Reaction of Bromomalonaldehyde with 3-Methylisocytosine (12). To 13 mL of water was added 0.117 g (0.94 mmol) of 3-methylisocytosine (12) and 0.143 g (0.95 mmol) of bromomalonaldehyde. The pH was adjusted to 4.3 with 2 N NaOH and the reaction mixture was heated to 60 °C under nitrogen atmosphere until the absorbance at 263 nm reached a maximum (6 days). The reaction was then neutralized with 2 N NaOH and the solvent removed in vacuo at 50 °C. The residue was then chromatographed on silica gel preparative-layer plates using 5% $MeOH/CH_2Cl_2$ as the solvent. The band with R_f 0.35 provided 0.026 g (0.15 mmol, 16%) of 8-methyl-3-formylimidazo[1,2-*a*]-pyrimidin-7(8*H*)-one (13) as pale yellow crystals: mp 178–181 °C; UV (H_2O) λ_{max} 264 nm (ϵ 1.51 × 10^4), 280 nm (ϵ 1.45 × 10^4); fluorescence (EtOH) excitation 302 nm and emission 424 nm; mass spectrum, *m/z* (relative intensity) 178 (M^+ + 1, 10.1), 177 (M^+, 100), 148 (M^+ – CHO, 18.3); ^1H NMR (Me_2SO-d_6) δ 3.54 (s, 3 H), 6.35 (d, 1 H, J = 7.8 Hz), 8.15 (s, 1 H), 8.80 (d, 1 H, J = 7.8 Hz), 9.71 (s, 1 H).

Anal. Calcd for $C_8H_7N_3O_2$: C, 54.23; H, 3.98; N, 23.72. Found: C, 53.81; H, 4.28; N, 23.49.

Another band found at R_f 0.25 afforded 0.086 g (0.58 mmol, 61%) of 8-methylimidazo[1,2-*a*]pyrimidin-7(8*H*)-one (14) as yellow crystals: mp 145–148 °C; UV (H_2O) λ_{max} 221 nm (ϵ 1.24 × 10^4); fluorescence (EtOH) excitation 309 nm and emission 455 nm; mass spectrum, *m/z* (relative intensity) 150 (M^+ + 1, 8.8), 149 (M^+, 100), 120 (64.7); ^1H NMR (Me_2SO-d_6) δ 3.48 (s, 3 H), 6.14 (d, 1 H, J = 7.8 Hz), 7.06 (d, 1 H, J < 1 Hz), 7.43 (d, 1 H, J < 1 Hz), 8.36 (d, 1 H, J = 7.3 Hz).

Anal. Calcd for $C_7H_7N_3O$: C, 56.37; H, 4.73; N, 28.17. Found: C, 56.80; H, 5.07; N, 28.28.

Reaction of Bromomalonaldehyde with Adenosine (16). To 170 mL of water was added 1.001 g (3.75 mmol) of adenosine and 0.873 g (5.78 mmol) of bromomalonaldehyde. The pH was adjusted to 4.5 with 2 N NaOH and the solution was heated to 60 °C under nitrogen atmosphere for 72 h. The solvent was then removed in vacuo at 50 °C and the brown residue which remained was separated on a column of Amberlite XAD-4 using 80:20 H_2O:ethanol as the solvent. 1,N^6-Ethenoadenosine (18a) was afforded as white crystals in 10% yield (0.109 g, 0.38 mmol, 13% conversion). The spectral data for 18a were consistent with literature values.[25] Also obtained was 1,N^6-ethenoadenosine-carboxaldehyde (18b) (0.218 g) (0.69 mmol, 18% yield, 24% conversion) as white crystals: mp 216–218 °C; UV (H_2O) λ_{max} 228 nm (ϵ 2.38 × 10^4), 325 nm (ϵ 1.75 × 10^4), 335 nm (ϵ 1.71 × 10^4); fluorescence (EtOH) excitation 270 nm and emission 410 nm; mass spectrum, *m/z* (relative intensity) 319 (M^+, 1.1), 187 (M^+ + H^+ – ribose, 100), 186 (M^+ – ribose, 31.0), 159 (base – CO, 6.3); ^1H NMR (Me_2SO-d_6) δ 4.59–6.12 (m, 9 H), 8.61 (s, 1 H), 8.81 (s, 1 H), 9.95 (s, 1 H), 10.02 (s, 1 H); ^{13}C NMR (Me_2SO-d_6) δ 61.0, 70.1, 74.3, 85.6, 87.9, 122.8, 124.7, 136.6, 141.4, 142.0, 144.7, 147.8, 179.1.

Anal. Calcd for $C_{13}H_{13}N_5O_5 \cdot H_2O$: C, 46.29; H, 4.48; N, 20.76. Found: C, 46.88; H, 4.43; N, 20.94.

Reaction of Bromomalonaldehyde with 9-Ethyladenine. To 60 mL of H_2O was added 0.452 g (2.77 mmol) of 9-ethyladenine (15) and 0.456 g (3.02 mmol) of bromomalonaldehyde. The pH was checked (3.3) and not adjusted. The reaction was then heated to 55 °C under nitrogen atmosphere for 72 h. The reaction was extracted with CH_2Cl_2 (3 × 40 mL) and the organic phase dried over Na_2SO_4. The solvent was removed in vacuo at 50 °C and the residue chromatographed on silica gel plates with 13% $MeOH/CH_2Cl_2$ as the solvent. The band with R_f 0.59 afforded 0.143 g (0.66 mmol, 24%) of 9-ethylethenoadeninecarboxaldehyde (17) as white crystals: mp 223–225 °C; UV (95% ethanol) λ_{max} 230 nm (ϵ 2.06 × 10^4), 328 nm (ϵ 1.51 × 10^4), 339 nm (ϵ 1.50 × 10^4); fluorescence (EtOH) excitation 270 nm and emission 410 nm; mass spectrum, *m/z* (relative intensity) 216 (M^+ + 1, 12.2), 215 (M^+, 100), 187 (M^+ – CO, 34.4), 186 (M^+ – Et, 34.4), 159 (M^+ – Et – CO, 13.5); ^1H NMR ($CDCl_3$) δ 1.62 (t, 3 H), 4.44 (q, 2 H), 8.13 (s, 1 H), 8.37 (s, 1 H), 10.02 (s, 1 H), 10.08 (s, 1 H); ^{13}C NMR (Me_2SO-d_6) δ 15.4, 38.4, 122.4, 124.7, 136.4, 139.6, 143.4, 145.1, 147.9, 179.0.

