	3.73 (d)	4.06 (d)	7.27[a] (d)	7.52[a] (d)
				$J_{6,7}$ = 7.5, $J_{7,9}$ = 1.5, $J_{8,9}$ = 0.5, $J_{2,2}$ = 17.5 Hz							
62154-49-8	**17**	6.70 (d)	4.80 (br t)	6.02 (m)	5.30 (br d)	5.52 (br s)	2.30 (br s)	3.92 1)d)	4.24 (d)	7.3–8.1 (m)	
				$J_{6,7}$ = 7.5, $J_{7,8}$ = 7.5, $J_{8,9}$ = 10.0, $J_{2,2}$ = 18.5 Hz							
62154-50-1	**18**	6.66 (d)	4.68 (dd)	1.79 (d)	5.05 (br s)	5.41 (br s)	1.95 (br s)	3.91 (d)	4.22 (d)	7.3–8.1 (m)	
				$J_{6,7}$ = 7.5, $J_{7,9}$ = 1.5, $J_{8,9}$ = 1.0, $J_{2,2}$ = 18.5 Hz							
62154-51-2	**20**	6.60 (dd)	4.71 (br t)	5.95 (m)	5.17 (br d)	5.42 (br s)	2.10 (br s)	3.87 (q)	1.25 (d)	7.1–7.6 (m)	
				$J_{6,7}$ = 7.5, $J_{7,8}$ = 7.5, $J_{8,9}$ = 10.0, $J_{6,8}$ = 0.5, $J_{2,2}$ = 7.5 Hz							
62154-52-3	**22**	6.63 (d)	4.66 (dd)	1.76 (d)	5.00 (br s)	5.40 (br s)	1.98 (br s)	3.96 (q)	1.31 (d)	7.2–7.7 (m)	
				$J_{6,7}$ = 7.5, $J_{7,9}$ = 1.5, $J_{8,9}$ = 1.0, $J_{2,2}$ = 7.5 Hz							
62154-53-4	**24**	6.63 (d)	4.75 (br t)	5.98 (m)	5.23 (br d)	5.42 (br s)	2.07 (br s)	3.60 (br d)	1.75[d] (m)	7.1–7.6 (m)	
				$J_{6,7}$ = 7.5, $J_{7,8}$ = 7.5, $J_{8,9}$ = 10.0, $J_{2,2}$ = 8.5 Hz							
62154-54-5	**25**	6.60 (d)	4.65 (dd)	1.75 (s)	5.00 (br s)	5.32 (br s)	1.93 (br s)	3.61 (br d)	1.75[e] (m)	7.1–7.6 (m)	
				$J_{6,7}$ = 7.5, $J_{7,9}$ = 1.5, $J_{2,2}$ = 8.5 Hz							
62154-55-6	**27**	6.74 (d)	4.78 (br t)	5.97 (m)	5.10 (br d)	5.40 (br s)	2.30 (br s)	4.91 (s)	*f*	7.1–7.7 (m)	
				$J_{6,7}$ = 7.5, $J_{7,8}$ = 7.5, $J_{8,9}$ = 10.0 Hz							
62154-56-7	**28**	6.71 (d)	4.67 (dd)	1.73 (d)	4.87 (br s)	5.30 (br s)	2.20 (br s)	4.90 (s)	*f*	7.1–7.7 (m)	
				$J_{6,7}$ = 7.5, $J_{7,9}$ = 2.0, $J_{8,9}$ = 1.0 Hz							
62154-57-8	**21**	7.23 (d)	5.68 (dt)	6.66 (br t)	6.40 (dd)			4.81 (q)	1.26 (d)	7.2–7.4 (m)	7.7–7.9 (m)
				$J_{6,7}$ = 7.5, $J_{7,8}$ = 7.5, $J_{8,9}$ = 10.0, $J_{7,9}$ = 1.5, $J_{6,8}$ = 1.5 Hz							

[a] Appeared as A_2B_2 patterns (J = 7.5–8.0 Hz). [b] Plus δ 2.31 (3 H, s). [c] Plus δ 2.33 (3 H, s). [d] Plus δ 0.98 (3 H, t, J = 7.5 Hz). [e] Plus δ 0.98 (3 H, t, J = 7.5 Hz). [f] Overlapped with signals at δ 7.1–7.7.

