solution was extracted with dichloromethane. The organic layer was washed with brine, dried ($MgSO_4$), and evaporated. The residue was purified by chromatography on neutral alumina (elution with hexane–ether). In the case of **4b**, the hydrolysis was carried out by using aqueous HCl (2 M, 0.3 mL) instead of aqueous H_2SO_4. The structures of **18a** (mp 95–97 °C),[21] **18c**,[22] **18d** (mp 81–84 °C),[23] **18e**,[24] **19a** (mp 57–58 °C),[25] and **19b**[26] were identified by comparison of their IR and NMR spectra with the reported ones. **18b**: pale yellow crystals, mp 55–56 °C; IR (KBr) 1740 cm^{-1}; NMR δ 1.6–1.9 (4 H, m), 2.0–2.5 (4 H, m), 4.56 (2 H, br s); MS, m/e (relative intensity) 138 (28), 109 (100), 81 (80). Anal. Calcd for $C_8H_{10}O_2$: C, 69.55; H, 7.29. Found: 69.40; H, 6.99.

Perillene (24). **4e** (116 mg, 0.59 mmol) was desulfurized by Raney Ni in a similar manner to that described for the synthesis of **13a** to give **24** (71 mg, 0.47 mmol, 80%). The NMR and MS spectra were in agreement with those reported.[13]

Rosefuran (25). 3-Methyl-2-(3-methyl-2-butenyl)furan (**26**) (165 mg, 0.84 mmol, 87%) was obtained from **4c** (124 mg, 0.97 mmol) in a similar manner to that described for **14a**; a colorless oil, bp 50 °C (0.2 mmHg); NMR δ 1.70 (6 H, br s), 1.89 (3 H, s), 2.20 (3 H, s), 3.20 (2 H, br d), 5.21 (1 H, m); MS, m/e (relative intensity) 196 (62), 181 (63), 128 (59), 41 (100). **26** (107 mg, 0.55 mmol) was desulfurized in a similar manner to that described for the synthesis of **13a** to give **25** (56 mg, 0.37 mmol, 68%). The NMR spectrum was in agreement with the reported one.[14]

Registry No. **1a**, 13636-88-9; **1b**, 17649-90-0; **1c**, 17649-86-4; **1d**, 4254-65-3; **1e**, 84735-54-6; **1f**, 57663-21-5; **1g**, 3275-23-8; **1h**, 91003-02-0; **2**, 6814-64-8; **3a**, 84735-55-7; **3b**, 84735-56-8; **3c**, 84735-58-0; **3d**, 91632-63-2; **3e**, 84735-57-9; **3f**, 91632-64-3; **3g**, 91632-65-4; **4a**, 84735-60-4; **4b**, 91632-66-5; **4c**, 84735-62-6; **4d**, 91632-67-6; **4e**, 84735-64-8; **4f**, 91632-68-7; **4h**, 91632-70-1; (*E*)-**5**, 84735-59-1; **7**, 91632-69-8; **13a**, 13679-41-9; **13b**, 91632-72-3; **14a**, 84735-61-5; **14b**, 91632-71-2; **15a**, 50552-26-6; **16a**, 21433-91-0; **17b**, 91632-73-4; **18a**, 1575-47-9; **18b**, 66309-76-0; **18c**, 6124-79-4; **18d**, 57200-23-4; **18e**, 61315-75-1; **19a**, 74528-46-4; **19b**, 68965-57-1; **24**, 539-52-6; **25**, 15186-51-3; **26**, 84735-63-7; prenyl bromide, 870-63-3.

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Syn–Anti Isomerism in the Opiate Hydrazones and Azines Derived from Naloxone, Naltrexone, and Oxymorphone

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Very recently we demonstrated by a ^{13}C NMR study that the long acting opiate drugs naloxone hydrazone, naltrexone hydrazone, and oxymorphone hydrazone exist as mixtures of their anti and syn isomers (*Life Sci., Suppl. 1* **1983**, *33*, 419–422). That finding indicated that the corresponding opiate azines, which are formed from the above hydrazones, and which are much longer acting than these hydrazones, may exist theoretically as three possible isomers—anti–anti, anti–syn, and syn–syn. In this study samples of naloxone azine, naltrexone azine, and oxymorphone azine have been analyzed by ^{13}C NMR and high-resolution ^1H NMR. The presence of all three isomers has been observed.

