for 36 h, and the solvent was removed in vacuo. The residue was dissolved in chloroform, and the solution was washed with saturated sodium bicarbonate solution. After drying, the solution was concentrated to provide 92 mg (61%) of an unstable yellow liquid. Attempted purification by column chromatography resulted in decomposition. Due to the instability of this material, satisfactory C and H analysis could not be obtained: ^{1}H NMR (300 MHz, $CDCl_3$) 7.38–7.26 (m, 5 H), 5.82 (br s, 2 H), 4.50 (AB q, $\Delta\nu$ = 12.1 Hz, J = 1.2 Hz, 2 H, $PhCH_2O$), 3.86 (dd, J = 4.0, 0.6 Hz, 1 H), 3.71 (m, 1 H), 3.61 (m, 2 H), 3.43 (dd, J = 5.7, 4.0 Hz, 1 H), 3.14 (br, 2-OH), o.02 (m, 1 H), 2.05–1.30 (m, 12 H), 0.89 (t, J = 6.6 Hz, 3 H) ppm; ^{13}C NMR (75.3 MHz, $CDCl_3$) 138.27, 128.41, 127.63, 126.82, 126.08, 75.23, 74.48, 73.08, 67.88, 58.42, 51.72, 36.03, 34.23 31.93, 31.83, 25.61, 22.65, 14.04 ppm; IR (neat) 3346 (br), 3087, 3062, 3031, 3005, 2953–2859, 1695, 1635, 1623, 1616, 1496, 1454, 1430, 1378, 1362, 1270, 1085, 1028, 1012 cm^{-1}; high-resolution MS (CI, isobutane) calcd for $C_{21}H_{34}NO_3$ 348.2539 ([M + H]$^+$), found 348.2542.

Registry No. 1, 57682-64-1; (±)-(*E*)-**4**, 116911-42-3; (±)-(*Z*)-**4**, 116949-70-3; (±)-**4** (aldehyde), 116949-69-0; **5**, 113999-42-1; **6**, 5663-96-7; **6** (methyl ester), 111-12-6; (*E*)-**7**, 7367-81-9; (*Z*)-**7**, 68854-59-1; (±)-**8**, 116911-40-1; (±)-**8** (glycol), 116911-41-2; (±)-**13**, 116911-43-4; (±)-**14**, 117019-43-9; (±)-**16**, 116911-46-7; (±)-**17**, 116949-71-4; (±)-**18**, 116911-44-5; (±)-**19**, 116911-45-6; (±)-**22**, 116911-47-8; $BnO(CH_2)_2CHO$, 19790-60-4.

Oxidative Deamination of *sec*-Alkyl Primary Amines with 3,5-Di-*tert*-butyl-1,2-benzoquinone: A Second Look[1]

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Corey's oxidative deamination with 3,5-di-*tert*-butyl-1,2-benzoquinone (1) was studied with four *sec*-alkyl primary amines: cyclohexylamine (**2a**), cycloheptylamine (**2b**), 2-butanamine (**2c**), and 3-pentanamine (**2d**). The condensation products of 1 with **2a–d** were identified as the respective Schiff bases (**4a–d**) of 2-amino-4,6-di-*tert*-butylphenol (**5**) resulting from rapid, spontaneous prototropic rearrangement of the intermediate quinone imines (**3a–d**). MNDO calculations on model systems confirm that the rearrangement is thermodynamically highly favored ($\Delta\Delta H_f$ = 16.5 kcal/mol). Acidic hydrolysis of **4a–d** gave the corresponding ketones (**6a–d**) and aminophenol **5** in high yields. Aminophenol **5** was identified as the source (via oxidative coupling) of the intensely blue 2,4,6,8-tetra-*tert*-butyl-1-phenoxazinone (**12**) accompanying all aerated reactions. Attempted regeneration of 1 via air oxidation/hydrolysis of **5** instead gave **12** in high yields; electrochemical or dichromate oxidation of **5** in strongly acidic media, however, gave 1 in 64 and 56% yield, respectively. Rapid hydrolysis of the corresponding quinone iminium ion to 1 was confirmed by cyclic voltammetry of **5** in acidic media, which displayed two cathodic waves (E_{p_c} = 0.409 and 0.307 V, respectively), the more negative corresponding to 1.

