cation **1**, and less so or even shielded in the secondary and tertiary ions. Despite the change in carbon shifts at carbocationic centers going from primary to tertiary ions (about 80 ppm), C_3 and C_4 show almost no change. The lack of variation of deshielded cyclopentadienyl carbons, C_3 and C_4, not only indicates positive charge delocalization into the ferrocenyl moiety at these positions, but also shows that the interaction between the iron atom and the carbocationic center is reduced going from primary to tertiary ions. One also finds that carbon–hydrogen coupling constants (J_{CH}, in hertz) at the carbenium centers are smaller than those in the cyclopentadienyl moiety, presumably caused by some interaction between iron and the carbenium center. The magnitude of J_{CH} is significantly different from those in, for example, dimethyl- and diphenylcarbenium ions (J_{CH} = 169 and 164 Hz, respectively).

The observed diastereotropism of the carbon pairs (C_2 and C_5, and C_3 and C_4) in the unsymmetrically substituted α-ferrocenylcarbenium ions (**2** and **4**) undoubtedly indicates slow rotation about the exocyclic C^+–C_1 bond, which could arise from either the double bond character between C^+ and C_1 or the direct interaction between iron and the carbocationic center.

The present ^{13}C NMR studies demonstrate that α-ferrocenylcarbenium ions indeed have the positive charge substantially delocalized into the metallocenyl moiety. Although the detailed mechanism for the interaction between the iron nucleus and the neighboring carbenium center is not yet clear, such interaction seems to be weaker in tertiary than in primary or secondary species.

Experimental Section

Materials. All α-ferrocenylcarbinols were prepared according to literature procedures.[5]

Carbon-13 NMR Spectra. A Varian Associates Model XL-100 NMR spectrometer equipped with a Fourier transform accessory, a spin decoupler, and a variable-temperature probe was used to obtain the carbon-13 NMR spectra. Carbon shifts were referred to external Me_4Si (capillary).

Preparation of the Ions. α-Ferrocenylcarbenium ions were prepared from corresponding alcohols in cold sulfuric acid solution at −10° and carefully transferred to NMR tubes for study.

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Registry No.—**1**, 12129-36-1; **2**, 12129-73-6; **3**, 12295-38-4; **4**, 12295-58-8.

References and Notes

(1) Part V: G. A. Olah and Y. K. Mo, *J. Organomet. Chem.*, **60**, 311 (1973).
(2) (a) M. Cais, *Rec. Chem. Prog.*, **27**, 177 (1966), and references cited therein; (b) T. G. Traylor, W. Hanstein, H. J. Berwin, N. A. Clinton, and R. S. Brown, *J. Am. Chem. Soc.*, **93**, 5715 (1971); (c) F. H. Gon and T. T. Tidwell, *J. Org. Chem.*, **37**, 1728 (1972); (d) P. B. Valkovich, G. W. Gokel, and I. K. Ugi, *Tetrahedron Lett.*, 2947 (1973); (e) D. Kaufman and R. Kupper, *J. Org. Chem.*, **39**, 1438 (1974); (f) R. L. Sime and R. J. Sime, *J. Am. Chem. Soc.*, **96**, 892 (1974); (g) R. D. Turbitt and W. E. Watts, *J. Chem. Soc., Chem. Commun.*, 182 (1973); (h) A. Eisenstadt and M. Cais, *ibid.*, 216 (1972); (i) R. Cleiter, R. Seeger, H. Binder, E. Fluck, and M. Cais, *Angew. Chem., Int. Ed. Engl.*, **11**, 1028 (1972); (j) R. Gleiter and R. Seeger, *Helv. Chim. Acta.*, **54**, 1217 (1971); (k) E. A. Hill, *J. Organomet. Chem.*, **24**, 457 (1970); *J. Am. Chem. Soc.*, **81**, 3484 (1959); (l) J. J. Dannenberg and J. H. Richards, *Tetrahedron Lett.*, 4747 (1967); (m) T. G. Traylor and J. C. Ware, *J. Am. Chem. Soc.*, **89**, 2304 (1967).
(3) (a) S. Braun and W. L. Watts, *J. Organomet. Chem.*, in press, and references cited therein; (b) V. I. Sokolov, P. v. Petrovskii, A. A. Koridze, and O. A. Reutov, *ibid.*, **76**, C15 (1974); (c) D. Seyferth, G. H. Williams, and D. D. Traficante, *J. Am. Chem. Soc.*, **96**, 604 (1974); (d) G. H. Williams, D. D. Traficante, and D. Seyferth, *J. Organomet. Chem.*, **60**, C53 (1973); (e) V. I. Sokolov, P. V. Petrovskii, and O. A. Reutov, *ibid.*, **59**, C27 (1973); (f) G. A. Olah and Y. K. Mo, *ibid.*, **60**, 311 (1973); (g) R. G. Sutherland, J. R. Sutton, and W. M. Horspool, *Tetrahedron Lett.*, 3283 (1973).
(4) See, for example, J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, N.Y., 1972.
(5) All the alcohol precursors were prepared according to literature procedures and gave satisfactory analysis.
(6) (a) J. J. Dannenberg, M. K. Levenberg, and J. H. Richards, *Tetrahedron*, **29**, 1575 (1973); (b) T. D. Turbitt and W. E. Watts, *J. Organomet. Chem.*, **49**, C30 (1973); (c) M. Hisatome and K. Yamakawa, *Tetrahedron*, **27**, 2101 (1971); (d) C. P. Lillya and R. A. Sahatjian, *J. Organomet. Chem.*, **32**, 371 (1971); (e) E. A. Hill and R. Wiesner, *J. Am. Chem. Soc.*, **91**, 509 (1969); (f) C. U. Pittman, Jr., *Tetrahedron Lett.*, 3619 (1967); (g) M. Cais, J. J. Dannenberg, A. Eisenstadt, M. I. Levenberg, and J. H. Richards, *ibid.*, 1695 (1966).