Introduction

Long lasting opiate antagonist naloxazone (I), which is the hydrazone of naloxone, drew considerable attention because of its ability to inhibit selectively the high affinity, or μ_1, binding sites and to block opiate analgesia with little effect on other classes of binding sites or on opiate-induced lethality.[2] Similarly, the hydrazone derivatives of naltrexone (II) and oxymorphone (III) are shown to be long acting opiate antagonist and agonist, respectively, both in vivo and in vitro[3] (Figure 1). The mechanism through which these hydrazones exert their long acting effects remains unknown. A possibility that covalent binding of these hydrazones to the opiate receptor sites occurs was considered.[3] Also, it was suggested that the long lasting action of these hydrazones may be due to the presence of the corresponding azines in the preparations of hydrazones.[2] These azines were found to irreversibly block opiate binding in vitro 20- to 40-fold more potently than the corresponding hydrazones.[2,4]

The mechanism through which the opiate azines exert their ultra long lasting effects has not been elucidated so far. Originally it was suggested that since the azines are dimeric opiates they may simultaneously occupy two binding sites at the receptor.[2] Recently, it was suggested that an irreversible chemical reaction between the receptor and the azine might be going on at the azine functional group.[5] In either mechanism, the knowledge of the exact stereochemistry of the azine opiates is of great importance for a proper mapping of the opiate receptor.

In a recent preliminary communication we have demonstrated by a ^{13}C NMR study that the long acting opiate hydrazones naloxazone (I), naltrexazone (II), and oxymorphazone (III) exist as mixtures of their anti and syn isomers[6] (Scheme I). The less crowded anti isomer was found to be the major product in all cases (Table I). No equilibration of the syn and anti isomers was observed

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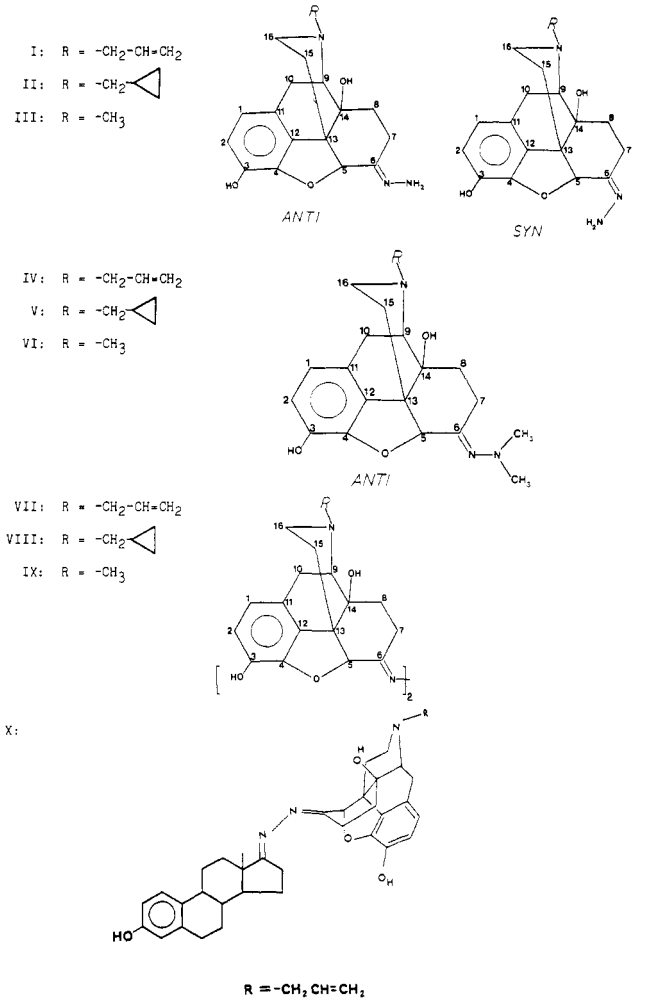


Figure 1. Structures of the compounds studied.

during the NMR experiment or on a prolonged standing. The finding that the opiate hydrazones are mixtures of their anti and syn isomers indicated that the corresponding opiate azines, which are formed from the hydrazones, may exist theoretically as three possible isomers—anti–anti, anti–syn, and syn–syn (Scheme II).[7-9] In this study samples of naloxone azine (VII), naltrexone azine (VIII), and oxymorphone azine (IX) have been analyzed by ^{13}C NMR and high-resolution ^1H NMR for the presence of these isomers.[11] The stereochemistry of the mixed estrone–naloxone azine (X)[12] was also studied.