Anal. Calcd for $C_{10}H_9N_5O$: C, 55.80; H, 4.21; N, 32.54. Found: C, 55.89; H, 4.11; N, 32.34.

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Registry No. 1 (R = Br), 2065-75-0; **2**, 71-30-7; **3**, 1122-47-0; **4**, 65-46-3; **5a**, 55662-66-3; **6a**, 45859-50-5; **6b**, 91898-74-7; **6c**, 91898-75-8; **7**, 91898-76-9; **8**, 91898-77-0; **9**, 108-53-2; **10** (R = H), 55662-68-5; **12**, 2417-17-6; **13**, 91898-78-1; **14**, 91898-79-2; **15**, 2715-68-6; **16**, 58-61-7; **17**, 91898-80-5; **18a**, 39007-51-7; **18b**, 91898-81-6; $Me_2NCH(OMe)_2$, 4637-24-5; N^2-[(dimethylamino)-methylene]-3-methylisocytosine, 91898-82-7.

A Synthesis of *N*-Acyl-1,2-dihydropyridines

Michael J. Wyle and Frank W. Fowler*

Department of Chemistry, State University of New York at Stony Brook, Stony Brook, New York 11794

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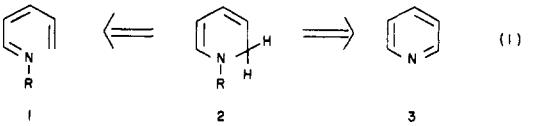
A new approach to the synthesis of *N*-acyl-1,2-dihydropyridines based on the cyclization of *N*-acyl-1-azatrienes is introduced. These latter compounds were not isolated but were produced in the gas phase as transient intermediates by the flash vacuum pyrolysis of *O*-methoxycarbonyl *N*-penta-1,3-dien-5-yl hydroxamic acid derivatives 8.

Simple 1,2-dihydropyridines are electron-rich dienes where the π-system is activated by the heterocyclic nitrogen atom. These compounds are known to undergo reactions characteristic of enamines as well as behaving as reactive partners in cycloaddition reactions.[1] Because of their diverse reactivity they would appear to possess considerable potential in synthetic chemistry. However, 1,2-dihydropyridines that do not contain electron-withdrawing substituents on the ring (2, R = alkyl) (eq 1), are



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relatively unstable with respect to dimerization, polymerization, and oxidation.[1] They are difficult to handle

(1) For reviews on dihydropyridines, see: Stout, D. M.; Meyers, A. I. *Chem. Rev.* **1982**, *82*, 223. Lyle, R. E. In "Heterocyclic Chemistry, Pyridine and Its Derivatives"; Abramovitch, R. A., Ed.; Wiley: New York, 1974; Vol. 14, Part 1, p 137. Eisner, U.; Kuthan, J. *Chem. Rev.* **1972**, 1.

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under normal laboratory conditions and usually require special methods for their preparation.[2] In contrast, the *N*-acyl-1,2-dihydropyridines **2** (R = acyl), because of the electron-withdrawing group on nitrogen, are relatively stable. Since the *N*-acyl group is removable or can be converted into other functional groups, *N*-acyl-1,2-dihydropyridines have attracted much attention as intermediates for the preparation of natural products.[3]

All the synthetically useful preparations of *N*-acyl-1,2-dihydropyridines require either pyridine or a derivative as a starting material.[1] The standard procedure usually involves treatment of the *N*-acylpyridinium salt with organometallic[4] or reducing agents.[5] Unfortunately, the unsubstituted *N*-acyl-1,2-dihydropyridines are not readily available using this method. Although the reduction of *N*-(methoxycarbonyl)pyridinium chloride proceeds in high yield, the reduction of pyridinium ions derived from other carboxylic acid chlorides proceeds in poor yield, if at all. A bromination–dehydrobromination sequence of tetrahydropyridines, that circumvents this problem, has recently been introduced.[6] This method holds considerable promise for the preparation of *N*-acyl-1,2-dihydropyridines.

An alternative synthetic scheme for the preparation of *N*-acyl-1,2-dihydropyridines could involve the electrocyclic ring closure[7] of a 1-azatriene (1). Although the 1,2-dihydropyridine and 1-azatriene equilibrium has been observed previously,[8] it has not been exploited as a general method for *N*-acyl-1,2-dihydropyridine synthesis. The *N*-acyl-1-azatrienes 1 (R = acyl) would be anticipated to be relatively unstable,[9] requiring special techniques for their preparation. Therefore, the major obstacle for the preparation of 1,2-dihydropyridines would probably be the synthesis of the precursor azatrienes 1.

