Jeolco Model C-60 spectrometer with Me_4Si as internal standard. Microanalyses were performed by Chemical Analytical Services, University of California, Berkeley, Calif. Commercial HMPT was distilled before use, bp 120–122° (21 mm). Other compounds not described below were commercially available and were used without further purification.

Benzoins (1). Conventional procedures[7] were employed for the synthesis of the benzoins listed in Table I as well as 4-methoxybenzoin (4). 4,4′-Dichlorobenzoin could not be crystallized and was oxidized with nitric acid to the corresponding benzil.[8] Reduction of this benzil with sodium dithionite[9] afforded the expected 4,4′-dichlorobenzoin.

2,3,5,6-Tetraarylpyridines (3). General Procedure. The benzoin (0.05 mol) was refluxed with 35 ml of HMPT until the pot temperature just exceeded 245° (15–60 min as shown in Table I). After cooling, the clear, dark orange reaction mixture was poured into 150 ml of cold water and the resulting mixture was saturated with sodium chloride. This mixture was extracted three times with benzene. The benzene solution was washed twice with brine, dried (anhydrous sodium sulfate), and reduced in volume on a rotary evaporator, leaving a residue of oil and crystals. Ethanol (100 ml) was added to the residue and the solution was heated briefly on a steam bath. Crystallization followed upon cooling. The product was recrystallized from ethanol–benzene. For example, benzoin (**1a**, 10.6 g, 0.05 mol) treated as above affords 15.05 g of crude reaction product as a dark orange oil. The ir spectrum (film) of the oil shows bands at 5.96 (benzoin C=O), 7.04 (tetraphenylpyridine), and 7.6–8.0 μ (organophosphorus P=O). Addition of ethanol at room temperature followed by standing for several hours afforded 1.73 g (18%) of **3a** as a light yellow solid. Recrystallization from ethanol–benzene gave white product of the reported melting point.

Reaction of 2-Hydroxycyclohexanone with HMPT. 2-Hydroxycyclohexanone (0.05 mol) was refluxed with 35 ml of HMPT. Ten minutes after the onset of reflux, a volatile material had formed which was distilled from the reaction vessel. Water (200 ml) was added to the reaction vessel and distillation was continued until no more organic material steam distilled. The distillate was extracted with ether, the ethereal solution was dried (anhydrous sodium sulfate), and the ether was evaporated, affording 2-dimethylaminocyclohexanone in 59% yield. The ir and NMR spectra of the product were identical with those of an authentic sample. The picrate melted at 110–113° (lit.[10] mp 113–114°).

Reaction of 4-Methoxybenzoin (4) with HMPT. 4-Methoxybenzoin (**4**) was refluxed with HMPT and worked up in the same manner as described above. The product, after two recrystallizations from ethanol–benzene, had mp 178–194°. The ir and NMR spectra of the product were virtually identical with those of authentic **5**.

Anal. Calcd for $C_{31}H_{25}O_2N_2$: C, 84.0; H, 5.6; N, 3.1. Found: C, 83.7; H, 5.7; N, 3.1.

The product was chromatographed on neutral alumina. Petroleum ether–benzene (3:7) as eluent gave fractions A and B, and petroleum ether–benzene (1:4) gave fraction C. Small amounts of intermediate materials having depressed melting points were also obtained.

1,3-Di(*p*-methoxybenzoyl)-1,3-diphenylpropane (9). This compound was prepared by the method used by Carpenter[3] for an analogous compound. Thus, benzyl *p*-methoxyphenyl ketone[11] (**8**) was treated with aqueous formaldehyde and potassium hydroxide in ethanol at room temperature to give crude **9** in 63% yield. The product was recrystallized twice from ethanol: mp 150–151°; ir (film) 5.99 and 6.26 μ.

Anal. Calcd for $C_{31}H_{28}O_4$: C, 80.2; H, 6.0. Found: C, 80.3; H, 6.1.