Experimental Section

Melting points (uncorrected) were determined on a Thomas-Hoover capillary melting point apparatus. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN. The ^{13}C and ^1H NMR spectra were taken on a Nicolet 200 instrument (200 MHz with respect to ^1H) and on an IBM-Bruker WM-400 instrument (400 MHz with respect to ^1H). ^1H NMR spectra were also taken on a Perkin-Elmer R-32 (90 MHz) instrument. All the samples were run in $CDCl_3$ solution with Me_4Si as the internal standard, unless otherwise noted. Some spectra were also taken on a Nicolet 360 instrument by Dr. Robert B. Clarkson, from the NSF Regional NMR Center at the University of Illinois (CHE-79-16100). Thanks are expressed to Dr. Clarkson for taking these high-resolution spectra for us.

The IR spectra were recorded on a Perkin-Elmer 297 spectrophotometer. The mass spectra were taken on the LKB-9000 by Peter Jahnke, and MS CH-5 by Dr. Richard M. Milberg, to whom thanks are expressed.

The preparative TLC was done on E. Merck plates (precoated PLC plates, silica gel 60F-254, layer thickness 2 mm, catalogue no. 5766). The TLC was done on E. Merck aluminum supported sheets (precoated TLC sheets, silica gel 60F-254, layer thickness 0.2 mm, catalogue no. 5539). The eluent used was $CHCl_3$:MeOH:concentrated NH_4OH 132:12:0.9.[2] For steroids, benzene:EtOAc 7:3 was also used. The spots were observed in UV, and in the case of steroids the plate was also sprayed with 50% H_2SO_4 and heated to over 100 °C.

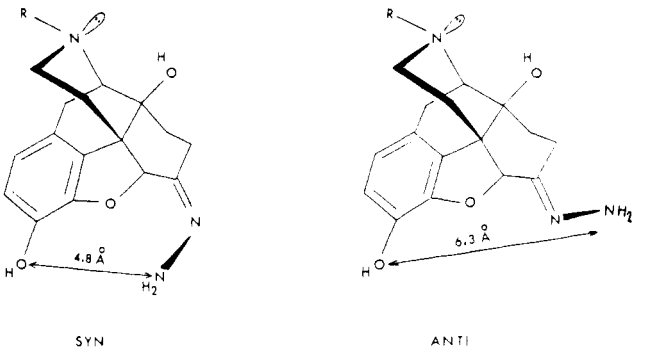
Syntheses of the Opiate Hydrazones and Azines (I–IX). The known hydrazones (I–III) were prepared as described in ref 3. The new hydrazones (IV–VI) were prepared in an analogous manner by using 1,1-dimethylhydrazine (Aldrich) instead of hydrazine. The ^{13}C NMR spectra of I–VI were given in our preliminary communication[6] but are also given here for a comparison with the azines (Table II). In this paper we are giving

Table I. The Anti–Syn Composition of the Hydrazones Studied as Determined by ^{13}C NMR

compd	anti, %	syn, %
I, crude powder	77	23
II, crude powder	82	18
III, crude powder	82	18
III, mp 189–190 °C	70	30
II, 1:1 complex with EtOH	ca. 100	trace
IV, V, VI	ca. 100	trace
estrone hydrazone, mp > 270 °C[a]	100	
Δ4-androstene-3,17-dione dihydrazone		
crude[b]	100 C-17	
recrystalized material	85.5 C-3	14.5 C-3
pregnenolone 3-acetate 20-hydrazone,[c] mp 238–240 °C ($EtOH-CHCl_3$)	100	

[a] See Experimental Section. [b] Reported in ref 10; prepared by a treatment of Δ4-androstene-3,17-dione with an excess of hydrazine hydrate in EtOH. [c] Prepared by a treatment of pregnenolone acetate (formed by reacting pregnenolone (Searle) with Ac_2O in pyridine) with an excess of hydrazine hydrate in EtOH.

