inant way in which four ethynes are linked by nickel catalysts en route to COT leaves the initial connectivity of the starting carbon pairs intact. This is currently best accommodated by the postulate of a zipper-stepwise-type mechanism.

Acknowledgment. This work was supported by NSF-CHE-79-03954 and the Director, Office of Energy Research, Office of Basic Energy Sciences, Chemical Sciences Division of the U. S. Department of Energy, under Contract W-7405-ENG-48. We are grateful for useful discussions with Dr. A. Falick on mass spectral analyses and the tireless efforts of L. Fanning expended on the recording of GC mass spectral data.

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(22) $HC{\equiv}{}^{13}CH$ (90% labeled), $Ni(acac)_2$, CaC_2, THF, N_2 (50–60 psig), 2–3 days, 85–90 °C. For this label purity the following values are calculated (standardized to *m/e* 165 = 100%, ^{13}C in $^{12}C \sim 1\%$) (*m/e*, 163, 164, 166, 167): zipper, 3.0, 38.2, 21.6, 1.7; cyclobutadiene, 4.6, 46.9, 29.3, 2.7; random, 7.3, 51.3, 33.5, 4.4; metal–benzene, 3.6, 43.6, 26.3, 2.0. Found: 7.0, 36.5, 20.4, 1.2.

2,3,4,4a,5,6,7,7a-Octahydro-1*H*-benzofuro[3,2-*e*]isoquinoline: A New Morphine Fragment

Engelbert Ciganek

Contribution No. 2892
Central Research and Development Department
E. I. du Pont de Nemours & Co.
Wilmington, Delaware 19898

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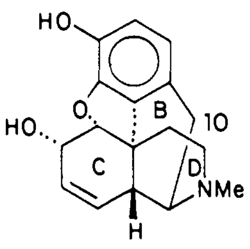
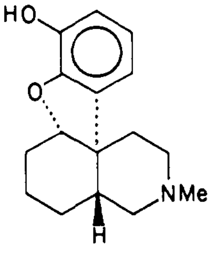
Generations of medicinal chemists have used the morphine molecule (**1**) as a model in their search for a strong, nonaddictive analgesic.[1] We now report the synthesis of a new morphine fragment, 2,3,4,4a,5,6,7,7a-octahydro-1*H*-benzofuro[3,2-*e*]isoquinoline (**2**), which lacks ring B but contains the complete skeleton of morphine with the exception of C-10.[2,3]



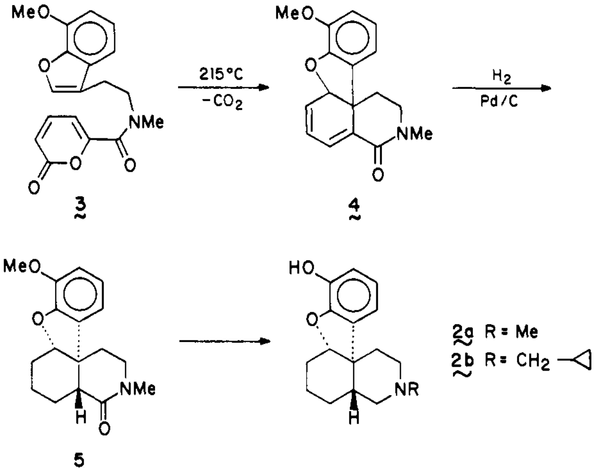
1



2

The key reaction in the synthesis of **2** is the intramolecular Diels–Alder reaction[4] (0.5% in 1,2,4-trichlorobenzene, reflux, 10 h) of *N*-(7-methoxy-3-benzofuranylethyl)-*N*-methyl-6α-pyronecarboxamide (**3**)[5] to give 9-methoxy-3-methyl-2,3-dihydro-1*H*-benzofuro[3,2-*e*]isoquinolin-4(7a*H*)-one (**4**)[6,7], mp 175–176 °C, in 53% yield.[8] The *N*-benzyl and *N*-cyclopropylmethyl analogues of **4** were obtained in the same manner in 50 and 67% yields, respectively. Diels–Alder additions involving benzofuran as the dienophile do not appear to have been reported previously;[9] the reverse reaction has been observed in the case of the Diels–Alder adducts of thebaine with esters of acetylenedicarboxylic acid.[10]

Catalytic hydrogenation of **4** (Pd/C, THF) stereospecifically introduced the trans C/D ring junction to give the lactam **5**[6,11] which on reduction (borane–methyl sulfide) and demethylation (*n*-PrSK, DMF) furnished 3-methyl-2,3,4,4a,5,6,7,7a-octahydro-1*H*-benzofuro[3,2-*e*]isoquinolin-9-ol (**2a**), mp 218–220 °C,[6] in 86% yield (based on **4**). The assigned structure was confirmed by a single-crystal x-ray structure determination[12] carried out on the cyclopropylmethyl analogue **2b**.[13]



