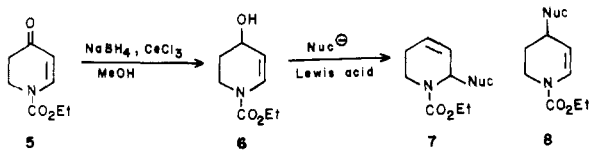

5 6 7 8

nium ion system (e.g., pyridinium ions).[2]

When **6** was exposed to thiophenol or ethanol with use of pyridinium *p*-toluenesulfonate as catalyst, the 4-substituted-Δ^2-piperidines **7f** and **7g** (Table I) resulted. Apparently, the regiochemical orientation observed here represents a thermodynamic result. While initial kinetic addition may occur at the 2-position, an anomeric effect weakened by nitrogen lone-pair interaction with the carbethoxy substituent and the consequent nonbonded interactions between the ortho-related substituents as well as the resonance stabilization of the enamido system lead to migration of the heteroatom nucleophile to the 4-position. With trimethylsilyl triflate as catalyst, **6** likewise reacted with ethanol to afford **7f** plus a small amount of the diaddition product, *N*-carbethoxy-2,4-diethoxypiperidine.[7]

The work described herein thus provides a useful entry to 2-substituted-Δ^3-piperidines (for carbon nucleophiles) via the nitrogen analogue of the Ferrier rearrangement process. The chemistry further reveals the importance of iminium salts as reactive intermediates for organic synthesis.[8,9]

Experimental procedures for the preparation of **6** and its transformation to **7a** and **7b** follow.

***N*-Carbethoxy-4-hydroxy-1,2,3,4-tetrahydropyridine (6).** To a stirred solution of the *N*-carbethoxy-4-oxo-1,2,3,4-tetrahydropyridine (**5**, 2.97 g, 17.6 mmol) and cerium(III) chloride hexahydrate (6.24 g, 17.6 mmol) in 44 mL of methanol was added sodium borohydride (678 mg, 17.6 mmol) in small portions at 0 °C over 20 min. The reaction mixture was diluted with 40 mL of water, concentrated in vacuo to ~40 mL, and extracted with ether (4 × 40 mL). The combined organic extracts were dried over anhydrous potassium carbonate, filtered, and concentrated to afford 2.81 g (93%) of the alcohol **6** as a colorless oil. This compound was used in all subsequent reactions without further purification. Attempted chromatographic purification of **6** resulted in decomposition: IR (thin film) 3439, 3023, 2930, 2884, 1708, 1648, 1462, 1415, 1377, 1344, 1335, 1326, 1296, 1228, 1164, 1059, 997, 948, 878, 859, 834, 770, 744 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.31 (t, 3 H, CH_3, J = 7.1 Hz), 1.60 (d, 1 H, OH, J = 5.5 Hz), 1.70–1.98 (m, 2 H, -CH_2CH_2N<), 3.41 (br t, 1 H, >CH_{ax}–N<, J = 11.1 Hz), 3.92 (m, 1 H, >CH_{eq}–N<), 4.10–4.32 (overlapping q and m, 3 H, CH_2CH_3, J = 7.1 Hz, >CHOH), 5.02 and 5.11 (two br s, 1 H, -CH=CHCHOH, collapsed to two d on irradiation at 4.22, J = 6.7 Hz), 6.98 (two br d, 1 H, -CH=CHCHOH, J = 8.1 Hz); mass spectrum (15 eV), m/z 171 (M^+), 154, 153, 152, 142, 124, 108, 102, 98, 80 (base), 74, 59, 45, 31, 29; exact mass calcd for $C_8H_{13}NO_3$ 171.0895; found 171.0887.