Introduction

Of a limited number of synthetic reagents for oxidative deamination of primary aliphatic amines,[2] the most elegant mimic the pyridoxal/pyridoxamine interconversion for biological transamination.[3] To date, the most efficient of the "biomimetic" reagents for oxidative deamination of *sec*-alkyl primary amines is 3,5-di-*tert*-butyl-1,2-benzoquinone, "Corey's Reagent" (1) (Scheme I).[4,5] In comparison with other similar reagents,[6] oxidation occurs under unusually gentle reaction conditions (without added base), excellent yields of the respective ketones are obtained, and product isolation is convenient, without derivatization or chromatography.

Scheme I

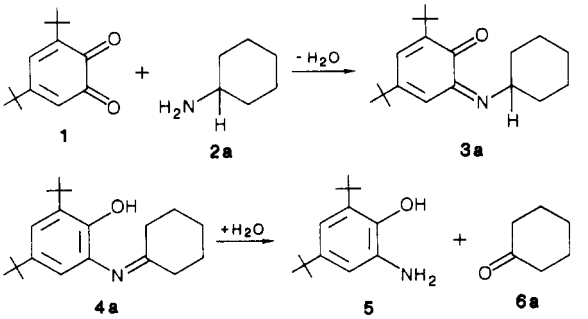


Table I. Oxidation of *sec*-Alkyl Primary Amines 2a–d with 3,5-Di-*tert*-butyl-1,2-benzoquinone (1)

compound	yield ketone,[a] %
cyclohexylamine (**2a**)	92.
cycloheptylamine (**2b**)	93.
2-butanamine (**2c**)	83.
3-pentanamine (**2d**)	87.

[a] All reactions performed with 2 g of amine, in anhydrous MeOH/THF (6:1), under N_2 at 25 °C; yields determined from mass of recrystallized 2,4-DNPH derivatives.

(1) Taken in part from the following: Bargas, L. M. M.S. Thesis, Georgetown University, Washington, DC 20057, April 24, 1987. Presented in part in a preliminary communication, see: Klein, R. F. X.; Bargas, L. M.; Horak, V.; Navarro, M. *Tetrahedron Lett.* **1988**, *29*, 851–2.

(2) For a review, see: (a) Baumgarten, R. J.; Curtis, V. A. In *The Chemistry of Amino, Nitroso and Nitro Compounds*; Patai, S., Ed.; Wiley: New York, 1982; Part 2, Supplement F. See also: (b) *The Chemistry of the Amino Group*; Patai, S., Ed.; Interscience: New York, 1968. (c) Baumgarten, R. J. *J. Chem. Ed.* **1966**, *43*, 398–408.

(3) (a) Dugas, H.; Penney, C. *Bioorganic Chemistry*; Springer-Verlag: New York, 1981. For a review of pyridoxal chemistry, see: (b) *Transaminases*; Christen, P., Metzler, D. E., Eds.; John Wiley and Sons: New York, 1985.

(4) Corey, E. J.; Achiwa, K. *J. Am. Chem. Soc.* **1969**, *91*, 1429–32.

(5) *o*-Quinone 1 is unsuitable for preparation of aldehydes due to preferential formation of substituted benzoxazoles. See: Corey, ref 4. In addition, α-amino acids undergo facile β-elimination to also give substituted benzoxazoles. See: Vander Zwan, M. C.; Hartner, F. W.; Reamer, R. A.; Tull, R. *J. Org. Chem.* **1978**, *43*, 509–11.

(6) (a) Buckley, T. F.; Rapoport, H. *J. Am. Chem. Soc.* **1982**, *104*, 4446–50. (b) Babler, J. H.; Invergo, B. J. *J. Org. Chem.* **1981**, *46*, 1937–8. (c) Dinizio, S. E.; Watt, D. S. *J. Am. Chem. Soc.* **1975**, *97*, 6900–1. (d) Calo, V.; Lopez, L.; Todesco, P. E. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1652–3.

0022-3263/88/1953-5994$01.50/0

Table II. MNDO-MO Parameters

compound	ΔH_f, kcal/mol
7	14.97
8	15.09
9	−1.54

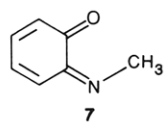
The success of **1** derives from its structural design; the *tert*-butyl groups screen the ring from nucleophilic attack (directing condensation with the C_1-carbonyl), the quinone/aromatic redox system thermodynamically favors the 1,5-prototropic rearrangement (vide infra), and the transamination byproduct, 2-amino-4,6-di-*tert*-butylphenol (**5**), is isolated as the anilinium salt in the workup, allowing clean separation of the carbonyl product.

Corey demonstrated the synthetic utility of **1** on a variety of *sec*-alkyl primary amines;[4,7] herein, we report the results of a followup study aimed toward (1) clarification of the mechanism and timing of the prototropic rearrangement, (2) regeneration of **1** from recovered **5**, and (3) identification of the intensely blue byproduct accompanying the reaction under aerated conditions.