Heating the *N*-(7-methoxy-3-benzofuranethyl)-*N*-(cyclopropylmethyl)amide of 2,4-pentadienoic acid (**6**)[14] in toluene (0.5% solution) to 240 °C for 10 h and isolating the product by HPLC gave the cis-fused intramolecular Diels–Alder adduct **7**[15] in 10%

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[1] Johnson, M. R.; Michne, G. M. In "Medicinal Chemistry", 4th ed.; Wolff, M. E., Ed.; Wiley Interscience: New York, 1981; Part III, p 699.

[2] Derivatives of ring system **2** having the unnatural cis C/D ring junction have been prepared previously: Schultz, A. G.; Lucci, R. D.; Fu, W. Y.; Berger, M. H.; Erhardt, J.; Hagmann, W. K. *J. Am. Chem. Soc.* **1978, 100**, 2150. Schultz, A. D.; Lucci, R. D. *J. Chem. Soc., Chem. Commun.* **1976**, 925.

[3] Some of the compounds described in this communication are claimed in patents, e.g.; Ciganek, E. U.S. Patent 4 243 668, 1981; *Eur. Pat. Appl.* 9780, 1980; *Chem. Abstr.* **1980**, *93*, 220720.

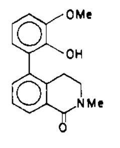
[4] For recent reviews, see: Brieger, G.; Bennett, J. N. *Chem. Rev.* **1980**, *80*, 63. Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10.

[5] Methyl *o*-vanillate was converted into 7-methoxy-3-benzofuranone according to the procedure of: Schroeder, D. C.; Corcoran, P. D.; Holden, C. A.; Mulligan, M. C. *J. Org. Chem.* **1962**, *27*, 586. Treatment of this ketone with [(carbomethoxy)methylene]triphenylphosphorane followed by hydrolysis gave 7-methoxy-3-benzofuranacetic acid. Reduction with borane–methyl sulfide, tosylation of the resulting 7-methoxy-3-benzofuranethanol, and treatment of the tosylate with methylamine gave 7-methoxy-*N*-methyl-3-benzofuranethylamine which was condensed with 6α-pyronecarbonyl chloride to give **3** in 22% overall yield [NMR (60 MHz in $CDCl_3$): τ 2.4 (s, 1 H), 2.5–3.8 (m, 6 H), 5.9 (s, 3 H), 6.1 (t, split further, 2 H), 6.7 (s, 3 H), and 6.8 (t, split further, 2 H).

[6] Correct elemental analyses have been obtained for all new compounds.

[7] NMR (220 MHz in $CDCl_3$): τ 3.1 (d, 1 H, *J* = 6 Hz), 3.3–3.5 (m, 2 H), 3.6 (d/d, 1 H, *J* = 6/2 Hz), 4.1 (d/d/d, 1 H, *J* = 10/6/2 Hz), 4.3 (d/d, 1 H, *J* = 10/2 Hz), 4.7 (narrow m, 1 H); 6.3 (s, 3 H), 6.6 (t/d, 1 H, *J* = 12/4 Hz), 6.9 (d/d/d, 1 H, *J* = 12/6/2 Hz), 7.7 (s, 3 H), 8.0 (t/d, 1 H, *J* = 12/6 Hz), 8.3 (d/d/d, 1 H, *J* = 12/4/2 Hz).

[8] Two other products were isolated in low yields: a Diels–Alder dimer of **4** of unknown regio- and stereochemistry and compound i, which was presumably formed by cleavage of the carbon–oxyen bond of the dihydrobenzofuran in **4** followed by phenyl migration and aromatization.



i

[9] For an intramolecular Diels–Alder reaction of a hexahydronaphthalene (diene) to a furan (dienophile), see: Ghisalberti, E. L.; Jefferies, P. R.; Payne, T. G. *Tetrahedron* **1974**, *30*, 3099.

[10] Rapoport, H.; Sheldrick, P. *J. Am. Chem. Soc.* **1963**, *85*, 1636.

[11] NMR (220 MHz in $CDCl_3$): τ 2.9–3.1 (m, 2 H), 3.2–3.4 (m, 1 H), 5.3 (d/d, *J* = 8/6 Hz, 1 H); 5.9 (s, 3 H), and 6.4–8.7 (m + s, 14 H).

[12] We are indebted to Dr. R. L. Harlow for this determination; details are available in the supplementary material.