***N*-Carbethoxy-2-allyl-1,2,5,6-tetrahydropyridine (7a).** To a stirred solution of the allylic alcohol **6** (2.01 g, 11.8 mmol) and allyltrimethylsilane (3.79 mL, 23.3 mmol) in 20 mL of methylene chloride cooled to −78 °C was added stannic chloride (1.70 mL, 14.5 mmol) dropwise over 5 min. After 30 min, the reaction mixture was quenched with saturated aqueous sodium bicarbonate solution, warmed to room temperature, and extracted with ether (4 × 50 mL). The combined organic extracts were dried over anhydrous potassium carbonate, filtered, and concentrated in vacuo. The residue was chromatographed on 200 g of silica gel with 3% ethyl acetate–hexanes as eluent to afford **8a** (30 mg) and a mixture of **7a** and **8a** (21 mg). On further elution, 2.06 g (90%) of **7a** was obtained as a colorless liquid: IR (thin film) 2904, 1695, 1456, 1352, 1326, 1243, 1195, 1103, 1034, 912, 767, 711 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.27 (t, 3 H, CH_3, J = 7.1 Hz), 1.89–2.02 (m, 1 H, >NCH_2CH_{ax}—), 2.20 (br s, 1 H, >NCH_2CH_{eq}—), 2.34 (t, 2 H, -CH_2CH=CH_2, J = 6.9 Hz), 2.90 (br s, 1 H, -$(CH_2)CH_{ax}N$<), 4.11–4.18 (m, 3H, -$CH_2CH_{eq}NC(O)OCH_2$-), 4.43 (br s, 1 H, >$NCHCH_2CH$=CH_2), 5.02–5.10 (m, 2 H, -CH_2CH=CH_2), 5.62–5.93 (m, 3 H, -CH=CH-, -CH=CH_2); mass spectrum (15 eV), m/z 196 (M^+ + 1), 154 (M^+ − CH_2CH=CH_2, base), 126, 82, 58, 43; exact mass calcd for $C_8H_{12}NO_2$ (M^+ − CH_2CH=CH_2) 154.0868, found 154.0868.

***N*-Carbethoxy-2-cyano-1,2,5,6-tetrahydropyridine (7b).** A stirred solution of the allylic alcohol **6** (34.2 mg, 0.200 mmol) and trimethylsilyl cyanide (160 μL, 1.20 mmol) in 8 mL of methylene chloride under a nitrogen atmosphere was cooled to −78 °C and treated with trimethylsilyl triflate (58.0 μL, 0.300 mmol). After 3 h, the reaction mixture was quenched with saturated aqueous sodium bicarbonate solution, warmed to room temperature, and extracted with ether (3 × 10 mL). The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel with 5% ethyl acetate–hexanes as eluent to give 25.2 mg (70%) of **7b** as an oil: IR (thin film) 2917, 1704, 1461, 1420, 1376, 1335, 1300, 1275, 1259, 1236, 1203, 1168, 1111, 1056, 1037, 987, 899, 770, 709 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.31 (t, 3 H, CH_3, J = 7.1 Hz), 2.06–2.40 (m, 2 H, CH_2CH=CH-), 2.95–3.21 (m, 1 H, >$CH_{ax}N$<), 4.10–4.40 (m, 3 H, -CH_2CH_3, >$CH_{eq}N$<), 5.25 and 5.38 (two br s, 1 H, >CHCN), 5.70 (br s, 1 H, -CH=CHCHCN), 6.11 (br s, 1 H, -CH=CHCH(CN)-); mass spectrum (15 eV), m/z 180 (M^+), 152, 151 (base), 135, 125, 108, 107, 81, 80, 68, 42, 29; exact mass calcd for $C_9H_{12}N_2O_2$ 180.0899; found 180.0897.

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Supplementary Material Available: Characterization data for **7c–g** (2 pages). Ordering information is given on any current masthead page.

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(8) For some other examples of the trapping of iminium salts by allylsilanes, see: Hart, D. J.; Tsai, Y.-M. *Tetrahedron Lett.* **1981**, *22*, 1567. Kraus, G. A.; Neuenschwander, K. *J. Chem. Soc., Chem. Commun.* **1982**, 134.

(9) For a report concerning the use of 2-cyano-Δ^3-piperidines as 5,6-dihydropyridinium salt equivalents, see: Grierson, D. S.; Harris, M.; Husson, H.-P. *Tetrahedron* **1983**, *39*, 3683 and references cited therein.

Intramolecular Reactions of Azidoalkenes. The 2-(Azidoalkyl)quinone Rearrangement

Summary: Rearrangements of 2-(azidopropyl)-1,4-benzo- and -1,4-naphthoquinones give 2-(2-Δ^1-pyrrolinyl)-4-cyclopentene-1,3-diones and pyrrolidino[2,1-*b*]azepine-1,5-diones via intermediate triazolines. Acid-catalyzed triazoline isomerization to an isolable diazo enedione is reported.