Results and Discussion

Reaction of **1** with amines **2a–d** followed by aqueous acidic hydrolysis and extraction gave the respective ketones **6a–d** in high yields (Table I). Additional workup; i.e., neutralization and extraction, gave **5**[8] in nearly quantitative yields.

In order to establish at what point in the reaction sequence the prototropic rearrangement **3** → **4** occurs (i.e., spontaneously following the initial condensation or as a first step during hydrolysis), the ongoing reactions between **1** and **2a–d** were examined by theoretical, chromatographic, and spectroscopic techniques. A priori, initial condensation results in a mixture of *cisoid*/*transoid* isomers of the quinone imines **3a–d**, which are in tautomeric equilibrium with the corresponding aromatic Schiff bases **4a–d**. MNDO calculations[9,10] on the model systems **7–9** (Table II) confirm the higher stability of **9** ($\Delta\Delta H_f$ = 16.5 kcal/mol) and suggest that **4a–d** are thermodynamically strongly favored in the equilibrium.



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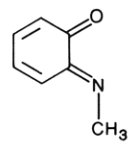

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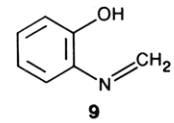


9

(7) Surprisingly, since introduction, **1** has been reported for oxidation of only a few specialized amines. See: (a) Boxler, D. L.; Brambilla, R.; Davies, D. H.; Mallams, A. K.; McCombie, S. W.; Morton, S. B.; Reichert, P.; Vernay, H. F. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2168–85 (aminoglycosides). (b) Krbechek, L. O.; Spitzner, E. B.; Clark, J. P. U.S. 4,252,732 (Cl. 260–397.3; C0759/00), 24 Feb 1981; *Chem. Abstr.* **1981**, *94*, P192569c (20-amino-3-oxopregnenes). (c) Paulsen, H.; Sumfleth, E. *Chem. Ber.* **1980**, *113*, 1723–45 (2-deoxystrepamines). (d) Lengstad, B.; Lonngren, J. *Carbohydr. Res.* **1979**, *72*, 312–4 (amino sugars). (e) Gleason, J. P. Ger. Offen. 2,627,126 (Cl. C07D501/00), 30 Dec 1976; *Chem. Abstr.* **1977**, *86*, P140073*b* (7-aminocephalosporins).

(8) (a) Fukata, G.; Sakamoto, N.; Tashiro, M. *J. Chem. Soc., Perkin Trans. 1* **1982**, 2841–8. (b) Schroeter, S. H. *J. Org. Chem.* **1969**, *34*, 4012–5. (c) Haeussler, H.; Jadamus, H. *Chem. Ber.* **1964**, *97*, 3051–5.

(9) (a) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899–907. For a recent update and several reviews, see: (b) Dewar, M. J. S. *J. Mol. Struct.* **1983**, *100*, 41–50. (c) Sadlej, J. *Semi-Empirical Methods of Quantum Chemistry*; Ellis-Horwood, Ltd.: Chicester, 1985. (d) Clark, T. *A Handbook of Computational Chemistry*; Wiley-Interscience: New York, 1985; Chapter 4.

(10) MOPAC (MNDO version 3.00; QCPE publication #455); Stewart, J. P.; Frank, J. Seiler Res. Lab., U.S. Air Force Academy, Colorodo Springs, CO 80840.

Table III. UV/Vis Parameters

compound	λ_{max}[a]	(ϵ)
1	402	(821)
4a	294	(980)[b]
5	288	(1070)
10	296	(1180)

[a] In nanometers; solvent: MeOH. [b] Approximate value; concentration assumed based on complete reaction of **1** and **2a**.

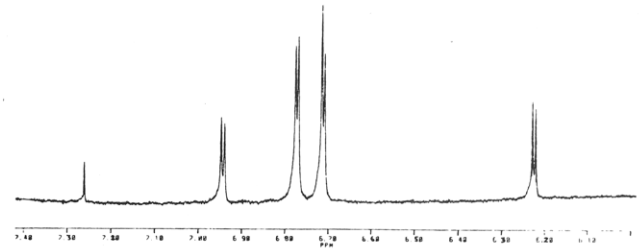
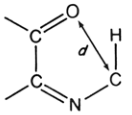


Figure 1. ^{1}H NMR (300 MHz, $CDCl_3$, δ vs Me_4Si) of the ongoing reaction between **1** and **2a**; expanded downfield region; time = 5100 s.