An Improved Procedure for the N-Demethylation of 6,7-Benzomorphans, Morphine, and Codeine

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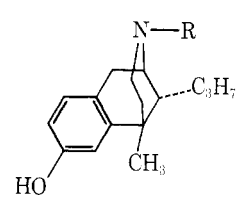
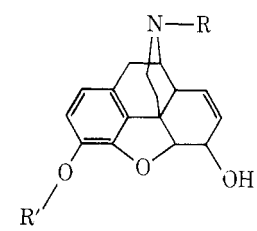
The N-demethylation of tertiary methylamines has been accomplished in several ways. The classic von Braun reaction,[1] using cyanogen bromide, was improved upon for many amines by the use of benzyl or ethyl chloroformate.[2] Further improvement involved the use of phenyl chloroformate;[2,3] the intermediate carbamate formed with this reagent proved easier to hydrolyze. Ethyl azodicarboxylate has been used[4] to demethylate thebaine and various 6-ester derivatives of morphine and codeine in reasonable yield. However, this procedure gave only ca. 40% yields of an *N*-nor-6,7-benzomorphan.[5] Recently, 2,2,2-trichloroethyl chloroformate[6] has been found to give a carbamate intermediate which could be cleaved by zinc in acetic acid or methanol. These reagents N-demethylated morphine in 75% yield. However, in our hands, the trichloroethyl chloroformate procedure gave poor yields (<40%) of the *N*-nor product from 2′-hydroxy-2,5-dimethyl-9α-propyl-6,7-benzomorphan (**1b**).



1a, R = H
b, R = CH_3



2a, R = R′ = H
b, R = CH_3; R′ = H
c, R = H; R′ = CH_3
d, R = R′ = CH_3

We utilized a modified phenyl chloroformate procedure to produce an intermediate carbamate, and have found that the carbamate can be easily cleaved with a 1:1 mixture of 64 and 95% hydrazine. The method has been applied to morphine (**2b**), codeine (**2d**), and 6,7-benzomorphans to give the *N*-nor compounds in excellent yield. Hydrazine has, of course, been used in the past to cleave amides in peptides and other compounds.[7]

The procedure of Abdel-Monem and Portoghese[3] for the preparation of *N*-normorphine involved the hydrolysis of *N*,3,6-tricarbophenoxynormorphine to *N*-carbophenoxynormorphine, its chromatography and crystallization, followed by cleavage with ethanolic KOH, in an overall yield of ca. 40%. We found it unnecessary in our procedure to isolate and purify the intermediate carbamate and, with the benzomorphan, the *N*-nor product precipitated from the hydrazine reaction mixture; washing and drying gave analytically pure product in 95% overall yield. *N*-Normorphine

and *N*-norcodeine were obtained in overall yields of 84 and 89%, respectively.