We have previously had success in the synthesis of analogous imines by the thermolysis of *O*-acyl hydroxamic acid derivatives.[10] Application of this method to the preparation of 1,2-dihydropyridines would require the hydroxamic acids 8. These compounds were readily prepared by first treating the hydroxamic acid derivative **5**[11] with 5-bromopenta-1,3-diene. Removal of the *t*-BOC protecting group followed by acylation of the resulting hydroxyl amine **7** with the desired acid chloride gave the hydroxamic acid derivatives 8. Evaporation of these hydroxamic acid derivatives through a hot tube gave the 1,2-dihydropyridines **9a–e** as the only isolable products in 32% to 58% yield (eq 2).

We speculate that this reaction is proceeding by an initial elimination of methyl bicarbonate from the hydroxamic acid derivative **8** to give the azatriene **10** (eq 3).

Because this latter compound contains a trans double bond, it cannot directly cyclize to the 1,2-dihydropyridine. Isomerization of the *trans*-azatriene **10** to the cis isomer **12** can occur by two electrocyclic processes involving the oxazine. We believe this to be a reasonable hypothesis since an isolable *N*-acylazadiene has been observed to readily interconvert with the isomeric oxazine **11**.[12]

Dihydropyridines bearing substituents at the position β to the nitrogen atom are often required in natural product synthesis. The use of 1-azatrienes is an attractive approach to a solution of this problem. The required precursor for the 1-azatriene **15** was prepared by the alkylation of the bromodiene **13**[13] with *N*,*O*-bis(methoxycarbonyl)hydroxylamine (eq 4). Evaporation of the hydroxamic acid derivative **14** through the reaction tube gave the 5-ethyl-*N*-(methoxycarbonyl)-1,2-dihydropyridine (**16**) as the main product. The structure of this compound was confirmed by comparison to an authentic sample (eq 5).

However, proton NMR analysis of the reaction mixture showed that dihydropyridine **16**, in contrast to the dihydropyridines **9a–e** produced in eq 2, was not pure, representing only 60–70% of the product mixture. The other products appear to arise by other pericyclic reactions (i.e., 1,5-hydrogen shifts) of the 1-azatriene **15** involving the

(2) For example, see: Beeken, F.; Bonfiglio, J. N.; Hasan, I.; Piwinski, J. J.; Weinstein, B.; Zollo, K. A. *J. Am. Chem. Soc.* **1979**, *101*, 6677.

(3) Dihydropyridines have been used in than several synthetic schemes for the preparation of alkaloids. For leading and recent references, see: (a) Ogawa, M.; Kuriya, N.; Natsume, M. *Tetrahedron Lett.* **1984**, *25*, 969. (b) Kunng, F.-A.; Gu, J.-M.; Chao, S.; Chen, Y.; Marlano, F. S. *J. Org. Chem.* **1983**, *48*, 4263. (c) Raucher, S.; Lawrence, R. F. *Tetrahedron Lett.* **1983**, *24*, 2927. (d) Comins, D. L.; Abdullah, A. H.; Smith, R. K. *Tetrahedron Lett.* **1983**, *24*, 2711. (e) Krow, G. R.; Carey, J. T.; Cannon, K. C.; Henz, K. J. *Tetrahedron Lett.* **1982**, *23*, 2527. (f) Szantay, C.; Keve, T.; Bolcskel, H.; Acs, T. *Tetrahedron Lett.* **1983**, *24*, 5539.

(4) See: Comins, D. L.; Stroud, E. D.; Herrick, J. J. *Heterocycles* **1984**, 22, 151 and references cited therein.

(5) Fowler, F. *J. Org. Chem.* **1972**, *37*, 1321.

(6) Fowler, F. W., unpublished results. This method has recently been improved and applied to the preparation of indole alkaloids (see ref 3c).

(7) Marvel, E. N. "Thermal Electrocyclic Reactions"; Academic Press: New York, 1980.

(8) Reference 7, p 323.

(9) Simple *N*-acyl imines are relatively unstable, usually being prepared as transient intermediates (for example, see: Weinreb, S. M.; Levin, J. I. *Heterocycles* **1979**, *12*, 949).

(10) Cheng, Y.-S.; Lupo, A., Jr.; Fowler, F. W. *J. Am. Chem. Soc.* **1983**, *105*, 7696.

(11) Zinner, G.; Nebel, G.; Hitz, M. *Arch. Pharm.* **1970**, *303*, 317.

(12) Overman, L. E.; Clizbe, L. A.; Freerks, R. L.; Marlowe, C. K. *J. Am. Chem. Soc.* **1981**, *103*, 2807.

(13) (a) Carpino, L. A.; Giza, C. A.; Carpino, B. A. *J. Am. Chem. Soc.* **1959**, *81*, 955. (b) Boyland, E.; Nery, R. *J. Chem. Soc. C* **1966**, 346.

ethyl group. Several attempts to purify this reaction mixture by gas–liquid, thin-layer, and column chromatography were not successful.

In summary, we have developed a new synthesis of N-acyl-1,2-dihydropyridines that is conceptually different from the available methods. The dihydropyridine is prepared by a cyclization process rather than by modification of an existing six-membered ring.

Experimental Section

Melting points were recorded on a Fischer-Johns melting point apparatus and are uncorrected; infrared spectra were recorded on a Perkin-Elmer 727 spectrometer. The absorption intensities are described as being either strong (s), medium (m), or weak (w) and were all referenced to the 1601.4 absorption of polystyrene. Proton NMR spectra were recorded on either a Varian EM-360, HFT-80, or a Nicolet NT-300 spectrometer. All chemical shifts were reported in ppm (δ units) from tetramethylsilane as an internal standard. Low-resolution mass spectra were recorded on a Hewlett-Packard 5980A spectrometer. High-resolution mass spectra were recorded on an AEI MS-30 spectrometer. Analytical gas chromatography were performed on a Hewlett-Packard 5830 chromatograph equipped with a flame ionization detector. Preparative gas chromatography were performed on a Varian 920 chromatograph equipped with a hot wire detector. Thin-layer chromatography were performed on 70–230 mesh silica gel 60 (E.M. Merck). All dry solvents were distilled from sodium benzophenone ketyl under a nitrogen atmosphere unless otherwise stated.