The tautomerization mechanism may involve either a stereoelectronically favored 1,5-sigmatropic rearrangement[11] of the *cisoid* isomer of **3** (d = 3.00 Å in **7**) with rapid concurrent isomerization of the *transoid* isomer[12] or a "push–pull" proton exchange with the solvent.



Experimentally, GC analysis of the ongoing reaction between **1** and **2a** showed smooth loss of both reactants and appearance of one major product at a much longer t_R. UV/vis spectroscopy displayed loss of **1** and formation of a new product (λ_{max} = 294 nm, $\epsilon \simeq 980$) spectroscopically similar to **5** or 3,5-di-*tert*-butylcatechol (**10**) (Table III). IR spectroscopy of the oily product showed no quinonoid carbonyl absorptions and presence of a phenolic hydroxyl (ν_{O-H} = 3330, ν_{C-O} = 1235 cm^{-1}). A time study using ^{1}H NMR spectroscopy ($CDCl_3$) displayed smooth loss of the two quinonoid proton doublets in **1** and concurrent formation of two new doublets with much closer chemical shifts ($\Delta\delta$ = 0.735 vs 0.085 ppm, respectively) comparable to that of **5** (Table IV, Figure 1). MO calculations predict a more similar chemical environment for the aromatic protons in **9** compared with the quinonoid protons in **7** (Table IV).[13] The data strongly supports spontaneous rearrangement of **3a** to **4a**.

(11) (a) Lehr, R. E.; Marchand, A. P. *Orbital Symmetry*; Academic Press: New York, 1972. (b) Gilchrist, T. L.; Storr, R. C. *Organic Reactions and Orbital Symmetry*; Cambridge University Press: London, 1972. (c) Woodward, R. B.; Hoffman, R. *The Conservation of Orbital Symmetry*; Verlag Chemie GmbH (Academic Press): Weinheim/Bergstr. (New York, NY), 1970. See also (d) Grigg, R. *Chem. Soc. Rev.* **1987**, *16*, 89–121.

(12) The *cis*/*trans* isomerization barrier for N-substituted quinoneimines is typically 19–23 kcal/mol. See: (a) McCarty, C. G. *Syn-Anti* Isomerizations and Rearrangements In *The Chemistry of the Carbon-Nitrogen Double Bond*; Patai, S., Ed.; Interscience: New York, 1970; pp 363–464. (b) Reiker, A.; Kessler, H. *Tetrahedron* **1967**, *23*, 3723–32. (c) Reeves, R. L. Formation of Carbon-Nitrogen Double Bonds In *The Chemistry of the Carbonyl Group*; Patai, S., Ed.; Interscience: New York, 1966; pp 567–619.

(13) MNDO-MO calculations are not generally utilized for chemical shift–charge density correlations; however, essentially identical results are obtained with other SCF-MO programs, e.g., see: Fraga, S.; Melgarejo, M. *CI–SCF Parameters for Conjugated Systems. X. Derivatives of Benzene*; Technical Report TC-6917; Department of Chemistry, University of Alberta: Alberta, Canada, 1969.

Table IV. ^{1}H NMR Chemical Shifts ($CDCl_3$) and MNDO-MO Net Atomic Charges

compound	δ_{H_4}[a]	δ_{H_6}[a]	(Δ)	q_{C_4}	q_{C_6}	(Δ)
1	6.965	6.230	(0.735)	−0.210[b]	−0.1204[b]	(0.0994)
4a	6.782	6.697	(0.085)			
4b	6.890	6.790	(0.100)			
4c	6.757	6.687	(0.070)			
4d	6.714	6.659	(0.055)			
5	6.905	6.788	(0.117)	−0.0399[b]	−0.0403[b]	(0.0004)
7				+0.0026	−0.0273	(0.0247)
9				−0.0322	−0.0277	(0.0045)

[a] In ppm, downfield from Me_4Si; assignments are assumed based on charge densities in the model systems. [b] Net atomic charges on 1 and 5 are from the unsubstituted parent systems (without *tert*-butyl groups).