[13] Mp 175 °C. NMR (220 MHz in $CDCl_3$): τ 2.5 (br s, 1 H), 3.1 (d, *J* = 6 Hz, split further, 1 H), 3.3 (m, 2 H), 5.6 (t, presumably d/d, *J* ≈ 5–6 Hz, 1 H), 6.9 (m, 2 H), 7.2–7.6 (m, 4 H), 7.9–9.2 (m, 10 H), 9.5 (m, 2 H), and 9.9 (m, 2 H).

[14] The amide **6** was prepared from 2,4-pentadienoic acid by treatment with methyl chloroformate (CH_2Cl_2, *i*-$PrNEt_2$, 0 °C) followed by *N*-(cyclopropylmethyl)-7-methoxy-3-benzofuranethylamine. NMR (60 MHz in $CDCl_3$): τ 2.5 (s, 1 H), 2.6–4.8 (m, 8 H), 6.0 (s, 3 H), 6.3 (m, 2 H), 6.4–7.2 (m, 4 H), and 8.8–9.9 (m, 5 H).

[15] NMR (220 MHz in $CDCl_3$): τ 3.1–3.2 (m, 3 H), 3.9 (d/d/d, *J* = 9/4/2 Hz, 1 H), 4.0 (m, 1 H); 5.3 (d/d, *J* = 5.5/7 Hz, 1 H), 6.1 (s, 3 H), and 6.2–9.8 (m, 14 H).

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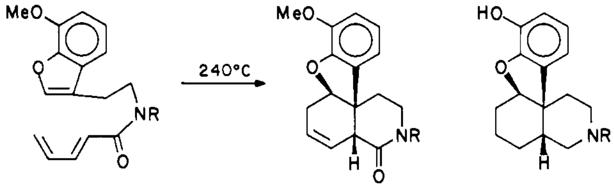
yield. Catalytic hydrogenation of **7** followed by borane reduction and demethylation furnished **8**,[6,16] the cis isomer of **2b**, mp 174–175 °C.



6 R=CH$_2$–◁ 7 8

Intramolecular Diels–Alder reactions have also been carried out with substrates **3** where the benzofuran oxyen was replaced by sulfur and nitrogen and by one[17] or two methylenes. Details will be reported in future publications.

Supplementary Material Available: X-ray structure determination of 3-(cyclopropylmethyl)-2,3,4,4a,5,6,7,7a-octahydro-1*H*-benzofuro[3,2-*e*]isoquinolin-9-ol (14 pages). Ordering information is given on any current masthead page.

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(16) NMR (220 MHz in CDCl$_3$): τ 3.2 (m, 1 H), 3.3 (m, 2 H), 5.7 (br s, width at half-height ca. 9 Hz, 1 H), 7.1–7.6 (br m, 4 H), 7.7 (d, *J* = 6 Hz, 2 H), 7.9–8.6 (br m, 9 H), 9.1 (m, 1 H); 9.5 (m, 2 H), and 9.9 (m, 2 H). The phenolic OH occurred as a very broad signal in the aromatic region.

(17) For an unsuccessful attempt to prepare decahydroindeno[1,2-*f*]isoquinolines, see: Smith, J. R. L.; Norman, R. O. C.; Rose, M. E.; Curran, A. C. W. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2863.

Experimental Measurement of the Electron Affinity of the Hydroperoxy Radical

Veronica M. Bierbaum,* Robert J. Schmitt,† and
Charles H. DePuy

Department of Chemistry, University of Colorado
Boulder, Colorado 80309

Roy D. Mead, P. A. Schulz, and W. C. Lineberger*

Department of Chemistry, University of Colorado
and Joint Institute for Laboratory Astrophysics
University of Colorado and National Bureau of Standards
Boulder, Colorado 80309

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The hydroperoxy radical, HO$_2$, plays an important role in the chemistry of the atmosphere, in combustion processes, and in a variety of biological and chemical oxidative systems. However, the electron affinity of this species has never been measured directly. An estimate by Weiss[1] placed this quantity at 4.6 eV. Recently, Benson and Nangia[2] have obtained 1.85 ± 0.12 eV on the basis of a thermochemical cycle employing solution data. Using the flowing afterglow technique we have experimentally bracketed the gas-phase acidity of hydrogen peroxide

$$H_2O_2 \rightarrow H^+ + HO_2^- \qquad \Delta H = \Delta H^\circ_{acid}(H_2O_2) \qquad (1)$$

to be 375.5 ± 3.3 kcal mol^{-1} and the electron affinity of the hydroperoxy radical

$$HO_2^- \rightarrow HO_2 + e^- \qquad \Delta H = EA(HO_2) \qquad (2)$$

to be 1.16 ± 0.15 eV. Using these results, we have performed threshold photodetachment of HO$_2^-$ to obtain a more precise value, EA(HO$_2$) = 1.19 ± 0.01 eV (27.4 ± 0.2 kcal mol^{-1}). Employing this value and well-established heats of formation of HO$_2$, H$_2$O$_2$, and H$^+$, we find $\Delta H_f^\circ(HO_2^-)$ = −24.9 ± 0.7 kcal mol^{-1} and $\Delta H^\circ_{acid}(H_2O_2)$ = 374.8 ± 0.7 kcal mol^{-1}.