N-(*tert*-Butoxycarbonyl)-O-(methoxycarbonyl)hydroxylamine (5). A cold solution of 1.25 g of sodium hydroxide in 12 mL of water was added dropwise over a period of 5–10 min to a precooled stirring mixture of 2.00 g of N-(*tert*-butoxycarbonyl)hydroxylamine,[13] 1.40 g of methyl chloroformate, and 20 mL of water. The reaction flask warmed to room temperature during the addition, and the mixture was allowed to stir for an additional 45 min. The mixture was then cooled in an ice bath, acidified with 6 M HCl, and extracted with ether. These were combined, dried over $MgSO_4$, and concentrated in vacuo to give 2.73 g (95%) of **5** as a yellow oil. Purification was obtained by passing the oil through a column of silica gel using petroleum ether and acetone (10/1), giving 2.25 g (78%) of a clear oil which crystallized on standing overnight. Repeated recrystallization (hexanes and ether) gave colorless needles: mp 53.5–54 °C (lit.[13] mp 53–55 °C), ^{1}H NMR ($CDCl_3$, EM-360) δ 1.53 (s, 9 H), 3.83 (s, 3 H), 8.30 (s, 1 H); IR (film) 3325 (m, NH), 3010 (m, CH_3), 1788 (s, C=O), 1740 cm^{-1} (s, C=O).

5-[N-(*tert*-Butoxycarbonyl)-O-(methoxycarbonyl)hydroxylamino]-1,3-pentadiene (6). The standard alkylation procedure: In a round-bottom flask, 10 mL of DMF, 1.54 g of 5-bromo-1,3-pentadiene[14] and 2.00 g of **5** were combined. Anhydrous potassium carbonate (2.90 g) was added over 2 min with stirring. The mixture was purged with nitrogen and then allowed to stir for 20 to 30 h. The mixture was diluted in 40 mL of water and extracted with ether. These were combined, washed with water, dried over $MgSO_4$, and concentrated in vacuo to give 2.36 g of a yellow oil. Passing this residue through a column of silica gel with hexanes and acetone (10/1) afforded 2.10 g (78%) of a clear oil showing greater than 95% purity by GC and homogeneous by TLC: ^{1}H NMR ($CDCl_3$, EM-360) δ 1.51 (s, 9 H), 3.81 (s, 3 H), 4.15 (d, J = 6.5 Hz, 2 H), 5.01–6.51 (m, 5 H); IR (film) 2915 (m, CH), 1795 (s, C=O), 1720 cm^{-1} (s, C=O); high-resolution MS, m/z (relative intensity) (M – C_4H_8) 201.0633 (0.15), $C_8H_{11}NO_5$ requires 201.0661.

5-[N,O-Bis(methoxycarbonyl)hydroxylamino]-1,3-pentadiene (8a). The required N,O-bis(methoxycarbonyl)-hydroxylamine was prepared by a modification of the Carpino procedure.[13a] To a stirring, ice bath cooled mixture of hydroxylamine hydrochloride (13.0 g), methyl chloroformate (17.1 g), and water (48 mL), was added 72 mL of a 20% sodium hydroxide solution. The addition was made dropwise over a period of 40 min, and the reaction was allowed to stir for an additional 90 min. Another equivalent of methyl chloroformate (16.2 g) was added dropwise over a period of 10 min. The ice bath was then removed, and 20% NaOH (50 mL) was added dropwise over a period of 10 min. The reaction was then allowed to stir for 60 min at room temperature. The mixture was cooled and acidified with 6 M HCl. The acidified mixture was extracted with ether, and these were combined and washed with water. The ethereal extract was then dried over $MgSO_4$ and concentrated in vacuo to afford 13.4 g (53%) of a yellow oil. The product was purified by bulb-to-bulb distillation and was shown to be homogeneous by TLC: ^{1}H NMR ($CDCl_3$, EM-360) δ 3.75 (s, 3 H), 3.85 (s, 3 H), 8.15 (s, 1 H); IR (film) 3315 (m, NH), 3001 (m, CH_3), 1790 (s, C=O), 1755 (s, C=O), 1608 (w, C=C) cm^{-1}. The standard alkylation procedure using N,O-bis(methoxycarbonyl)hydroxylamine and 5-bromo-1,3-pentadiene afforded **8a** as a yellow oil. Silica gel column chromatography with petroleum ether and acetone (10/1) gave a clear oil (55%) showing 99% purity by GC and homogeneous by TLC: ^{1}H NMR ($CDCl_3$, EM-360) δ 3.72 (s, 3 H), 3.81 (s, 3 H), 4.18 (d, J = 6 Hz, 2 H), 4.97–6.43 (m, 5 H); IR (film) 2995 (m, CH), 1795 (s, C=O), 1735 (s, C=O), 1608 cm^{-1} (w, C=C); high-resolution MS, m/z (relative intensity) (M – CO_2CH_3) 140.0720 (14.7), $C_7H_{10}NO_2$ requires 140.0712.