Table V. Electrochemical Parameters

compound	buffer[a]	E_{p_c}[b]	E_{p_a}	ΔE_p	i_{o_c}[c]	i_{o_a}
1	a	0.285	0.489	0.204	24.75	28.38
	b	−0.064	0.083	0.147	25.88	23.18
	c	−0.155	0.490	0.645	28.48	9.50
5	a #1	0.409	0.538	0.129	10.69	19.71
	#2	0.307		0.231	11.57	
	b	−0.030	0.049	0.079	16.28	14.75
	c	−0.083	−0.072	0.011	12.33	13.63
10	a	0.260	0.450	0.190	25.50	33.13
	b	−0.101	0.035	0.136	27.88	26.90
	c	−0.240	−0.132	0.108[d]	36.98	38.15

[a] Buffers: (a) $HClO_4$, pH 1.2; (b) phosphate, pH 7.6; (c) borate, pH 8.6. [b] In volts vs Ag/AgCl. [c] In microamps. [d] The large difference between 1 and 10 in E_{p_a} is due to borate complex formation. See: Goulart, M. O. F.; Sant'Ana, A. E. G.; Horak, V. *Mikrochimica Acta [Wien]* **1986**, *I*, 23–6.

To unambiguously differentiate **3a** from **4a**, the latter was directly synthesized by an independent route. Aminophenol **5** was prepared via nitration[14] and reduction[15] of 2,4-di-*tert*-butylphenol (**11**). Condensation of **5** with cyclohexanone (**6a**) gave authentic **4a**; spectroscopic and chromatographic comparisons with the product obtained from reaction of **1** with **2a** under the same conditions were essentially identical, confirming spontaneous rearrangement **3a** → **4a** following initial condensation of **1** and **2a**. Comparable results were observed with amines **2b–d** (Table IV).

No spectroscopic or chromatographic evidence of **3a** was observed in reactions in $CHCl_3$,[16] suggesting a low steady-state concentration. The ^{1}H NMR derived kinetics ($CDCl_3$, complete in 4 h) showed initially curvilinear fits to the expected second-order plots; at linearity, the second-order rate constant for consumption of **1** (= **2a**) was, typically, 5.2×10^{-3} L mol^{-1} s^{-1}. The rate of the reaction was unaffected by light or by addition of up to equimolar amounts of DBN; however, the induction period (to linearity) was reduced from ca. 5400 to 1600 s in kinetic runs utilizing moistened $CDCl_3$, suggesting possible autocatalysis by H_2O produced in the initial condensation.

Reaction of **1** and **2a** in MeOH proceeded much more rapidly than in $CHCl_3$ (complete in 10 min). ^{1}H NMR (MeOH-d_4) displayed, in addition to **1** and **4a**, two new doublets (J = 2.51 Hz, $\Delta\delta$ = 0.696 ppm), indicating the presence of a third reaction component in low concentration. The similarities of the coupling constants and chemical shift difference with **1** (in MeOH-d_4: J = 2.21 Hz, $\Delta\delta$ = 0.524 ppm) vs **4a** (in MeOH-d_4: J = 1.80 Hz, $\Delta\delta$ = 0.036 ppm) were consistent with the quinone imine **3a**. The ^{1}H NMR derived kinetics (MeOH-d_4, 10 min) were ill-behaved, however, displaying negative mass balance (suggesting additional unidentified intermediates) and nonlinear second-order plots. The approximate second-order rate constant for consumption of **1** (= **2a**) was 1×10^{-1} L mol^{-1} s^{-1}. The rate of the reaction was unaffected by light but showed slight enhancement upon addition of an equimolar amount of DBN (ca. 12% faster to 50% consumption of **1**).

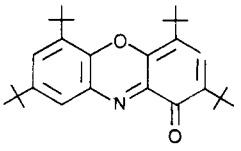
The overall results suggest: (A) that formation of **3** is rate determining, (B) that no anionic intermediate(s) lie on the reaction coordinate (as shown by the lack of rate enhancement in $CDCl_3$ and the negligible rate enhancement in MeOH-d_4 upon addition of DBN), and (C) that the prototropic rearrangement occurs with solvent participation in the transition state (as shown by the dramatic rate increase in MeOH-d_4 vs $CDCl_3$ and the rate enhancement in moistened $CDCl_3$).[17]

As noted above (vide supra), the transamination byproduct (aminophenol **5**) may be isolated in clean and nearly quantitative yields by additional workup of the reaction mixtures. This recovery was explored for regeneration of **1** via oxidation/hydrolysis.