Scheme I[a]



[a] Molecular structures of the syn and anti isomers of naloxozone (R = allyl) (I), naltrexazone (R = cyclopropylmethyl) (II), and oxymorphazone (R = methyl) (III). Observe different geometric dispositions of the NH_2 group of the syn and anti hydrazones (the distances are approximate based on Dreiding molecular models: the conformation of the ring C is uncertain, see discussion in the text).

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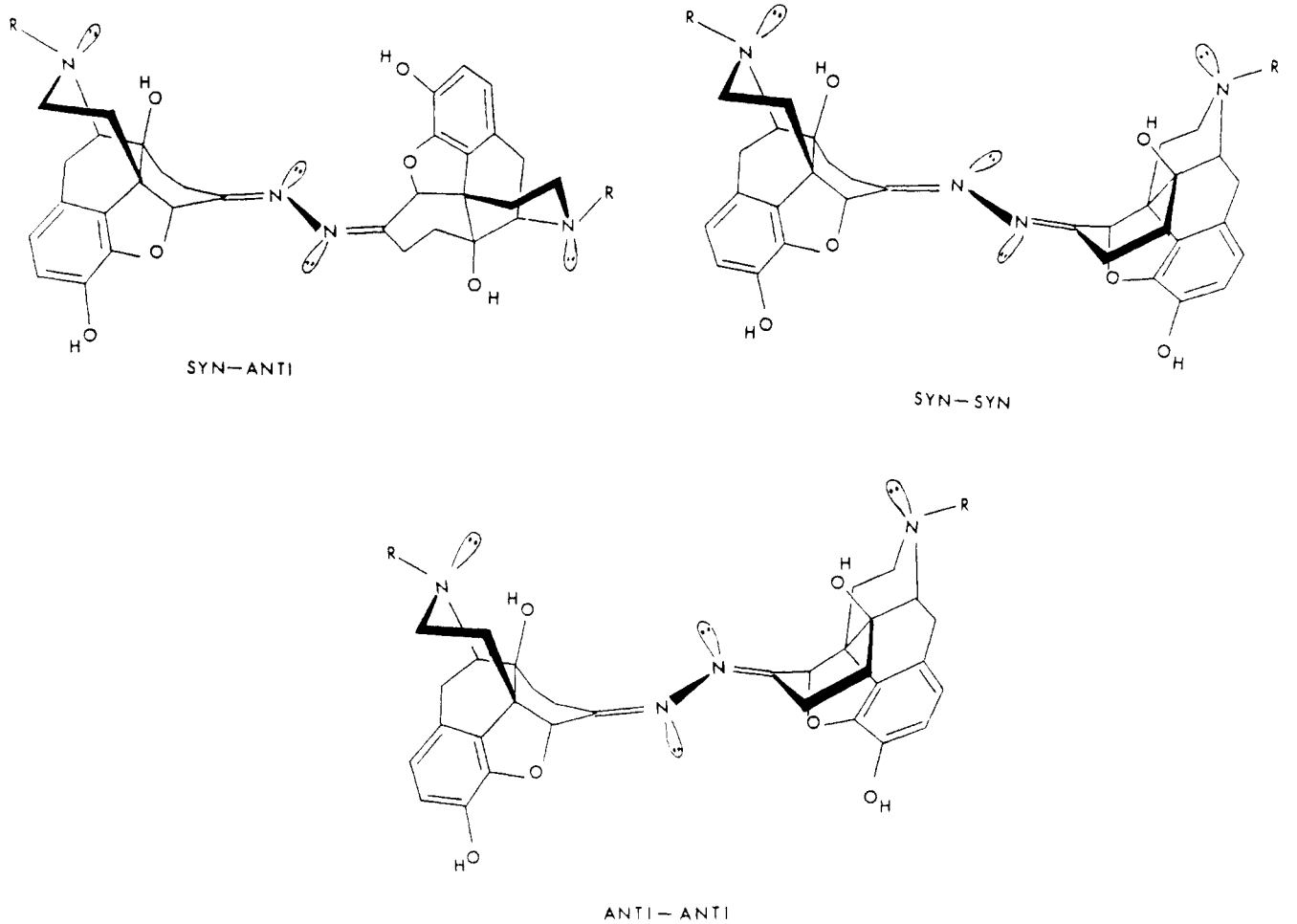
Scheme II[a]