Scheme I



Scheme II



10–53% yields (Scheme I). On the other hand, reactions with dimethylhydrazone methiodides of propiophenone, *n*-butyrophenone, and benzyl phenyl ketone, **19, 23,** and **26,** in which disubstituted azirines must be formed, did not take place at room temperature, but, by heating the reaction mixtures, the corresponding 2,3-disubstituted dihydropyridotriazines **20, 22, 24, 25,** and **27–29** were obtained in 12–57% yields (Scheme II). The compound **29** was also formed in 38% yield by the reaction of quinolinium *N*-imine dimer **30** with the methiodide **26.** Strange to say, dehydro compound **21** was obtained in 30% yield for only one time during our several runs of the reaction of the salt **1** with the methiodide **19,** but our attempts to reproduce this phenomenon were unsuccessful.

The structures of products **6–9, 11, 12, 14, 15, 17, 18, 20, 22, 24, 25,** and **27–29** were determined by physical and spectral means and by comparisons with those of known dihydropyridotriazines synthesized earlier by us.[1,2] In particular, the large similarity of the chemical shifts (Table I) of the products **11, 12, 14, 15, 17, 18, 20, 22, 24, 25, 27,** and **28** with those of known dihydropyridotriazines supported strongly our proposed structures. All new compounds gave satisfactory analyses, and all melting points and IR and NMR spectral patterns of compounds **6–9** and **29** were in good accord with those of pyridotriazines prepared by the reactions of pyridinium *N*-imines with 2-phenylazirine or 2,3-diphenylazirine.[2]

The NMR spectrum of compound **21** exhibited signals at

Table II. Results and Some Properties of Pyridotriazines

Compd[a,d]	Reactant: N-Imine[e]	Reactant: Methiodide[f]	Yield, %	Mp, °C	IR (KBr), cm^{-1}: NH	IR (KBr), cm^{-1}: C=C or C=N
6[b]	1	5	29	98–100		
7[b]	2	5	23	114–117		
8[b]	3	5	53	127–129		
9[b]	4	5	10	158–160		
11	1	10	29	124–126	3272	1635
12	2	10	25	131–133	3200	1653
14	1	13	38	116–118	3258	1636
15	2	13	23	130–132	3222	1652
17	1	16	26	168–170	3208	1633
18	2	16	31	142–143	3216	1655
20	1	19	35	65–68	3225	1637
21	1	19	30	Oil		1644[c]
22	2	19	42	79–81	3278	1661
24	1	23	57	68–70	3278	1637
25	2	23	57	105–107	3268	1656
27	1	26	15	132–134	3255	1637
28	2	26	12	113–115	3273	1655
29[b]	3	26	24	184–186		
29[b]	30	26	38	184–186		

[a] **11.** Anal. Calcd for $C_{14}H_{15}N_3$: C, 74.64; H, 6.71; N, 18.65. Found: C, 74.34; H, 6.90; N, 18.66. **12.** Calcd for $C_{15}H_{17}N_3$: C, 75.28; H, 7.16; N, 17.56. Found: C, 75.09; H, 7.25; N, 17.63. **14.** Calcd for $C_{13}H_{12}N_3Cl$: C, 63.54; H, 4.92; N, 17.10. Found: C, 63.32; H, 4.91; N, 17.24. **15.** Calcd for $C_{14}H_{14}N_3Cl$: C, 64.73; H, 5.43; N, 16.18. Found: C, 64.76; H, 5.41; N, 16.16. **17.** Calcd for $C_{17}H_{15}N_3$: C, 78.13; H, 5.79; N, 16.08. Found: C, 78.32; H, 5.78; N, 15.86. **18.** Calcd for $C_{18}H_{17}N_3$: C, 78.51; H, 6.22; N, 15.26. Found: C, 78.56; H, 6.31; N, 15.14. **20.** Calcd for $C_{14}H_{15}N_3$: C, 74.64; H, 6.71; N, 18.65. Found: C, 74.45; H, 6.87; N, 18.38. **21** (its picrate, mp 178–181 °C). Calcd for $C_{20}H_{16}N_6O_7$: C, 53.10; H, 3.57; N, 18.58. Found: C, 53.08; H, 3.60; N, 18.67. **22.** Calcd for $C_{15}H_{17}N_3$: C, 75.28; H, 7.16; N, 17.56. Found: C, 75.01; H, 7.19; N, 17.40. **24.** Calcd for $C_{15}H_{17}N_3$: C, 75.28; H, 7.16; N, 17.56. Found: C, 75.01; H, 7.19; N, 17.41. **25.** Calcd for $C_{16}H_{19}N_3$: C, 75.85; H, 7.56; N, 16.59. Found: C, 75.87; H, 7.62; N, 16.54. **27.** Calcd for $C_{19}H_{17}N_3$: C, 79.41; H, 5.96; N, 14.62. Found: C, 79.13; H, 6.03; N, 14.46. **28.** Calcd for $C_{20}H_{19}N_3$: C, 79.70; H, 6.35; N, 13.94. Found: C, 79.43; H, 6.25; N, 13.80. [b] See ref 2. [c] Neat. [d] Registry no.: **6,** 54855-55-9; **7,** 54855-56-0; **8,** 59065-86-0; **9,** 59247-65-3; **29,** 59247-66-4. [e] Registry no.: **1,** 6295-87-0; **2,** 7583-92-8; **3,** 39996-55-9; **4,** 39996-57-1; **30,** 7184-52-3. [f] Registry no.: **5,** 33785-82-9; **10,** 33785-84-1; **13,** 33777-73-0; **16,** 33777-77-4; **19,** 19679-61-9; **23,** 33777-79-6; **26,** 33777-82-1.