Aminophenol **5** is moderately unstable in air, displaying rapid blue coloration in solution; similar coloration was observed in all reactions of **1** and **2a–d** in which anaerobic conditions were not strictly maintained. Intentional reaction and workup of **1** with **2a** under O_2 gave, in addition to **5** and **6a**, the intensely blue 2,4,6,8-tetra-*tert*-butyl-1-phenoxazinone (**12**);[8a,18] the latter was also recovered from reaction of equimolar methanolic solutions of **1** and **5** under N_2 or from oxygenation of a methanolic solution of **5** alone, suggesting formation via oxidative coupling.[8a,18] The results confirmed that **1** cannot be regenerated from

(14) Elder, J. W.; Mariella, R. P. *Can. J. Chem.* **1963**, *41*, 1653–6.
(15) Han, B. H.; Shin, D. H.; Cho, S. V. *Tetrahedron Lett.* **1985**, *26*, 6233–4.
(16) High GC column temperatures rapidly complete the prototropic rearrangement. TLC and C_{18}-reverse-phase HPLC hydrolyze **3a** and **4a**; only **1**, **2a**, **5**, and **6a** are observed. The chromophore of **1** (probably) overlays **3a** in UV/vis and the ^{1}H NMR ($CDCl_3$) does not display any additional doublets attributable to **3a**.
(17) Sigmatropic rearrangements are relatively insensitive to solvent changes; see ref 11. In addition, it is pertinent to note that a closely analogous reaction with 2,6-di-*tert*-butyl-1,4-benzoquinone (in which a sigmatropic rearrangement cannot occur) proceeds in boiling H_2O only. See: Nishinaga, A.; Shimizu, T.; Matsuura, T. *J. Chem. Soc., Chem. Commun.* **1979**, 970–1.
(18) Schroeter, H. B.; Scheffler, K.; Stoecker, F.; Buerk, H. *Chem. Ber.* **1968**, *101*, 262–71.

5 by oxidation/hydrolysis in neutral media.



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However, quinone imines are highly susceptible to acidic hydrolysis,[19] conditions which preclude formation of **12** due to protonation of **5**. Cyclic voltammetry of **5**[20] displayed quasi-reversible character in basic, neutral, and acidic media (Table V). The results were similar to 3,5-di-*tert*-butylcatechol (**10**)[21] except in acidic media; the anodic peak potential was shifted positively (due to protonation of the amine moiety) and a second cathodic peak (E_{p_c} = 0.307 V, corresponding to reduction of **1**) is seen in the reverse scan. The results confirmed in situ formation of **1** via hydrolysis of the corresponding quinone iminium ion within the timescale of the voltammogram.

The facile oxidation/hydrolysis of **5** in acidic media was utilized for preparative recovery of **1**. Controlled current electrooxidation of **5** (0.2 M $HClO_4$, 12 V vs Ag/AgCl) gave **1** in 64% yield; similarly, $Na_2Cr_2O_7$ oxidation (1.0 M H_2SO_4/CH_2Cl_2, 1:1) gave **1** in 56% yield.[22]

Experimental Section

Instrumentation. Melting points were recorded on a Fisher-Johns melting point apparatus and are uncorrected. GC analyses were carried out on Varian Aerograph 980-00 equipped with a 6 ft × $^1/_4$ in. o.d. stainless steel column packed with 15% SE-30 on Chromosorb W-GW-DMCS 60/80. All NMR spectra were recorded on a Bruker AM-300 WB NMR spectrometer (operating at 300 MHz for ^1H and 75.5 MHz for ^{13}C) with internal Me_4Si as a calibration standard. IR spectra were recorded on a Sargent-Welch 3-100 IR spectrophotometer; polystyrene was used as a calibration standard. UV/vis spectra were recorded on a Hewlett-Packard 854-1A diode-array UV/vis spectrophotometer. Mass spectra (70 eV-EI) were recorded on a Finnigan-MAT CH5-DF mass spectrometer. Electrochemical studies were carried out with an IBM EC 225 voltammetric analyzer with an IBM 7424 MT X-Y-T recorder. Glassy carbon (Bioanalytical Systems; area = 0.07 cm^2) was utilized as the working, Ag/AgCl as the reference, and Pt wire as the auxiliary electrode.

Molecular Orbital Calculations. MNDO[9] calculations were executed by using the MOPAC program,[10] installed on a VAX/VMS version V4.3 or V4.5. Initial molecular geometries were estimated from standard tables in the literature.[23] All geometric parameters (bond lengths, bond angles, and dihedral angles) were optimized without any specific assumptions.

Reagents and Chromatographic Methods. 3,5-Di-*tert*-butyl-1,2-benzoquinone, 98% (**1**) (Aldrich), was utilized as is; amines **2a–d** (Aldrich) were distilled prior to use. **2-Amino-4,6-di-*tert*-butylphenol (5)**, mp 171–3 °C (lit.[8] mp 169 °C), was synthesized in two steps from **2,4-di-*tert*-butylphenol** (**11**) (Aldrich); **11** was nitrated via the procedure by Elder[14] to give **4,6-di-*tert*-butyl-2-nitrophenol**, mp 58 °C (lit.[24] mp 59–61 °C), which was reduced following the procedure by Han.[15] All other chemicals were reagent grade or better and utilized directly.