[a] Molecular structures of the syn-anti, syn-syn, and anti-anti isomers of naloxone azine (R = allyl) (VII), naltrexone azine (R = cyclopropylmethyl) (VIII), and oxymorphone azine (R = methyl) (IX). Observe that in the syn-anti isomer the piperidine nitrogens of the two opioid units are on the opposite ("up" and "down") sides from each other, while in the other two isomers they are on the same ("up") side. All three isomers have limited conformational freedom with respect to rotation about the N-N bond of the azine linkage, since certain conformations are energetically unfavorable due to the clashing of the two opioid units. (On the basis of Dreiding molecular models, the conformation of the ring C is uncertain, see discussion in the text.)

also the ^{1}H NMR spectra (Table III) as well as some other spectral and physical data.

The azines VII–IX were prepared from the corresponding hydrazones I–III which were mixtures of ca. 80% of anti and 20% of syn isomers[6] according to the published procedure[2] or a slight modification of it. In ref 2 the opiate ketones (naloxone, naltrexone, and oxymorphone) were allowed to react with a $^1/_3$ molar amount of the corresponding hydrazones (I, II, and III, respectively). The azines thus formed, VII–IX, were separated by the preparative thick-layer chromatography. In a modified procedure, a 1:1 molar ratio of ketone to hydrazone was used. In some cases acid catalyst (HCl) was also used. The ^{13}C NMR spectra of VII–IX are given in Table II, and the ^{1}H NMR in Table III.

Synthesis of the Mixed Estrone–Naloxone Azine (X).[12] X was prepared by reacting naloxone free base with estrone hydrazone in a 1:1 molar ratio. Naloxone·HCl (Endo) was dissolved in water and poured into a separatory funnel containing dilute borax solution and $CHCl_3$. The mixture was extracted with $CHCl_3$ three times. The combined $CHCl_3$ extracts were dried and evaporated giving naloxone free base as a white crystalline solid in 100% yield. Estrone hydrazone was prepared and identified as described in ref 13. Estrone hydrazone crystallized out of the reaction mixture, mp >270 °C. Its ^{13}C NMR revealed only one, anti, isomer at C-17.

Estrone hydrazone (0.0757 g, 2.66×10^{-4} mol) was dissolved in 5 mL of boiling EtOH (100%). To this hot solution naloxone free base (0.0881 g, 2.69×10^{-4} mol) was added, and the mixture was briefly boiled and then left to stir at room temperature in the dark. The progress of the reaction was followed by TLC by using two different ways to detect spots: observing them under UV light and observing the color development after the TLC plate was sprayed with 50% H_2SO_4 and heated to over 100 °C. Naloxone shows up very strongly in the UV while estrone hydrazone shows up only very faintly. The product, which has higher R_f values than either naloxone or estrone hydrazone, shows up very strongly in the UV. By using the color development method, one can detect very easily both estrone hydrazone (red) and the product (orange), while naloxone does not show up at all. After only traces of naloxone and estrone hydrazone were detected by TLC, the reaction was quenched by pouring into ice. The white solid thus formed was filtered off and dried in a vacuum oven, giving 0.1303 g (82.3% yield) of X, mp >190 °C dec. X was recrystallized from $CHCl_3$ and gave a satisfactory C, H, N analysis. Its IR, ^{1}H NMR, and ^{13}C NMR were in agreement with the proposed structure. ^{13}C NMR revealed that the azine bond is configurationally pure, i.e., anti–anti. The MS (electron impact) did not give the parent peak as opposed to, e.g., the hydrazones studied (I–VI).