5-[N-(Phenylacetyl)-O-(methoxycarbonyl)hydroxylamino]-1,3-pentadiene (8b). The Standard Hydrolysis/Acylation Procedure. A cooled (ca. –10 °C) round-bottomed flask containing 300 mg of **6** and 3 mL of nitromethane was treated with a stream of HCl gas for 8 min. The reaction mixture was then removed from the ice–acetone bath and concentrated in vacuo. To this residue (the hydroxylamine **7**) was added 3 mL of methylene chloride, 182 mg of phenylacetyl chloride, and 300 mg of sodium carbonate. The reaction mixture was allowed to stir for 1 h. The mixture was filtered, and concentrated in vacuo to afford a red-brown oil. Silica gel column chromatography afforded 288 mg (90%) of a clear oil showing 100% purity by GC, homogeneous by TLC: ^{1}H NMR ($CDCl_3$, CFT-20) δ 3.65 (s, 2 H), 3.79 (s, 3 H), 4.32 (d, J = 6.4 Hz, 2 H), 5.03–6.40 (m, 5 H), 7.23 (s, 5 H); IR (film) 3008 (w, CH), 2933 (w, CH), 1788 (s, C=O), 1673 (s, C=O), 1600 cm^{-1} (w, C=C); high-resolution MS, m/z (relative intensity) (M$^+$) 275.1157 (0.23), $C_{15}H_{17}NO_4$ requires 275.1157.

5-[N-Acetyl-O-(methoxycarbonyl)hydroxylamino]-1,3-pentadiene (8c). The standard hydrolysis and acylation procedure followed by silica gel column chromatography afforded a clear oil (62%) showing greater than 97% purity by GC, homogeneous by TLC: ^{1}H NMR ($CDCl_3$, CFT-20) δ 2.07 (s, 3 H), 3.89 (s, 3 H), 4.34 (d, J = 6 Hz, 2 H), 5.04–6.44 (m, 5 H); IR (film) 3055 (w, CH), 3000 (w, CH), 1790 (s, C=O), 1690 (s, C=O), 1610 cm^{-1} (w, C=C); high-resolution MS, m/z (relative intensity) (M – OCO_2CH_3) 124.0764 (22.4), $C_7H_{10}NO$ requires 124.0762.

5-[N-Benzoyl-O-(methoxycarbonyl)hydroxylamino]-1,3-pentadiene (8d). The standard hydrolysis and acylation procedure followed by silica gel column chromatography afforded a clear oil (88%) showing 99% purity by GC, homogeneous by TLC: ^{1}H NMR ($CDCl_3$, CFT-20) δ 3.77 (s, 3 H), 4.38 (d, J = 5.6 Hz, 2 H), 5.04–6.45 (m, 5 H), 7.30–7.62 (m, 5 H); IR (film) 3015 (w, Ar CH), 2945 (w, CH), 1790 (s, C=O), 1675 (s, C=O), 1600 cm^{-1} (w, C=C); high-resolution MS, m/z (relative intensity) (M$^+$) 261.1019 (0.69), $C_{14}H_{15}NO_4$ requires 261.1001.

5-[N-5-Hexenoyl-O-(methoxycarbonyl)hydroxylamino]-1,3-pentadiene (8e). The required hex-5-enoyl chloride was prepared from hex-5-enoic acid[15] by using thionyl chloride: ^{1}H NMR ($CDCl_3$, EM-360) δ 1.33–2.32 (m, 5 H), 2.83 (t, J = 6 Hz, 2 H), 4.83–6.07 (m, 3 H). The standard hydrolysis and acylation procedure followed by silica gel column chromatography afforded a clear oil (60%), showing 99% purity by GC, homogeneous by TLC: ^{1}H NMR ($CDCl_3$, CFT-20) δ 1.67–2.40 (m, 6 H), 3.88 (s, 3 H), 4.32 (d, J = 6.8 Hz, 2 H), 4.87–6.42 (m, 8 H); IR (film) 2933 (m, CH), 1784 (s, C=O), 1674 (s, C=O), 1604 cm^{-1} (w, C=C); high-resolution MS, (relative intensity) (M – OCO_2CH_3) 178.1218 (23), $C_{11}H_{16}NO$ requires 178.1231.

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Standard Pyrolysis Procedure. Using an apparatus analogous to the one previously described,[10] 25–100 mg of the hydroxamic acid derivatives **8a–e** were converted to the 1,2-dihydropyridines **9a–e**. Unless otherwise stated, the crude products were purified by being passed through a short silica gel column with methylene chloride and acetone (20/1).

***N*-(Methoxycarbonyl)-1,2-dihydropyridine (9a).** Using the standard pyrolysis procedure, 64 mg of 5-[*N*,*O*-bis(methoxycarbonyl)hydroxylamino]-1,3-pentadiene afforded 18 mg (43%) of the 1,2-dihydropyridine, showing 95% purity by GC, homogeneous by TLC. The spectral data were consistent with those previously reported for **9a**:[5] ^{1}H NMR ($CDCl_3$, CFT-20) δ 3.75 (s, 3 H), 4.34 (d of d, J = 4.2 Hz, 2 H), 5.11 (t, J = 7 Hz, 1 H), 5.35 (m, 2 H), 6.55–6.80 (m, 1 H); IR (film) 2955 (w, CH), 1800 (w), 1720 (s, C=O), 1660 cm^{-1} (m).

***N*-(Phenylacetyl)-1,2-dihydropyridine (9b).** The standard pyrolysis procedure with 62 mg of 5-[*N*-(phenylacetyl)-*O*-(methoxycarbonyl)hydroxylamino]-1,3-pentadiene (**8b**) afforded 20 mg (45%) of the 1,2-dihydropyridine **9b** showing greater than 95% purity by GC, homogeneous TLC: ^{1}H NMR ($CDCl_3$, EM-360) δ 3.68 (s, 2 H), 4.38 (m, 2 H), 4.90–5.23 (m, 1 H), 5.56–6.00 (m, 2 H), 6.51 (d, J = 8 Hz, 1 H), 7.23 (s, 5 H); IR (film) 3025 (w), 1635 (s, C=O), 1581 (m), 1492 (w), 1452 (m) cm^{-1}; high resolution MS, m/z (relative intensity) (M^+) 199.0982 (19.90), $C_{13}H_{13}NO$ requires 199.0997.