2,6-Di(*p*-methoxyphenyl)-3,5-diphenylpyridine (5). This compound was prepared by the method used by Carpenter[3] for an analogous compound. Thus, **9** (1.0 g) and hydroxylamine hydrochloride (0.35 g) were dissolved in 40 ml of absolute ethanol and heated in a closed tube at 150° for 21 hr. Upon cooling, the mixture yielded 0.29 g of crude **5** which was recrystallized from benzene–ethanol: mp 203–204°; ir (film) 6.23 and 6.35 μ; NMR (CCl_4) δ 4.04 (s, 6, CH_3O), 7.02 (d, 4, J = 9 Hz), 7.61 (m, 11), 7.86 (d, 4, J = 9 Hz).

Anal. Calcd for $C_{31}H_{25}O_2N_2$: C, 84.0; H, 5.6; N, 3.1. Found: C, 84.0; H, 5.7; N, 3.1.

Registry No.—**1a**, 119-53-9; **1b**, 1218-89-9; **1c**, 119-52-8; **1d**, 53458-15-4; **1e**, 4254-20-0; **1f**, 5623-25-6; **3a**, 24301-97-1; **3b**, 54932-37-5; **3c**, 54932-38-6; **3d**, 54932-39-7; **3e**, 54932-40-0; **3f**, 54932-41-1; **4**, 4254-17-5; **5**, 54932-42-2; **8**, 1023-17-2; **9**, 54932-43-3; 2-hydroxycyclohexanone, 533-60-8; hexamethylphosphoric triamide, 680-31-9; 2-dimethylaminocyclohexanone, 6970-60-1; 2-dimethylaminocyclohexanone piciate, 54932-44-4.

References and Notes

(1) Previous papers in this series on reactions in HMPT are (a) R. S. Monson and A. Baraze, *Tetrahedron*, in press; (b) R. S. Monson and B. M. Broline, *Can. J. Chem.*, **51**, 942 (1973), and references cited therein.
(2) R. S. Monson and D. N. Priest, *Chem. Commun.*, 1018 (1971).
(3) H. Carpenter, *Justus Liebigs Ann. Chem.*, **302**, 223 (1898).
(4) (a) D. Davidson, M. Weiss, and M. Jelling, *J. Org. Chem.*, **2**, 328 (1937). (b) cf. ref 1a and 6c; see also G. R. Newkome and D. L. Fishel, *J. Org. Chem.*, **37**, 1329 (1972).
(5) V. J. Traynelis and R. H. Ode, *J. Org. Chem.*, **35**, 2207 (1970).
(6) (a) E. B. Pederson and S.-O. Lawesson, *Tetrahedron*, **30**, 875 (1974); (b) S. Arimatsu, R. Yamaguchi, and M. Kawanisi, *Bull. Chem. Soc. Jpn.*, **47**, 1553 (1974); (c) R. S. Monson, D. N. Priest, and J. C. Ullrey, *Tetrahedron Lett.*, 929 (1972).
(7) W. S. Ide and J. S. Buck, *Org. React.*, **4**, 269 (1948).
(8) R. Adams and C. S. Marvel, *Org. Syn.*, **1**, 25 (1921).
(9) T. van Es and O. G. Backegerg, *J. Chem. Soc.*, 1371 (1963).
(10) M. Mousserson, J. Jullien, and Y. Jolchine, *Bull. Soc. Chim. Fr.*, 757 (1952).
(11) J. S. Buck and W. S. Ide, *J. Am. Chem. Soc.*, **54**, 3012 (1932).

Identification of C-22 Epimers in Steroids by Carbon-13 Nuclear Magnetic Resonance Spectroscopy[1a]

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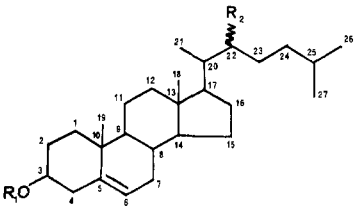
A recent communication reported a ^1H NMR analytical method to identify (20*R*,22*R*)- and (20*R*,22*S*)-dihydroxy steroidal isomers.[2] However, the same study indicated that ^1H NMR spectroscopy failed to differentiate (22*R*)- and (22*S*)-hydroxy cholesterols.[2]

We wish to report the utility of ^{13}C NMR in this case and provide an easy method to determine the absolute configuration at C-22 of steroids substituted at this center and having the cholestane side chain.