In the flowing afterglow which has been described in detail previously,[3,4] ion–molecule reactions are carried out in helium buffer gas under thermal energy conditions. In order to determine the acidity of H$_2$O$_2$, the bracketing acids must have well-known acidities which are similar to that of H$_2$O$_2$. Moreover, they must react with HO$_2^-$ exclusively by a simple proton-transfer process. This is a stringent requirement since HO$_2^-$ has been found to be a potent gas-phase oxidant.[5] Fluoroform and hydrofluoric acid fulfill these requirements:

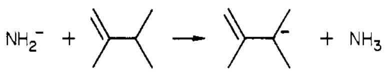
$$CF_3^- + H_2O_2 \rightleftarrows HO_2^- + HCF_3 \qquad (3)$$

$$F^- + H_2O_2 \rightleftarrows HO_2^- + HF \qquad (4)$$

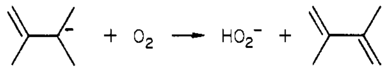
We have found that proton-transfer equilibria involving HO$_2^-$ and H$_2$O$_2$ cannot be experimentally established because a rapid competing process occurs.

$$HO_2^- + H_2O_2 \rightarrow OH^- + H_2O + O_2 \qquad (5)$$

Therefore equilibrium constants for reactions 3 and 4 were determined from measurements of forward and reverse rate constants, and a source of each ion which did not involve its conjugate acid was employed so that back reactions were minimized. CF$_3^-$ was generated by electron impact on CF$_4$, F$^-$ was produced by electron impact on NF$_3$, and HO$_2^-$ was formed by chemical reaction.



(6)



(7)

Neutral reactants were added through a movable inlet, and rate constants were measured by monitoring the reactant ion density as a function of reaction distance. The flow rates of H$_2$O$_2$ (97.5%) and HCF$_3$ were determined by monitoring the pressure increase in a calibrated volume, while HF flow was determined by using a calibrated mass flowmeter. A limit of the extent of possible decomposition of H$_2$O$_2$ was evaluated and included in the error limits.

The experimental results for reaction 3 are $k_f = 2.2 \times 10^{-10}$ cm^3 molecule^{-1} s^{-1} and $k_r = 6.4 \times 10^{-11}$ cm^3 molecule^{-1} s^{-1}, yielding ΔH = −1.3 kcal mol^{-1}.[6] Using $\Delta H^\circ_{acid}(HCF_3)$ = 376.6 kcal mol^{-1} [7] yields $\Delta H^\circ_{acid}(H_2O_2)$ = 375.3 kcal mol^{-1}.

For reaction 4 $k_f = 2.0 \times 10^{-12}$ cm^3 molecule^{-1} s^{-1} and $k_r = 2.8 \times 10^{-10}$ cm^3 molecule^{-1} s^{-1}, yielding ΔH = +4.4 kcal mol^{-1}.[6] Using $\Delta H^\circ_{acid}(HF)$ = 371.3 kcal mol^{-1} [7] yields $\Delta H^\circ_{acid}(H_2O_2)$ = 375.7 kcal mol^{-1}.

Employing the average value $\Delta H^\circ_{acid}(H_2O_2)$ = 375.5 kcal mol,$^{-1}$ reaction 1, $\Delta H_f^\circ(H^+)$ = 367.2 kcal mol^{-1},[8] and $\Delta H_f^\circ(H_2O_2)$ = −32.5 kcal mol^{-1} [8,9] yields $\Delta H_f^\circ(HO_2^-)$ = −24.2 kcal mol^{-1}. Finally, using this latter value, reaction 2, and a recently determined value,[10] $\Delta H_f^\circ(HO_2)$ = 2.5 kcal mol^{-1}, yields EA(HO$_2$) = 1.16 ± 0.15 eV (26.7 ± 3.4 kcal mol^{-1}).

Once the results of the flowing afterglow experiments were available, a more precise determination of the EA using threshold

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† Physical Organic Chemistry Department, SRI International, Menlo Park, CA 94025.

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(6) Standard entropies for H$_2$O$_2$, HCF$_3$, HF, and F$^-$ were obtained from ref 8 and 9. Entropies for CF$_3^-$ and HO$_2^-$ were estimated from those of isoelectronic neutrals.

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