***N*-Acetyl-1,2-dihydropyridine (9c).** The standard pyrolysis procedure with 60 mg of 5-[*N*-acetyl-*O*-(methoxycarbonyl)-hydroxylamino]-1,3-pentadiene (**8c**) afforded 12 mg (32%) of the 1,2-dihydropyridine **9c** showing greater than 95% purity by GC, homogeneous TLC: ^{1}H NMR ($CDCl_3$, CFT-20) δ 2.13 (s, 3 H), 4.41 (d of d, J = 4, 1.5 Hz, 2 H), 5.18 (t, J = 8 Hz, 1 H), 5.45–6.00 (m, 2 H), 6.45 (d, J = 4 Hz, 1 H); IR (film) 1727 (m), 1640 (s, C=O), 1588 (m), 1425 cm^{-1} (s); high-resolution MS, m/z (relative intensity) (M^+) 123.0686 (7.17), C_7H_9NO requires 123.0684.

***N*-Benzoyl-1,2-dihydropyridine (9d).** The standard pyrolysis procedure with 55 mg of 5-[*N*-benzoyl-*O*-(methoxycarbonyl)-hydroxylamino]-1,3-pentadiene (**8d**) afforded 17 mg (41%) of the 1,2-dihydropyridine **9d** showing 98% purity by GC, homogeneous by TLC: ^{1}H NMR ($CDCl_3$, CFT-20) δ 4.50 (d of d, J = 4, 2 Hz, 2 H), 5.15 (t, J = 8 Hz, 1 H), 5.50–6.00 (m, 2 H), 6.41 (d, J = 8 Hz, 1 H), 7.17–7.60 (m, 5 H); IR (film) 3050 (w), 1722 (m), 1640 (s, C=O), 1580 cm^{-1} (m); high-resolution MS, m/z (relative intensity) (M^+) 185.0837 (26.1), $C_{12}H_{11}NO$ requires 185.0841.

***N*-5-Hexenoyl-1,2-dihydropyridine (9e).** The standard pyrolysis procedure with 49 mg of 5-[*N*-5-hexenoyl-*O*-(methoxycarbonyl)hydroxylamino]-1,3-pentadiene (**8e**) afforded 20 mg (58%) of the 1,2-dihydropyridine **9e** showing greater than 95% purity by GC, homogeneous by TLC: ^{1}H NMR ($CDCl_3$, EM-360) δ 1.50–2.50 (m, 6 H), 4.35 (d, J = 3 Hz, 2 H), 4.70–5.27 (m, 3 H), 5.40–6.10 (m, 3 H), 6.44 (d, J = 7.4 Hz, 1 H); IR (film) 3120 (w), 2975 (m, CH), 1650 (s, C=O), 1585 (m); high resolution MS, m/z (relative intensity) (M^+) 177.1173 (3.24), $C_{11}H_{15}NO$ requires 177.1154.

4-[[*N*,*O*-Bis(methoxycarbonyl)hydroxylamino]methyl]-hexa-1,3-diene (14). The required bromo diene **13** was prepared in three steps from acrolein and ethyl 2-bromobutyrate by using the Wittig reaction.[17a] Refluxing of acrolein (2 g) and ethyl 2-(triphenylphosphoranylidene)butyrate[16] (7 g) for 17 h followed by a bulb-to-bulb distillation of the product gave ethyl 2-ethylpenta-2,4-dieneoate[17b] in 64% yield that was homogeneous by TLC: ^{1}H NMR ($CDCl_3$, EM-360) δ 0.75–1.44 (m, 6 H), 2.39 (q, J = 7 Hz, 2 H), 4.12 (q, 7 Hz, 2 H), 5.25–5.60 (m, 2 H), 6.28–7.11 (m, 2 H); IR (film) 3018 (m, CH), 1708 (s, C=O), 1630 (w, C=C), 1590 (w, C=C), 1275 (m), 1240 (s), 1172 (m), 1105 cm^{-1} (m). Reduction of 1.08 g of this unsaturated ester with 0.608 mg of $LiAlH_4$ in 10 mL of dry ether for 3 h at room temperature followed by workup with 10% NaOH and $MgSO_4$ drying gave 4-ethyl-1,3-pentadien-5-ol in 76% yield: ^{1}H NMR ($CDCl_3$, EM-360) δ 1.03 (t, J = 7 Hz, 3 H), 1.49 (t, J = 6 Hz, 1 H) 2.18 (q, J = 7 Hz, 2 H), 4.00 (d, J = 5 Hz, 2 H), 4.93–5.23 (m, 2 H), 5.83–6.79 (m, 2 H); IR (film) 3325 (m, OH), 2970 (m, CH), 1655 (w, C=C), 1603 cm^{-1} (w, C=C). The bromide **13** was obtained by treating 110 mg of the above alcohol with 300 mg of PBr_3 in 2 mL of ether at 0 °C for 3.5 h. The reaction was worked up by stirring for 30 min with 1.5 g of solid $NaCO_3$ followed by filtration and concentration in vacuo to give 137 mg (80%) of **13** that was homogeneous by TLC: ^{1}H NMR ($CDCl_3$, EM-360) δ 1.04 (t, J = 7 Hz, 3 H), 2.33 (d, J = 7 Hz, 2 H), 3.96 (s, 2 H), 5.01–5.34 (m, 2 H), 5.97–6.81 (m, 2 H); IR (film) 3000 (s), 1460 (w), 1435 (w), 1415 (w), 1250 (m), 1200 (s), 980 (s), 703 (s). This bromo diene was used immediately for the next step. The standard alkylation procedure using *N*,*O*-bis(methoxycarbonyl)hydroxylamine and 5-bromo-4-ethyl-1,3-pentadiene followed by silica gel column chromatography (hexanes and ethyl acetate, 8/1) afforded a clear oil in 68% yield showing 99% purity by GC, homogeneous by TLC: ^{1}H NMR ($CDCl_3$, CFT-20) δ 1.03 (t, J = 7 Hz, 3 H), 2.25 (q, J = 7 Hz, 2 H), 3.79 (s, 3 H), 3.86 (s, 3 H), 4.23 (s, 2 H), 5.05–5.30 (m, 2 H), 5.90 (d, J = 10.5 Hz, 1 H), 6.33–6.80 (m, 1 H); IR (film) 3000 (m, CH), 1790 (s, C=O), 1725 (s, C=O), 1445 (s); high-resolution MS, m/z (relative intensity) ($M - OCO_2CH_3$) 168.1014, $C_9H_{14}NO_2$ requires 168.1025.