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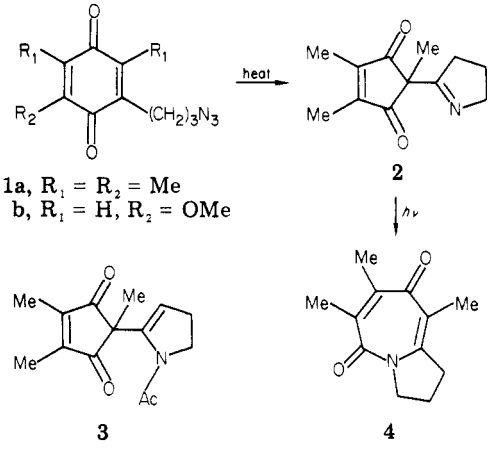
Sir: Alkyl- and aryl-substituted 1,4-benzo- and 1,4-naphthoquinones[1] undergo reaction with hydrazoic acid to give 2,5-azepinediones in 60–80% yields;[2] however, product composition critically depends on reaction conditions, and in certain cases butenolides and other products of quinone ring contraction have been isolated.[1] Very little is known about the reaction of quinones with organic azides: reactions of phenyl azide with 1,4-benzoquinone and 1,4-naphthoquinone give products of ring contraction via rearrangement of presumed intermediate *N*-phenyltriazolines.[3]

In this communication, we present the first study of thermal intramolecular rearrangements of 2-(azidoalkyl)-1,4-benzo- and -1,4-naphthoquinones.[4] Products of ring contraction and expansion (e.g., **2** and **4**) and reaction conditions that provide selective access to either isomeric series are described.

Construction of 2-(3-azidopropyl)-3,5,6-trimethyl-1,4-benzoquinone (**1a**) begins with hydroboration of the *O*-



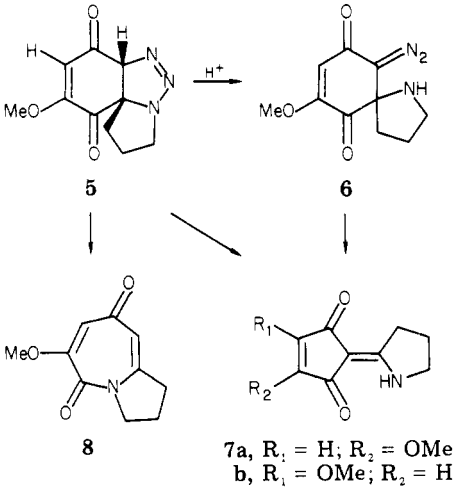
1a, $R_1 = R_2 = Me$
b, $R_1 = H$, $R_2 = OMe$

2 **3** **4**

benzyl ether of 2-allyl-3,5,6-trimethylphenol[5] and makes use of methodology already described in detail.[6] Heating a solution of **1a** in dry benzene at reflux temperature in the dark gives a mixture (3:2) of 2,4,5-trimethyl-2-(2-Δ^1-pyrrolinyl)-4-cyclopentene-1,3-dione (**2**) and pyrrolidino-[2,1-*b*]-4,6,7-trimethylazepine-1,5-dione (**4**) in quantitative yield.[7] Control experiments demonstrate that **2** and **4** do not interconvert in refluxing benzene solution in the dark. More selective formation of ring-contracted **2** (oil, 82% chromatographically isolated yield) occurs on heating (40 °C) a methylene chloride or benzene solution of **1a** in the presence of Brønsted acids. For purposes of additional characterization, imine **2** is converted to enamide **3** on treatment with acetic anhydride at 100 °C.

We desired a method for selective preparation of azepinedione **4**. A priori, compounds **2** and **4** might be interconverted by 1,3-acyl group migrations. Similar rearrangements are performed photochemically,[8a] and we were pleased to find that **2** undergoes photorearrangement[8b] to **4** (48% isolated yield, mp 97–98 °C).

Thermolysis studies with 2-(3-azidopropyl)-6-methoxy-1,4-benzoquinone (**1b**) (bright yellow crystals, mp 60–65 °C, dec) provide mechanistic insight. At 40 °C, in either benzene or refluxing methylene chloride solution, **1b** undergoes intramolecular azide–olefin cycloaddition to give triazoline **5**. The progress of reaction can be conveniently followed by ^1H NMR spectroscopy (C_6D_6 solvent). After ~2.5 h triazoline **5** (~50%) and azidoquinone **1b** (~25%) are observed, together with ring-contracted 4-cyclopentene-1,3-diones **7a** + **7b**, azepinedione **8** and a trace of diazo enedione **6**.[9] Continued heating at 40 °C results in eventual consumption of **1b** and formation of a mixture (1:1) of azepinedione **8** (mp 150–151 °C) and 4-cyclopentene-1,3-diones **7a** + **7b** at the expense of triazoline **5**. On the other hand, triazoline **5** is rapidly converted to