δ 1.26 (3 H, d, J = 7.5 Hz, C_2CH_3), 4.81 (1 H, q, J = 7.5 Hz, C_2 H), 5.68 (1 H, dt, J = 7.5, 7.5, and 1.5 Hz, C_7 H), 6.40 (1 H, dd, J = 10.0 and 1.5 Hz, C_9 H), 6.66 (1 H, bt, J = 10.0 and 7.5 Hz, C_8 H), 7.23 (1 H, dd, J = 7.5 and 1.0 Hz, C_6 H), 7.2–7.4 (3 H, m, meta, meta′, and para protons of C_3 phenyl), and 7.7–7.9 (2 H, m, ortho and ortho′ protons of C_3 phenyl). Compared with the dihydro isomer **20,** the largely shifted signals to lower region and the disappearances of both a 9a and an amino proton signal were observed in the NMR spectrum of compound **21,** which corresponds clearly to the change from 1,9a-dihydro-2*H*-pyridotriazine to its dehydro 2*H* isomer as seen in our earlier work.[10] This structural assignment was also supported by the dehydrogenation of compound **20,** in which 2*H*-pyridotriazine **21** was obtained in 15% yield.

$$\mathbf{20} \xrightarrow[\text{in benzene}]{\text{palladium on carbon (5\%)}} \mathbf{21}$$

This reaction, though yields are generally lower than those of the reactions using isolated 2-phenylazirine, has a high utility because the possibility of its extension from stable to fleeting or nonisolable azirines is realized.

Experimental Section[11]

Materials. 1-Aminopyridinium salts **1–4** were prepared by Gösl's[12] and Tamura's methods[13] and quinolinium *N*-imine dimer **30** was obtained by alkaline treatment of salt **3.**[14] Dimethylhydrazone methiodides **5, 10, 13, 16, 19, 23,** and **26** were prepared by the reactions of acetophenone, *p*-methyl-, *p*-chloroacetophenone, 2-acenaphthone, propio-, *n*-butyrophenone, and benzyl phenyl ketone with *N,N*-dimethylhydrazine, followed by the quaternizations of the resulting dimethylhydrazones with methyl iodide.[9]

Preparations of 2*H*-Pyridotriazine Derivatives. Method A. An equimolar mixture (2 mmol) of 1-aminopyridinium salt and dimethylhydrazone methiodide was treated with potassium *tert*-butoxide (4 mmol) in tetrahydrofuran (50 mL) at room temperature for 1 day and then the reaction mixture was filtered to remove the insoluble substances. The filtrate was concentrated under reduced pressure and the residual oil was separated by column chromatography (alumina) using *n*-hexane at first and then ether as an eluent. Recrystallizations of crude products from *n*-hexane or ether–*n*-hexane gave pale yellow to yellow needles of 1,9a-dihydro-2*H*-pyrido[1,2-*b*]-*as*-triazines **6–9, 11, 12, 14, 15, 17,** and **18.**

Method B. A similar reaction mixture was allowed to react in tetrahydrofuran at the reflux temperature for 10–20 min in the reactions of salts **1** and **2** with methiodides **19, 23,** and **26,** or for 60 min in that of salt **3** with methiodides **26.** Usual workup gave the corresponding dihydropyridotriazines **20, 22, 24, 25,** and **27–29.** Dehydro compound **21** was also obtained in 30% yield for only one time during our several runs of the reaction of salt **1** with methiodide **19.** When the reactions of salts **1** and **2** with methiodides **19, 23,** and **26** were carried out for a prolonged reflux time (50–60 min), decreased yields of dihydropyridotriazines **20, 22, 24, 25, 27,** and **28** were observed.