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Table II. ^{13}C NMR Chemical Shifts of the Opiate Hydrazones and Azines as Compared to the Parent Ketones

	naloxone series (R = $CH_2CH{=}CH_2$)				
C	I anti	I syn	IV anti	VII major isomer[a]	naloxone
1	119.17	119.52	119.20	119.41	119.81
2	117.99[b]	117.99[b]	117.72	118.29[b]	118.03
3	138.95	138.95	139.21	139.18	138.93
4	143.66	143.15	143.88	143.81	143.61
5	88.72	86.47	88.67	87.73	90.43
6	149.65	147.63	166.70	161.23	209.80
7	18.97	26.80	21.88	21.42[c]	36.10
8	27.83	29.01	29.75	29.65[d]	31.21
9	62.35	62.64	62.30	62.09	62.18
10	22.87	23.06	22.76	22.63[c]	22.70
11	124.04	124.29	124.04	123.92	124.01
12	130.42	130.42	130.18	129.64	129.01
13	47.68	48.02	48.91	49.51	50.94
14	70.18	70.18	70.19	70.27	70.63
15	31.63	31.07	30.97	30.39[d]	30.43
16	43.48	43.48	43.59	43.53	43.34
17	57.73	56.29	57.70	57.61	57.64
18	135.36	135.36	135.33	135.22	135.20
19	117.88[b]	117.88[b]	117.86	117.93[b]	118.03
NCH_3			47.11		

	naltrexone series (R = CH_2–$\overline{CHCH_2CH_2}$)				
C	II anti	II syn	V anti	VIII major isomer[a]	naltrexone
1	119.17	119.51	119.30	119.42	119.77
2	117.86	117.68	117.89	118.27, 117.72	117.94
3	138.83	138.83	139.41	139.25	138.90
4	143.61	143.12	143.68	143.95	143.59
5	88.79	86.55	88.27	88.06	90.46
6	149.80	147.75	167.61	161.05	209.90
7	18.97	26.89	22.24	21.44[c]	36.15
8	27.96	29.06	29.85	29.85[d]	31.29
9	62.11	62.35	62.08	62.11	61.94
10	22.77	22.61	22.62	22.71[c]	22.61
11	124.23	124.45	123.91	124.13	124.04
12	130.47	130.47	130.04	129.89	129.06
13	47.80	48.05	49.07	46.68	50.99
14	70.03	70.10	70.09	70.21	70.48
15	31.69	31.22	30.80	30.69[d]	30.57
16	43.78	43.78	43.95	43.90	43.60
17	59.27	59.27	59.20	59.27	59.19
18	9.40	9.40	9.41	9.41	9.37
19	4.03[b]	4.03[b]	4.01[b]	4.00[e]	4.01
20	3.71[b]	3.71[b]	3.72[b]	3.80[e]	3.78
NCH_3			47.11		

	oxymorphone series (R = CH_3)				
C	III anti	III syn	VI anti	IX major isomer[a]	oxymorphone[f]
1	119.17	119.53	119.22	119.48	119.81
2	117.93	117.76	117.73	118.53	117.96
3	138.87	138.87	139.22	139.42	139.10
4	143.66	143.16	143.83	143.68	143.67
5	88.86	86.59	88.54	87.68	90.43
6	149.39	147.40	166.85	162.18	209.51
7	18.91	26.79	21.95	21.69[b]	36.14
8	27.83	29.02	29.72	29.78[c]	31.28
9	64.73	64.94	64.92	64.51	64.56
10	22.11	21.94	22.14	21.92[b]	21.98
11	124.24	124.46	124.07	123.99	124.05
12	130.39	130.39	130.06	129.49	128.99
13	47.13	47.46	48.35	49.06	50.41
14	70.29	70.29	70.30	70.31	70.64
15	31.61	31.02	30.82	30.26[c]	30.48
16	45.36	45.36	45.48	45.20	45.28
17	42.85	42.77	42.79	42.72	42.72
NCH_3			47.09		

[a] Splitting of the peaks was observed. In VIII all the peaks were split, most into three peaks, but some into more than three. The latter could indicate the presence of various conformers. [b–e] The shifts with the same footnote may be interchanged. [f] $CDCl_3$ + acetone-d_6.