Oxidation of *sec*-Alkyl Primary Amines with 3,5-Di-*tert*-butyl-1,2-benzoquinone (1). General Procedure. (**Note**: In order to preclude formation of **12** in oxidations of *sec*-alkyl primary amines with **1**, all procedures must be done under N_2). Via a variation of Corey's procedure,[4] the amine (20 mmol) is dissolved in MeOH/THF (6:1) (50 mL) at 25 °C with stirring (additional THF may be added to aid solvation). After 10 min, **1** (4.41 g, 20 mmol) is added; a deep red color results. The color fades to light green over 20 min–3 h; after the reaction is complete (by GC) first H_2O (10 mL) and then oxalic acid (3.15 g, 25 mmol) is added. After 1 h, additional H_2O (100 mL) is added; extraction with CCl_4 or c-C_6H_{12} (3 × 50 mL; more polar solvents partially extract protonated **5**) gives the ketone. Neutralization of the aqueous layer ($NaHCO_3$) followed by extraction with $CHCl_3$ (3 × 50 mL) gives moderately pure **5** (suitable for oxidation to **1**; vide infra). Column chromatography (silica gel, $CHCl_3$) gives analytically pure **5**; melting point and TLC data were identical with those of an authentic sample.

3,5-Di-*tert*-butyl-1,2-benzoquinone (1). Method A, Electrooxidation. Aminophenol **5** (100 mg, 0.455 mmol) was dissolved in 0.2 M $HClO_4$ (20 mL) and electrooxidized at 12 V cell potential in a standard H-cell equipped with a carbon cloth anode (16 cm^2, WCA carbon cloth, Union Carbide) and a spiral lead wire cathode. A deep violet color rapidly developed; during the course of the electrolysis, the color faded and insoluble **1** precipitated on the anode and cell walls. After 2 h, the current dropped from 96 to 72 mA, and the reaction was stopped. The crude product was recovered by washing (EtOH or CH_2Cl_2); purification via column chromatography (silica gel, *n*-C_6H_{14}/MeOH 95:5) gave pure **1** (64 mg, 64% yield) as dark red crystals; melting point and TLC data were identical with those of the commercial sample.

Method B, Chemical Oxidation. Aminophenol **5** (200 mg, 0.91 mmol) was dissolved in 1 M H_2SO_4 (5 mL) and added to a biphasic mixture of 1 M H_2SO_4 (20 mL) and CH_2Cl_2 (20 mL) containing $Na_2Cr_2O_7$ (224 mg, 0.91 mmol) with stirring at 25 °C. After 12 h, the organic layer was separated, washed with H_2O (3 × 20 mL) and dilute $NaHCO_3$ (20 mL), dried (anhyd Na_2SO_4), and purified as above to give pure **1** (112 mg, 56% yield) identical with that obtained via method A.[22]

2,4,6,8-Tetra-*tert*-butyl-1-phenoxazinone (12). Method A. Aminophenol **5** (107 mg, 0.484 mmol) and *o*-quinone **1** (104 mg, 0.472 mmol) were dissolved in CH_2Cl_2 (50 mL) under N_2 at 25 °C. A rapid deep blue coloration was observed; after 2 h, the solvent was removed under N_2 to give an oily, dark blue solid. Column chromatography (silica gel, $CHCl_3$) gave an amorphous dark blue solid. Dissolution in MeOH followed by dropwise addition of H_2O with stirring precipitated pure **12** (25 mg, 42% yield) as a fine blue-black powder: mp 218 °C (lit.[8a,18] mp 220–1 °C); ^1H-coupled ^{13}C NMR, corrected ($CDCl_3$) δ 179.7 (d, $J_{C_1-H_3}$ = 12 Hz).[25]

Method B. Aminophenol **5** (660 mg, 2.99 mmol) was dissolved in MeOH (100 mL) at 25 °C and bubbled with O_2; a rapid deep blue coloration was observed. After 72 h, workup as above gave pure **12** (440 mg, 77% yield) identical with that prepared above (or isolated from reaction of **1** and amines **2a–d** under aerated conditions).