These results and some properties of these pyridotriazine derivatives are summarized in Table II.

Reaction of Quinolinium *N*-Imine Dimer with Methiodide 26. A mixture of quinolinium *N*-imine dimer **30** (1 mmol) and methiodide **26** (2 mmol) was heated under reflux in tetrahydrofuran (50 mL) for 60 min in the presence of potassium *tert*-butoxide (2 mmol). Similar separation of the reaction mixture gave dihydropyridotriazine **29** in 38% yield.

Dehydrogenation of Dihydropyridotriazine 20. A benzene solution (50 mL) of dihydropyridotriazine **20** (170 mg) was stirred with palladium on carbon (5%, 1.0 g) at room temperature until the material disappeared (by TLC). The resulting mixture was then filtered and the filtrate was concentrated under reduced pressure. Usual separation of the residual oil gave 2-methyl-3-phenyl-2*H*-pyrido[1,2-*b*]-*as*-triazine (**21,** 25 mg, 15%) as a yellow oil. The IR spectrum and the melting point (its picrate, 179–181 °C) of this product were in good accord with those of compound **21** obtained above.

Registry No.—**21** picrate, 62154-58-9.

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Andalusol, a New Diterpenoid from a *Sideritis arborescens* Salzm. Subspecie. Chemical and X-Ray Structure Determination[1]

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Continuing our studies[2] on diterpenoids from a subspecie of *Sideritis arborescens* Salzm. (family Labiatae) we have now isolated a new compound, andalusol (**1**, $C_{20}H_{34}O_3$), the UV spectrum of which showed characteristic absorption (λ_{max} 224 nm, ϵ 11 000) for a monosubstituted conjugated diene grouping.[3] Treatment of compound **1** with acetic anhydride in pyridine solution gave the diacetate **2** plus a minor triacetyl derivative (**3**), thus establishing the hydroxylic nature of the three oxygen atoms of the molecule of andalusol. The ^1H NMR spectrum of **3** showed signals for an exocyclic methylene (δ 4.98, 2 H, broad singlet) and a vinyl group (δ_X 6.34, 1 H, quartet, and δ_A, δ_B 5.00–5.54, 2 H, multiplet), responsible for the UV diene absorption.

Hydroxylation of the diacetate **2** with osmium tetroxide gave a product which without further characterization was treated with HIO_4 to yield the lactone **4**.

With the preceding information a single-crystal x-ray determination of the structure of **4** was undertaken in order to establish the structure and relative stereochemistry of andalusol. A computer-generated drawing of the final x-ray model is shown in Figure 1. This model shows that the hydroxyl groups in andalusol are at C-6 (eq), C-8 (eq), and C-18 on a labdane skeleton. The lactone ring presents approximately an envelope conformation, being C-8, C-11, and C-9 at −0.12, 0.08, and 0.70 Å, respectively, out of the plane defined by C-12, C-13, O-25, and O-26. This envelope conformation is related to the special geometry displayed by the planar group: C-11–C-12 = 1.50, C-12–C-13 = 1.49, C-13–O-26 = 1.19, C-13–O-25 = 1.33, O-25–C-8 = 1.48 Å, C-11–C-12–C-13 = 119.8, C-12–C-13–O-26 = 121.7, C-12–C-13–O-25 = 119.7, O-25–C-13–O-26 = 118.6, C-13–O-25–C-8 = 122.2°. Both acetyl groups are coplanar with the carbon atoms at which they are bonded (C-6, C-18), the carbonyl oxygen atoms being at the cis positions. Electronic repulsion between all three methyl groups causes a bending effect on the main plane of the molecule. Distances between these groups follow: C-19–C-20 = 3.33 and C-17–C-20 = 3.24 Å. (For most details on x-ray structure determination see Experimental Section.)