Table III. ^1H NMR Chemical Shifts (δ) for the H-5 of the Opiate Hydrazones and Azines Studied (I–IX) as Compared to Their Parent Ketones

	naloxone series (R = $CH_2CH{=}CH_2$)				
naloxone	I anti	I syn	IV anti	VII major	VII minor
4.78	4.95	5.29	4.88	4.96	5.23 4.93

	naltrexone series (R = –CH_2–$\overline{CHCH_2CH_2}$)				
naltrexone	II anti	II syn	V anti	VIII major	VIII minor
4.78	4.96	5.28	4.86	4.95	5.17 4.87

	oxymorphone series (R = CH_3)				
oxymorphone	III anti	III syn	VI anti	IX major	IX minor
4.68[a]	4.94[a]	5.26[a]	4.87[a]	4.93[a]	5.13[a] 4.62[a]
				4.87[b]	5.07[b] 4.56[b]

[a] In $CDCl_3$ + acetone-d_6. [b] In $CDCl_3$ + 2 drops of Me_2SO-d_6.

Results and Discussion

The analysis of the ^{13}C NMR spectra of the opiate azines revealed that none of the samples contained the corresponding ketones or hydrazones as evidenced by the absence of the C-6 peaks at ca. 210 ppm and ca. 150 ppm for the carbonyl and hydrazone carbons, respectively, as well as the absence of all other characteristic peaks of the corresponding ketones and hydrazones. A new peak for the C-6 of the azine group was observed at ca. 160 ppm. In all the spectra of the azines multiple peaks for carbons were observed which were assigned to the three isomers—anti–anti, anti–syn, and syn–syn. One major isomer was observed in each case, which was tentatively assigned to be the anti–anti isomer, based on the extreme similarity of its C-5 and H-5 NMR shifts with those of the corresponding anti hydrazones (Tables II and III, respectively) and also because the starting hydrazones from which the azines were made were 80% anti. The assignments of the carbon shifts of the major isomer of the azines VII–IX given in Table II were based on the data in ref 14–16, which deal with the ^{13}C NMR's of various hydrazones and oximes, other than the opiate ones, and ref 6, which deals with the ^{13}C NMR's of the opiate hydrazones. The comparison of the chemical shifts of the carbons of the major azine isomers with those of the corresponding anti hydrazones reveals the expected similarities, except for the C-6, and, with their corresponding ketones, the expected differences in the shifts of the C-7 and C-8 in particular, in addition to the C-6 (Table II). The assignments of the two minor sets of peaks to the anti–syn and syn–syn isomers are tentative at this stage of the work in the sense that they may be interchanged and thus are not given.

Very significantly, we have observed additional sets of peaks in the ^{13}C NMR spectrum of VIII, i.e., in excess of those expected for the three isomers. Particularly interesting are, e.g., the splittings of the C-6 carbons, since similar splitting was observed in the spectra of naloxone hydrazone isomers and naloxone·HCl, which was interpreted as suggesting the presence of different conforma-

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tions of the ring C. The additional peaks in the azines could indicate the presence of various additional conformations arising from the partially restricted rotations around the azine bond. This aspect of the spectra is now under investigation.

Data shown in Table III indicate that the chemical shift of H-5 can be used as an indication of the presence of the azine as well as hydrazone isomers. Also, the splitting in the aromatic region, i.e., for H-1 and H-2, occurs when isomers are present. The presence of various conformers, which is indicated in the ^{13}C NMR, is shown also in the proton spectra.

The mixed estrone–naloxone azine (X) which was formed by treating 100% *anti*-estrone hydrazone with naloxone is configurationally pure anti–anti azine, based on both ^{13}C and ^{1}H NMR spectra. Thus, only one C-5 signal was observed (at 87.80 ppm), one C-6 azine carbon of the opiate (at 162.30 ppm), and one azine carbon at C-17 of the steroid (at 175.79 ppm). Only one H-5 of the opiate moiety was observed (at 5.044 ppm), and only one signal for the angular CH_3 group at 0.788 ppm.