Noise and single frequency decoupled ^{13}C NMR spectra were recorded for the (22*R*)- and (22*S*)-substituted cholesterol derivatives[3,4] **2–7** and for cholesteryl benzoate **1**. Application of chemical shift rules[5] as well as previous analysis of the ^{13}C NMR spectrum of cholesterol[6] led to the signal assignments shown in Table I.

Compared to the respective resonance positions in the spectrum of **1**, C-22, C-20, and C-23 are deshielded while C-17, C-21, and C-24 are shielded in all the compounds studied. These chemical shift variations are easily understood from the qualitative point of view as a consequence of α, β, and γ effects.[5,7] However, inspection of Table I indicates that the magnitude of the β effects is totally different for the 22*S* and 22*R* compounds. Considering the spectra of **2, 3, 5,** and **6,** the average β effect on C-20 is 4.1 and 6.8 ppm in the *S* and *R* series, respectively. On the chemical shift of C-23 an even more pronounced difference is observed between the two series. The β effect in this case is



1 R_1=COC_6H_5 ; R_2= H
2 R_1=COC_6H_5 ; R_2=OH (22S)
3 R_1= H ; R_2=NH_2(22S)
4 R_1=COC_6H_5 ; R_2=N_3 (22S)
5 R_1=COC_6H_5 ; R_2=OH (22R)
6 R_1=H ; R_2=NH_2(22R)
7 R_1=COC_6H_5 ; R_2=N_3 (22R)

Table I
^{13}C Chemical Shift [a]

Compd	C-17	C-18	C-20	C-21	C-22	C-23	C-24	C-25	C-26	C-27
1	56.3	11.9	35.8	18.8	36.3	23.9	39.6	28.0	22.6	22.8
2	52.6	11.8	40.3	11.6	73.8	33.3	35.7	27.8	22.6	22.6
3	52.9	11.8	39.5	11.3	52.9	34.2	36.2	27.6	22.6	22.6
4	53.2	11.8	40.5	12.7	66.5	30.5	36.1	28.1	22.6	22.6
5	53.2	11.9	42.6	12.5	74.0	27.5	36.1	27.9	22.5	22.9
6	53.3	11.8	42.7	12.3	53.3	27.6	36.6	28.2	22.3	23.0
7	52.8	11.8	40.1	13.5	66.9	25.4	36.7	28.0	22.4	22.9

[a] ^{13}C NMR spectra were recorded (at room temperature) in 0.3 *M* $CDCl_3$ solution on a Bruker HX-90E Fourier transform spectrometer at 22.63 MHz. Chemical shifts (±0.1 ppm) are given with respect to Me_4Si used as an internal standard. Resonance positions of the following carbons were only slightly affected by the structural changes of the side chain: C-1 (δ 38.2 ± 0.1); C-2 (δ 28.0 ± 0.2); C-3 (δ 74.5 ± 0.1); C-4 (δ 37.0 ± 0.1); C-5 (δ 139.7 ± 0.2); C-6 (δ 122.6 ± 0.1); C-7 (δ 31.9 ± 0.1); C-8 (δ 31.9 ± 0.1); C-9 (δ 50.0 ± 0.1); C-10 (δ 36.6 ± 0.1); C-11 (δ 21.1 ± 0.1); C-12 (δ 39.8 ± 0.1); C-13 (δ 42.3 ± 0.2); C-14 (δ 56.4 ± 0.3); C-15 (δ 24.2 ± 0.2); C-16 (δ 28.1 ± 0.2); C-19 (δ 19.4 ± 0.1); CO (δ 165.9 ± 0.1); substituted aromatic carbon (δ 132.6 ± 0.1) para carbon (δ 130.8 ± 0.1); specific assignment for the ortho and meta carbons cannot be made (δ 129.5 ± 0.1 and 128.2 ± 0.1). The (22*S*)- and (22*R*)-amino compounds **3** and **6** were examined with a free hydroxyl group at C-3. Chemical shifts for these two compounds from C-1 to C-16 and C-19 were identical with those published previously.[6] In the spectrum of (22*S*)-hydroxycholesterol-*20,22,23,23-d*$_4$ the 40.3-, 73.8-, and 33.3-ppm signals of **2** were not detectable, while the A- and B-ring carbons showed resonances which were identical with those observed in the spectra of **3** and **6**.