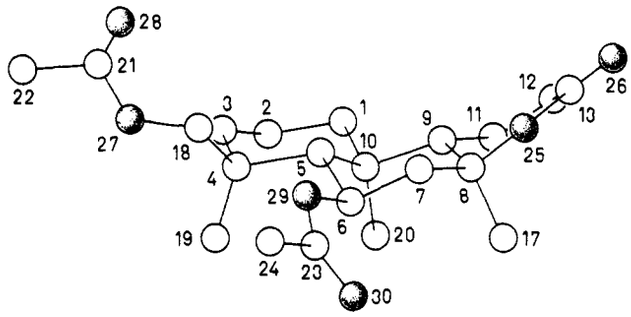
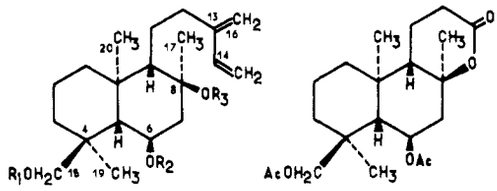


Figure 1. Computer-generated perspective drawing of *ent*-6 α,18-diacetoxy-14,15,16-trinorlabdan-13,8α-olide (**4**).

The absolute stereochemistry of the diterpenoid was established as follows. Treatment of compound **1** with benzoyl chloride in pyridine solution under controlled conditions yielded the monobenzoate **5**. Horeau's method[4] of partial resolution applied to product **5** afforded (+)-α-phenylbutyric acid, defining as 6*R* the absolute configuration of this center. On the other hand, application of Brewster's "benzoate rule"[5] to compounds **5** and **6** confirmed the above assignation.

Therefore andalusol is *ent*-13(16),14-labdadiene-6α,8α,18-triol (**1**).



1, $R_1 = R_2 = R_3 = H$
2, $R_1 = R_2 = Ac$; $R_3 = H$
3, $R_1 = R_2 = R_3 = Ac$
5, $R_1 = COPh$; $R_2 = R_3 = H$
6, $R_1 = R_2 = COPh$; $R_3 = H$

4

Experimental Section

All melting points were determined in a Kofler apparatus and are uncorrected. The optical rotations were measured with a Perkin-Elmer 141 polarimeter with 1-dm cells; the UV spectra were recorded on a Perkin-Elmer 402 spectrophotometer and the IR spectra on a Perkin-Elmer 257 spectrometer. The ^1H NMR spectra were obtained on a 60-MHz Perkin-Elmer R-12 or a 100-MHz Varian XL-100 apparatus with Me_4Si as an internal standard. The mass spectra were determined on an Hitachi Perkin-Elmer RMU 6MG apparatus. Elemental analyses were carried out in this laboratory with the help of an automatic analyzer.

Isolation of Andalusol (1). Dried and finely powdered *S. arborescens* Salzm. subspecie plants (5 kg), collected near Barbate (Cádiz), were extracted with light petroleum (16 L) in a Soxhlet apparatus during 120 h. The extract was concentrated under vacuum to 2 L and repeatedly extracted with 90% aqueous methanol (6 × 200 mL). The methanolic extracts were concentrated to 0.5 L, diluted with water (3 L), and extracted with chloroform (6 × 200 mL). The chloroform extracts were dried, filtered, and concentrated under vacuum to leave a residue (52 g) which was chromatographed on an Al_2O_3 (1.5 kg) (grade III) column with C_6H_6–EtOAc (19:1) as eluent, yielding the following compounds in order of elution: siderol[6] (320 mg), barbatol[2] (136 mg), and andalusol **1** (7.3 g) [mp 167–170 °C (acetone–*n*-hexane); $[\alpha]^{20}D$ −38.2° (*c* 0.69, EtOH); UV (EtOH) λ_{max} 224 nm (ϵ 11 000); IR (KBr) 3270, 3200, 3090, 3020, 1640, 1600, 1047, 920, 895 cm^{-1}; mass spectrum M^+ *m/e* 322]. Anal. Calcd for $C_{20}H_{34}O_3$: C, 74.49; H, 10.63. Found: C, 74.17; H, 10.51.

Acetylation of 1. Compounds 2 and 3. Acetic anhydride (5 mL) was added to a solution of **1** (300 mg) in pyridine (2.5 mL) and the mixture placed for 24 h at room temperature, poured into ice–water, and extracted with chloroform. Vacuum distillation of the solvent left