5 **6**

8

7a, $R_1 = H$; $R_2 = OMe$
b, $R_1 = OMe$; $R_2 = H$

diazo enedione **6** (mp ~107 °C, decomposition with gas evolution) in the presence of a trace of acid[10a] or by attempted silica gel chromatography[10b] of the thermolysis reaction mixture. To our knowledge, the spectroscopic and chemical data associated with **5** represent the first direct characterization of a triazoline obtained from cycloaddition

(1) For a review of the reactions of quinones with hydrazoic acid and organic azides, see: Moore, H. W.; Wilkholm, R. J. In "The Chemistry of Quinonoid Compounds", Part 1; Patai, S., Ed.; Wiley: New York, 1974; p 446.

(2) (a) Misti, D.; Moore, H. W.; Folkers, K. *Tetrahedron Lett.* **1965**, 1071. (b) Misti, D.; Moore, H. W.; Folkers, K. *Tetrahedron* **1966**, *22*, 1201. (c) Richards, R. W.; Smith, R. M. *Tetrahedron Lett.* **1966**, 2361. (d) Bedford, G. R.; Jones, G.; Webster, B. R. *Ibid.* **1966**, 2367.

(3) (a) Wolff, L. *Liebigs Ann. Chem.* **1912**, *394*, 68, 86. (b) Wolff, L. *Ibid.* **1913**, *299*, 274.

(4) For an investigation of the intramolecular reactivity of 2-[(2-azidoethyl)thio]-2-cycloalkenones, see: Schultz, A. G.; Ravichandran, R. *J. Org. Chem.* **1980**, *45*, 5008.

(5) Smith, L. I.; Hoehn, H. H.; Whitney, A. G. *J. Am. Chem. Soc.* **1940**, *62*, 1863.

(6) Schultz, A. G.; Dittami, J. P.; Myong, S. O.; Sha, C.-K. *J. Am. Chem. Soc.* **1983**, *105*, 3273. For the conversion of phenols to benzoquinones using potassium nitrosodisulfonate (Fremy's salt), see: Zimmer, H.; Lankin, D. C.; Horgan, S. W. *Chem. Rev.* **1971**, *71*, 230. Benzoquinone **1b** is prepared from 6-allyl-2-methoxyphenol benzyl ether. Naphthoquinones **9a** and **9b** are prepared from 2-allyl-1,4-dimethoxynaphthalene and 2-allyl-3-methyl-1,4-dimethoxynaphthalene. Methods for ceric ammonium nitrate oxidation of 1,4-dimethoxynaphthalenes to naphthoquinones are found in Jacob, P., Jr.; Callery, P. S.; Shulgin, A. T.; Castagnoli, N., Jr. *J. Org. Chem.* **1976**, *41*, 3627.

(7) Satisfactory combustion analyses for C, H, and N were obtained for **2–4**, **6**, **7a** + **7b**, **8**, **10**, **11a**, and **11b**. All new compounds involved in the preparation of azides **1a**, **1b**, **9a**, and **9b** gave satisfactory combustion analyses. Chemical ionization mass spectrometry provided molecular ions for all new compounds reported, including azides **1a**, **1b**, **9a**, and **9b**.

(8) (a) Photochemical conversion of **2** into **3** is performed in argon-purged methylene chloride solution by using a 450-W medium-pressure arc lamp and Pyrex glassware. (b) For photo-Fries and related photorearrangements, see: Bellus, D. In "Advances in Photochemistry"; Pitts, J. N., Jr., Hammond, G. S., Noyes, W. A., Jr., Eds.; Wiley-Interscience: New York, 1971; Vol. 8, p 109.

(9) ^1H NMR monitoring of the thermolysis of **1a** in C_6D_6 has not provided NMR spectral characterization of a triazoline; instead, **1a** is slowly converted to mainly **2** and a trace of **4** (~50% consumption of **1a** in 24 h). These observations suggest that, in contrast to **1b**, the thermal equilibrium between **1a** and triazoline is heavily weighted in favor of **1a**.