Care should be exercised in the preparation of the carbamate to ensure continuous, efficient stirring, especially in larger scale preparations. Inefficient mixing could be responsible for localized acid formation which might promote the formation of acid-catalyzed by-products from the *N*-normorphine and codeine carbamates to give, possibly, the epimeric 6-hydroxyl (6-iso) or 8-hydroxyl (from allylic rearrangement) *N*-normorphine (or codeine). Efficient stirring and an increased (over the former procedure[3]) amount of base tended to eliminate by-products.

A further precaution involved the use of 64% hydrazine in the hydrazine mixture which ensured the presence of hydrazine hydrate in the vapor of the refluxed mixture, rather than the air-sensitive (explosive) anhydrous hydrazine; safety shields should also be employed.

Experimental Section

Melting points were determined in open capillary tubes using a Thomas-Hoover apparatus and are corrected. Microanalyses were performed by the Laboratory's Section on Microanalytical Services and Instrumentation. Ir (Perkin-Elmer 21), NMR (Varian A-60 or HR-220), and mass (Hitachi Perkin-Elmer RMU 6E) spectra were consistent with the assigned structures.

(±)-5-Methyl-2′-hydroxy-9α-propyl-6,7-benzomorphan (1a). In a modification of the usual procedure,[3] phenyl chloroformate (26.0 g, 166 mmol) was added to a slurry of (±)-2,5-dimethyl-2′-hydroxy-9α-propyl-6,7-benzomorphan (**1b**, 5.0 g, 19.3 mmol) in $CHCl_3$ (500 ml). After stirring for several minutes the reaction mixture became homogenous and $KHCO_3$ (34.0 g, 340 mmol) was added. The mixture was refluxed for 48 hr and cooled and water (200 ml) was added. When the inorganic material had dissolved, the $CHCl_3$ was separated and washed with 1 *N* HCl (50 ml) and water (100 ml). The $CHCl_3$ was evaporated in vacuo and to the residue was added MeOH (310 ml) and a solution of KOH (14.5 g, 220 mmol) and $KHCO_3$ (22 g, 220 mmol) in H_2O (220 ml). After stirring at 25° overnight, the solution was acidified with 37% HCl and concentrated in vacuo until KCl separated. The aqueous suspension was washed with Et_2O and the combined extracts were dried ($MgSO_4$) and solvent was removed. The major portion of the residual phenol by-product was removed by distillation under high vacuum (bath 100–120°), to give a gum which was dissolved in Et_2O and filtered through a layer of silica gel (70–230 mesh). The silica gel was washed with Et_2O and the combined filtrate and washings were evaporated to yield the crude *N*-carbophenoxy derivative of **1a** (9.6 g) as a yellow foam that resisted crystallization from a variety of solvents and which still contained some phenol. To this material was added 64% hydrazine (35 ml) and 95% hydrazine (35 ml). The mixture was stirred (under N_2), and refluxed (behind a safety shield) for 1.5 hr. Crystalline **1a** separated from the reaction mixture. After an additional 18 hr of refluxing, the reaction mixture was cooled. The white solid was filtered and washed well with H_2O and then Et_2O (20 ml). The resulting white solid was dried in vacuo at 65° to yield 4.52 g (95.5%) of analytically pure **1a** directly, as small, irregular prisms, mp 248.5–250.5°.

Anal. Calcd for $C_{16}H_{23}NO$: C, 78.32; H, 9.45; N, 5.71. Found: C, 78.07; H, 9.25; N, 5.73.

Normorphine (2a). To a suspension of anhydrous morphine (**2b**, 2.50 g, 8.76 mmol) and finely divided $KHCO_3$ (15.0 g, 150 mmol) in $CHCl_3$ (250 ml) was added phenyl chloroformate (11.5 g, 73.4 mmol). The reaction mixture was vigorously stirred, refluxed for 60 hr, and cooled, most of the $CHCl_3$ was decanted, and the remaining inorganic material was dissolved in H_2O (100 ml). This solution was added to the decanted $CHCl_3$ and after shaking well the $CHCl_3$ was separated and washed with H_2O (50 ml) and then with 1 *N* HCl (50 ml). The $CHCl_3$ was dried ($MgSO_4$) and evaporated in vacuo, and most of the phenol was evaporated from the residue under high vacuum (bath 100–110°). To the residue was added 64% hydrazine (20 ml) and 95% hydrazine (20 ml) and the solution was refluxed (safety shield) under N_2 for 60 hr. The mixture was cooled, H_2O (100 ml) was added, and the solvent was removed in vacuo. The phenol remaining was evaporated under high vacuum (bath 100–120°), H_2O (20 ml) was added, and 37% HCl was added to pH 2.0 (Hydrion paper). The solutions was filtered, and the filtrate was made alkaline with NH_4OH. When crystallization (at 5°) was complete, the solid was filtered, washed with cold H_2O, and dried to give **2a**·$2H_2O$ (2.24 g, 84%), mp 275–277° dec (lit.[8] mp 276–277°).