greater for the *S* than for the *R* compounds (average value 9.8 and 3.6 ppm). Small differences are also observed for the γ carbons C-21 and C-24 of the respective isomers; these signals appear slightly downfield in the *R* compared to the *S* compounds.[11] Similar stereochemical effects on the chemical shifts of the aliphatic β- and γ-carbon resonances have been reported in C-15 epimeric prostaglandins.[10]

The interpretation of the magnitude of the observed effects is not easy; however, these results seem to be structurally diagnostic and may be helpful for stereochemical assignments of C-22 epimers in steroids.

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Registry No.—**1**, 604-32-0; **2**, 17954-95-9; **3**, 50921-62-5; **4**, 50921-61-4; **5**, 17954-94-8; **6**, 50921-65-8; **7**, 50921-64-7.

References and Notes

(1) (a) Résonance Magnétique Nucléaire du ^{13}C de Produits Naturels et Apparentés. XXII. For Part XVIII, see K. Tori, T. Komeno, M. Sangaré, B. Septe, B. Delpech, A. Ahond, and G. Lukacs, *Tetrahedron Lett.*, 1157 (1974). (b) Institut de Chimie des Substances Naturelles du Centre National de la Recherche Scientifique. (c) Worcester Foundation for Experimental Biology.
(2) T. A. Wittstruck, *J. Org. Chem.*, **38**, 1426 (1973). The (20*R*,22*R*)- and (20*R*,22*S*)-dihydroxy steroids described in the cited paper were mistakenly called 20*S*,22*R* and 20*S*,22*S* isomers.
(3) E. P. Burrows, G. H. Hornby, and E. Caspi, *J. Org. Chem.*, **34**, 103 (1969).
(4) Q. Khuong-Huu, Y. Letourneux, M. Gut, and R. Goutarel, *J. Org. Chem.*, **39**, 1065 (1974).
(5) J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, N.Y., 1972.
(6) (a) H. J. Reich, M. Jautelat, M. T. Messe, F. J. Weigert, and J. D. Roberts, *J. Am. Chem. Soc.*, **91**, 7445 (1969); (b) H. Eggert and C. Djerassi, *J. Org. Chem.*, **38**, 3788 (1973).
(7) In azido compounds the β nitrogen of the azide has a normal γ effect: A. Pancrazi, I. Kaboré, Q. Khuong-Huu, and G. Lukacs, unpublished results. In view of this observation on many model compounds, C-20 and C-23 of **7** are more shielded than the same carbons of **5** and **6**. While the C-23 shift of **4** is easy to interpret, the C-20 resonance of **4** is not understood at the present time.
(8) G. Lukacs and C. R. Bennett, *Bull. Soc. Chim. Fr.*, 3996 (1972).
(9) (a) H. Hikino and Y. Hikino, *Prog. Chem. Org. Nat. Prod.*, **28**, 256 (1970); (b) K. Nakanishi, *Pure Appl. Chem.*, **25**, 167 (1971).
(10) G. F. Cooper and J. E. Fried, *Proc. Natl. Acad. Sci. U.S.*, **70**, 1579 (1973).
(11) Reported chemical shift values in pyridine solution for C-20 (41.9 ppm) and C-23 (25.3 ppm) of α-ecdysone[8] are in agreement with the known *R* configuration[9] at C-22 of the hydroxyl group of this natural product. As a result of the γ effect on C-23 of the C-25 hydroxyl group of α-ecdysone, the C-23 shift of this compound is expected to be shielded by about 3 ppm[5] with respect to the resonance position of C-23 in **5**.