Thermolysis of 14. 5-Ethyl-*N*-(methoxycarbonyl)-1,2-dihydropyridine. Using the standard pyrolysis procedure, 50 mg of 4-[[*N*,*O*-bis(methoxycarbonyl)hydroxylamino]methyl]hexa-1,3-diene (**14**) gave 32 mg (100%) of crude product mixture. A comparison of the NMR spectrum of this reaction mixture with an authentic sample of 5-ethyl-*N*-(methoxycarbonyl)-1,2-dihydropyridine[6] clearly showed that it was the major product in this reaction mixture. Efforts at purification using silica gel, alumina, and preparative GC (SE-30 column, 6 ft) all failed to isolate the dihydropyridine in a pure state.

5-Ethyl-*N*-(methoxycarbonyl)-1,2-dihydropyridine (16). An authentic sample of **16** was prepared according to the following scheme. To 1.00 g of $NaBH_4$ and 5.07 g of 3-ethyl-*N*-(methoxycarbonyl)-1,2-dihydropyridine in 30 mL of dry benzene cooled to ca. 5 °C was added 7 mL of trifluoroacetic acid over 15 min. The reaction mixture was allowed to stir for an additional 15 min and 30 mL of 20% NaOH was added slowly at such a rate to prevent excessive foaming. The ice bath was removed and the mixture was allowed to stir for an additional 30–45 min. The mixture was extracted with ether. The ethereal extracts were combined, washed with 10% HCl and water, and dried with anhydrous magnesium sulfate. Removal of the ether in vacuo and bulb-to-bulb distillation (0.5 torr) of the residue gave 2.6 g (55%) of the tetrahydropyridine **18**. This compound, without further purification, was dissolved in 30 mL of methylene chloride, cooled to −80 °C; and treated with 2.40 g of bromine dissolved in 3 mL of methylene chloride. After allowing the reaction mixture to stir for 30 min at −80 °C, it was allowed to warm to room temperature and the solvent was removed in vacuo. Pentane was added to the residue and the slightly cloudy yellow solution was treated with decolorizing carbon. The colorless solution on cooling gave a colorless precipitate. Recrystallization from pentane gave an analytically pure sample of the dibromide, mp 53–55 °C. The 1,2-dihydropyridine **16** was prepared by treating 0.75 g of the dibromide with 1.25 g of 1,4-diazabicyclo[2.2.2]octane in 1.0 mL of dimethylformamide. The reaction was refluxed in an oil bath under nitrogen for 3 min. During this time the reactants dissolved and a precipitate formed. The reaction mixture was cooled, diluted with water, and extracted with ether. The ether extracts were washed with 10% HCl and water and dried with anhydrous magnesium sulfate. Removal of the solvent gave 0.175 g of the 1,2-dihydropyridine **16**. The properties of all of the above compounds are consistent with those previously reported.[4]

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Registry No. **4**, 1001-93-0; **5**, 27920-29-2; (*E*)-**6**, 91760-04-2; (*E*)-**7**, 91760-05-3; (*E*)-**8a**, 91760-06-4; (*E*)-**8b**, 91760-07-5; (*E*)-**8c**, 91760-08-6; (*E*)-**8d**, 91760-09-7; (*E*)-**8e**, 91760-10-0; **9a**, 33707-36-7; **9b**, 91760-11-1; **9c**, 91760-12-2; **9d**, 91760-13-3; **9e**, 91760-14-4; (*E*)-**13**, 91760-15-5; (*E*)-**14**, 91760-16-6; **16**, 72298-15-8; **17**,

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72019-96-6; 18, 77612-52-3; 18 dibromide, 91760-19-9; t-BuOC(O)NHOH, 36016-38-3; $ClC(O)OCH_3$, 79-22-1; $NH_2OH·HCl$, 5470-11-1; $MeOC(O)NHOC(O)OMe$, 6092-55-3; $PhCH_2C(O)Cl$, 103-80-0; $CH_2=CH(CH_2)_3C(O)Cl$, 36394-07-7; $CH_2=CH(CH_2)_3CO_2H$, 1577-22-6; $CH_3CH_2C(=PPh_3)C(O)OEt$, 22592-13-8; $CH_3CH_2C(Br)HC(O)OEt$, 533-68-6; $CH_2=CHCH=C(Et)C(O)OEt$, 91760-17-7; $HOCH_2C(Et)=CHCH=CH_2$, 91760-18-8; Ph_3P, 603-35-0; acrolein, 107-02-8.