The data from Table I show that in the hydrazones I–III the less crowded anti isomer is the major product, which suggests that the formation of these hydrazone isomers is sterically controlled. The latter suggestion is supported by our finding that in the more sterically encumbered hydrazones IV–VI, the anti isomers were obtained almost exclusively. We found a similar steric control of hydrazone formation in the case of a steroidal hydrazone, Δ4-androstene-3,17-dione dihydrazone.[10] In this steroid case only the anti isomer was obtained at the C-17 position, since at this position the syn isomer would be sterically very crowded, while a mixture of the anti and syn isomers was obtained at the less crowded position 3. Estrone hydrazone gave 100% anti hydrazone at C-17 and pregnenolone acetate hydrazone afforded 100% anti hydrazone at C-20. These steroidal hydrazones were used in syntheses of mixed azines between opiates and steroids;[12] one representative compound, X, is described here.

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The biological tests of the compounds in this study were done by Dr. Lars Terenius and Ahmet Koman to whom thanks are expressed. The biological data will be published separately.[17]

Registry No. I anti, 91797-50-1; I syn, 91797-51-2; II anti, 91796-59-7; II syn, 91796-60-0; III anti, 91796-61-1; III syn, 91797-52-3; IV anti, 91796-62-2; V anti, 91796-63-3; VI anti, 91712-58-2; VII isomer 1, 91796-64-4; VII isomer 2, 91796-65-5; VII isomer 3, 91796-66-6; VIII isomer 1, 91797-53-4; VIII isomer 2, 91796-67-7; VIII isomer 3, 91796-68-8; IX isomer 1, 91796-69-9; IX isomer 2, 91796-70-2; IX isomer 3, 91796-71-3; X, 91712-59-3; *anti*-estrone hydrazone, 91796-72-4; *anti*-pregnenolone 3-acetate 20-hydrazone, 91796-73-5; pregnenolone acetate, 1778-02-5; pregnenolone, 145-13-1; naloxone hydrochloride, 357-08-4; naltrexone, 16590-41-3; oxymorphone, 76-41-5; dimethyl hydrazine, 30260-66-3; naloxone, 465-65-6.

(17) Kolb, V. M.; Koman, A.; Terenius, L. 8th International Symposium on Medicinal Chemistry, to be held in Uppsala, Sweden, in August, 1984. Proceedings from this Symposium will be published in December, 1984, by Swedish Pharmaceutical Press, J. L. G. Nilsson and R. Dahbom, Eds.

Notes

Phenylfluorocarbene from Phenylfluorodiazirine. The Crown Ether Test for Free Carbenes Revisited

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A decade ago, we found that phenylbromocarbene and phenylchlorocarbene, generated by the action of potassium tert-butoxide on the corresponding benzal halides, were not free carbenes. Their selectivities toward a standard set of alkenes differed from those of the formally identical carbenes photolytically produced from the 3-halo-3-phenyldiazirines. In the presence of the macrocyclic polyether 18-crown-6, however, the selectivities of the KO-*t*-Bu-generated species became identical with those of the photogenerated carbenes.[1] It was concluded that the diazirine photolysis gave free phenylhalocarbenes, that the same intermediates could be generated from benzal halides by using a base–crown complex, and that α-elimination in the absence of crown ether gave phenylhalocarbenoids.[1,2]

We extended this work by examining the olefinic selectivity of PhCF, generated by the action of KO-*t*-Bu on PhCHBrF in the presence and absence of 18-crown-6;[3] cf. below. Over the years, others have carried out analogous studies to either test or ensure the "freeness" of (e.g.) alkylidenecarbenes,[4] alkenylidenecarbenes,[5] cyclo-

(1) Moss, R. A.; Pilkiewicz, F. G. *J. Am. Chem. Soc.* **1974**, *96*, 5632 and references therein.
(2) The structure of the carbenoid was undefined, but most likely involved complexation of PhCX with either KX or KO-*t*-Bu.
(3) Moss, R. A.; Joyce, M. A.; Pilkiewicz, F. G. *Tetrahedron Lett.* **1975**, 2425. Joyce, M. A. Ph.D. Thesis, Rutgers University, New Brunswick, NJ, 1979.
(4) Stang, P. J.; Mangum, M. G. *J. Am. Chem. Soc.* **1975**, *97*, 1459, 6478.
(5) Patrick, T. B.; Schmidt, D. J. *J. Org. Chem.* **1977**, *42*, 3354.

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