Anal. Calcd for $C_{16}H_{17}NO_3 \cdot 2H_2O$: C, 62.52; H, 6.89; N, 4.56. Found: C, 62.45; H, 6.77; N, 4.60.

Norcodeine (2c). To a solution of codeine (**2d**, 2.99 g, 10 mmol) in $CHCl_3$ (250 ml) was added $NaHCO_3$ (21.0 g, 250 mmol) and phenyl chloroformate (11.5 g, 73.4 mmol). The reaction mixture was refluxed with efficient stirring for 18 hr, cooled, filtered, and evaporated. To the resulting syrup (14.1 g) was slowly added 95% hydrazine (5 ml). When the strongly exothermic reaction was over, additional 95% hydrazine (10 ml) and 64% hydrazine (10 ml) were added. The solution, under N_2, was refluxed (safety shield) for 24 hr and cooled, and H_2O was added and then removed (twice, 100 ml each) in vacuo. Most of the remaining phenol was removed (high vacuum, bath 100–120°) to give a semisolid which was dissolved in a mixture of $CHCl_3$ (150 ml) and H_2O (75 ml). The aqueous phase was made alkaline with NH_4OH, and the $CHCl_3$ was separated and extracted with sufficient 10% KOH to remove the remaining phenol. The $CHCl_3$ solution was washed with H_2O (50 ml), dried (Na_2SO_4), and evaporated to give 2.54 g (89%) of norcodeine (**2c**), mp 183.5–185° (lit.[9] mp 185°).

Registry No.—**1a**, 55058-87-2; **1b**, 55058-88-3; **2a**, 466-97-7; **2b**, 57-27-2; **2c**, 467-15-2; **2d**, 76-57-3; phenyl chloroformate, 1885-14-9.

References and Notes

(1) H. A. Hageman, *Org. React.*, **7**, 198 (1953).
(2) J. D. Hobson and J. G. McCluskey, *J. Chem. Soc.*, 2015 (1967).
(3) M. M. Abdel-Monem and P. S. Portoghese, *J. Med. Chem.*, **15**, 208 (1972).
(4) A. Pohland and H. R. Sullivan, Jr., U.S. Patent 3,342,824 (Sept 19, 1967).
(5) K. Kanematsu, M. Takeda, A. E. Jacobson, and E. L. May, *J. Med. Chem.*, **12**, 405 (1969).
(6) T. A. Montzka, J. D. Matiskella, and R. A. Partyka, *Tetrahedron Lett.*, **No. 14**, 1325 (1974).
(7) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol. I, Wiley-Interscience, New York, N.Y., 1967, pp 442–444.
(8) D. G. Stecher, Ed., "Merck Index", 8th ed, Merck and Co., Inc., Rahway, N.J., 1968, p 749.
(9) Reference 8, p 747.

Formation of *gem*-Dinitrates from Acetaldehyde and Trifluoroacetaldehyde[1]

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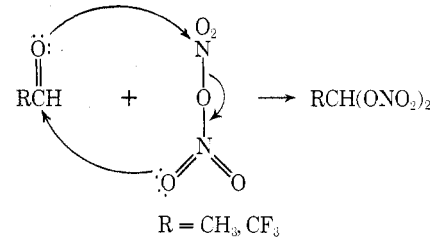
The new *gem*-dinitrates 1,1-dinitratoethane, $CH_3CH(O\text{-}NO_2)_2$, and 1,1,1-trifluoro-2,2-dinitratoethane, $CF_3CH(O\text{-}NO_2)_2$, have been synthesized by the reaction between dinitrogen pentoxide and acetaldehyde and trifluoroacetaldehyde. The combination of the aldehydes and N_2O_5 in a 1:1 mole ratio can be explained by the heterolytic cleavage of the latter involving a nucleophilic oxygen atom attack, i.e.



R = CH_3, CF_3

although the reaction need not be concerted.[2] This route is also similar to that for perchlorate formation reported by