Thermal Reorganizations of 1,2:3,4-Dibenzotropilidene (5*H*-Dibenzo[*a*,*c*]cycloheptene), 7,7′-Bi(1,2:3,4-dibenzotropyl) [5,5′-Bi(5*H*-dibenzo[*a*,*c*]cycloheptenyl)], and the 1,2:3,4-Dibenzotropyl (Dibenzo[*a*,*c*]cycloheptenyl) Free Radical

Martin Pomerantz,* Nissanke L. Dassanayake, Timothy R. McManus,[1] and Charles H. Reynolds[1]

Department of Chemistry, The University of Texas at Arlington, Arlington, Texas 76019-0065

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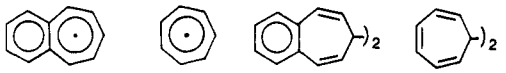
1,2:3,4-Dibenzotropilidene (5*H*-dibenzo[*a*,*c*]cycloheptene, **8**) has been shown to thermally produce phenanthrene (**12**), 9-methylphenanthrene (**13**), 9,10-dihydrophenanthrene (**14**), and 1,2:3,4-dibenzocycloheptadiene (6,7-dihydro-5*H*-dibenzo[*a*,*c*]cycloheptene, **15**). With added naphthalene, to trap the extruded one-carbon species, 1,2-benzotropilidene (**16**), α-methyl- and β-methylnaphthalene (**17** and **18**), 1,2-benzo-1,3-cycloheptadiene (**19**), and benzocycloheptene (**20**) were also produced. Reaction of 1,2-benzotropilidene with phenanthrene produced 1,2:3,4-dibenzotropilidene (**8**) and naphthalene, showing the reversibility of this thermal carbon extrusion reaction. 7,7-Bi(1,2:3,4-dibenzotropyl) [5,5′-bi(5*H*-dibenzo[*a*,*c*]cycloheptenyl), **10**] was prepared by VCl_2 reduction of the 1,2:3,4-dibenzotropylium cation. Thermally it underwent the same reactions as **8**, demonstrating that it is the 1,2:3,4-dibenzotropyl (dibenzo[*a*,*c*]cycloheptenyl) free radical (**9**) which lost a carbon atom (CH group) to the aromatic acceptor. At 200 °C the dimer **10** produced significant quantities of 9-methylphenanthrene (**13**), shown not to arise from **8**, in addition to phenanthrene, **12**. Mechanisms for the thermal transfer of a CH group from **9** to an aromatic acceptor and for the production of **13** from **9** are presented.

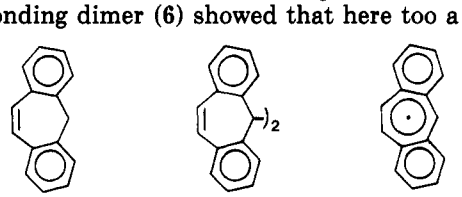
A number of years ago we noted that a one-carbon fragment could be thermally extruded from benzotropilidene[2,3] and this extruded species could be trapped by an aromatic acceptor such as benzene to produce naphthalene and toluene. The yield of naphthalene was in the range of 5–20%, showing that this pathway, while somewhat important, was not the major one. We further noted that in the thermolysis of the parent, tropilidene, the yield of benzene, also produced by the loss of a one carbon species, was only about 2–3%. In these cases the reactive intermediates were shown to be the benzotropyl (**1**) and tropyl (**2**) radicals by independent production from



1 **2** **3** **4**

their respective dimers, **3** and **4**,[2,4] and it was postulated that these radicals transferred a CH group to the aromatic acceptor.

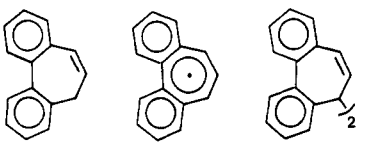
Examination of 1,2:5,6-dibenzotropilidene (**5**) and the corresponding dimer (**6**) showed that here too a carbon



5 **6** **7**

atom (CH group) was lost from the intermediate radical **7** and anthracene was produced. The yields of anthracene (up to about 45% absolute yield) were considerably higher than the yields of naphthalene from benzotropilidene and dimer **3**, and thus CH loss represents an important pathway for radical **7**.

We now report on the thermal extrusion of a one-carbon species from 1,2:3,4-dibenzotropilidene (5*H*-dibenzo[*a*,*c*]-cycloheptene, **8**) and from the 1,2:3,4-dibenzotropyl (5*H*-



8 **9** **10**

dibenzo[*a*,*c*]cycloheptenyl) free radical (**9**) and its transfer to an aromatic acceptor (naphthalene). Radical **9** was formed independently from the dimer 7,7-bi(1,2:3,4-dibenzotropyl) [5,5′-bi(5*H*-dibenzo[*a*,*c*]cycloheptenyl), **10**] by thermal cleavage of the central C–C bond. Absolute yields of up to 93% were observed, showing that this CH transfer is now the overwhelmingly preferred reaction.

Results

Preparation and Pyrolysis of 1,2:3,4-Dibenzotropilidene (8). 1,2:3,4-Dibenzotropilidene (**8**) was prepared by the reactions shown in Scheme I.[5,6] The sequence for preparation of alcohol **11** was the same as that in the literature.[5,6] Although 1,2:3,4-dibenzotropilidene (**8**) has been prepared previously by other methods,[7,8] we prepared it by refluxing the alcohol (**11**) with *p*-toluenesulfonyl chloride in pyridine.

Two types of pyrolyses were run. Those we call "low pressure", which involved heating 20–40 mg of **8** in an evacuated 125-mL Pyrex ampule for 1 h at the specified

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