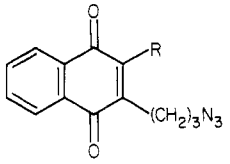
(10) (a) Phenols were found to be sufficiently acidic to catalyze rearrangements of triazolines. For this reason, it is extremely important to remove trace quantities of phenolic precursors of 2-(azidoalkyl)quinones. (b) For a related intermolecular addition of an organic azide to 2*H*-thiopyran-3(6*H*)-one to give a diazo ketone, see: Skinnemoen, K.; Undheim, K. *Heterocycles* **1981**, *16*, 929. A silica gel chromatographic separation preceded isolation of the diazo ketone. (c) For thermal rearrangement of related diazo ketones to 2-acyl-4-cyclopentene-1,3-diones, see: Cajipe, G. J. B.; Landen, G.; Semler, B.; Moore, H. W. *J. Org. Chem.* **1975**, *40*, 3874.

of an azide with a 1,4-benzoquinone.

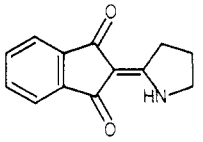
Diazo enedione **6** is stable in benzene solution at 40 °C for at least 21 h but is quantitatively converted to a mixture of **7a** and **7b** in refluxing toluene solution (1 h).[10c] Azepinedione **8** is not detected under these reaction conditions. Furthermore, **8** and **7a + 7b** do not interconvert in refluxing toluene solution.

These results indicate that diazo enedione **6** cannot be an intermediate in the conversion of triazoline **5** to **8** and **7a + 7b**. Instead, rearrangement might result from an intermediate betaine (formed by heterolytic N–N bond cleavage)[11a] and/or concerted [$\sigma^2s + \sigma^2s + \pi^2s$] cycloreversion of triazoline **5** to **8**, **7a + 7b** and N_2.[11b,4] Isomerization of triazoline **5** to diazo enedione **6** presumably follows an acid-catalyzed reaction pathway.[11c]

The 2-(azidoalkyl)quinone rearrangement also is observed with 1,4-naphthoquinones. Heating a solution of **9a** in benzene to reflux temperature for 18 h gives a mixture of **10** and **11a** in approximately quantitative yield.



9a, R = H
b, R = Me



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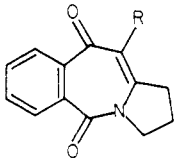
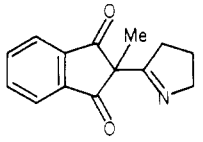


11a, R = H
b, R = Me



12

Chromatography on silica gel and crystallization gives **10** (53%, mp 240 °C, dec) and **11a** (26%, mp 130–131 °C).

Similarly, **9b** is converted to ring-expanded **11b** (mp 93–94 °C) and ring-contracted **12**.[12,13]

The 2-(azidoalkyl)quinone rearrangement should provide a generally useful route for synthesis of fused ring azepine-1,5-diones and 4-cyclopentene-1,3-diones. Preliminary studies demonstrate that in certain cases, selective access to either ring-contracted or ring-expanded systems is possible by (1) careful control of reaction temperature and (2) photochemical 1,3-acyl imine rearrangement. Acid-catalyzed isomerization of triazolines of type **5** should provide a general route to novel spirocyclic diazo enediones of type **6**. Continuing studies are directed at (1) a determination of the effect on product distribution of connecting chain length and composition and (2) the potential of other intramolecular 1,3-dipole-initiated quinone rearrangements.

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Supplementary Material Available: Listing of spectral and analytical data for all new compounds prepared in this work (5 pages). Ordering information is given on any current masthead page.

(11) (a) Hermes, M. E.; Marsh, F. D. *J. Org. Chem.* **1972**, *37*, 2969. (b) For recent observations of concerted denitrogenation of related 1,2-diazenes, see: Sheridan, R. S. *J. Am. Chem. Soc.* **1983**, *105*, 5140 and references cited therein. Engel, P. S. *Chem. Rev.* **1980**, *80*, 99. (c) Smith, P. A. S. "Derivatives of Hydrazine and other Hydronitrogens Having N–N bonds"; Benjamin/Cummings: Reading, MA, 1983; p 263.

(12) The nonenolizable diketo imine **12** proved to be unstable to chromatography on silica gel, neutral alumina, and Florisil; attempted chromatographic isolation gave only 2-methyl-4,5-benzocyclopentene-1,3-dione (mp 84–85 °C).

(13) For an alternative synthesis of the 2-benzazepine-1,5-dione ring system, see: Mazzocchi, P. H.; Wilson, P.; Khachik, F.; Klinger, L.; Minamikawa, S. *J. Org. Chem.* **1983**, *48*, 2981.

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