^1H NMR Kinetics. General Procedures. All kinetic runs were performed under N_2 at 25 °C. *o*-Quinone **1** (88 mg, 0.4 mmol) and cyclohexylamine (**2a**, 39 mg, 0.4 mmol) were each dissolved in $CDCl_3$ (1 mL), mixed, and immediately placed in a pretuned 5-mm NMR tube. Data was accumulated every 500 s over 3 h. Acquisition parameters: number scans, 16; acquisition time, 4.76 s/scan; relaxation delay, 3.24 s/scan. Integration values were normalized vs the $CHCl_3$ impurity peak. Kinetic runs in moist $CDCl_3$: $CDCl_3$ was thoroughly mixed with deionized H_2O and allowed to equilibrate for 30 min prior to use. Kinetic runs with DBN: DBN was added immediately after mixing—four exper-

(19) (a) Nickel, U.; Jaenicke, W. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1601–5. (b) Adams, R. N. *Electrochemistry at Solid Electrode Surfaces*; Marcel Dekker, Inc.: New York, 1969. See also: Patai, ref 12a.

(20) To date, **5** has not been examined by electrochemical methods; for a related study (3,5-di-*tert*-butyl-2-aminophenol), see: Harmalker, S. P.; Sawyer, D. T. *J. Org. Chem.* **1984**, *49*, 3579–83.

(21) *o*-Quinone **1** and catechol **10** have been the subjects of several studies, e.g., see: (a) Bodini, M. E.; Copia, G.; Robinson, R.; Sawyer, D. T. *Inorg. Chem.* **1983**, *22*, 126–9 and refs cited therein (1). (b) Stallings, M. D.; Morrison, M. M.; Sawyer, D. T. *Inorg. Chem.* **1981**, *20*, 2655–60 (**10**). For a review of the electrochemistry of catechols and *o*-quinones, see: (c) Chambers, J. Q. Electrochemistry of Quinones In *The Chemistry of the Quinonoid Compounds*; Patai, S., Ed.; John Wiley and Sons: New York, 1974; pp 737–91. For reviews of the electrochemistry of quinone imines, see: Adams, ref 19b. (d) Reed, R. C.; Wightman, R. M. *Encycl. Electrochem. Elem.* **1984**, *15*, 1–165. (e) Lund, H. Electrochemistry of the Carbon-Nitrogen Double Bond In Patai, ref 12a.

(22) Optimization of more sophisticated procedures should result in higher yields than those reported.

(23) March, J. *Advanced Organic Chemistry*, 3rd Ed.; Wiley-Interscience: New York, 1985; pp 18–21 and references cited therein.

(24) Cross, G. G.; Fischer, A.; Henderson, G. N. *Can. J. Chem.* **1984**, *62*, 2803–12.

(25) Incorrectly reported by Fukata, ref 8a, as a singlet.

iments were run: 1 drop (10 mg, 0.08 mmol), 3 drops, 5 drops (0.4 mmol), and 0.5 g (4 mmol). Kinetic runs in MeOH-d_4: concentrations identical; data was accumulated every 30 s over 15 min. Acquisition parameters: number scans, 4; acquisition time, 4.76 s/scan; relaxation delay, 2.24 s/scan; 2 drops $CHCl_3$ were added to each reaction mixture as an integration standard. Kinetic runs with DBN: solutions were diluted 1:10; an equilmolar amount of DBN was added to the solution containing **2a** just prior to mixing.

Cyclic Voltammetry. General Procedure. One milliliter of the substrate (0.01 M in EtOH) was added to 9 mL of deaerated buffer/EtOH (70:30) and deaerated with N_2 bubbling for 15 min (buffer systems are listed in Table V). The glassy carbon electrode was polished with 0.05 μm alumina prior to each scan. The scan rate was 50 mV s^{-1}. The reported data (Table V) are the average of two runs.

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Supplementary Material Available: Spectroscopic parameters for **4a**, **5**, 12, and 4,6-di-*tert*-butyl-2-nitrophenol (^1H and ^{13}C NMR, IR, UV/vis (12) and MS (12)); MNDO-MO optimized geometries (Cartesian coordinates) for *un*substituted **1**, **5**, and model systems **7–9**; IR and ^1H-NMR direct comparisons of **4a** from **1** and **2a** vs **5** and **6a**; cyclic voltammetry plot of **5** in acidic media, kinetic plots (13 pages). Ordering information is given on any current masthead page.

The 1-Aza-Cope Rearrangement. 2[1]

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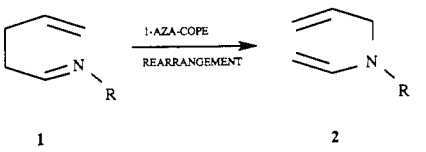
The 1-aza-Cope rearrangement of 4-vinylcyclohexene analogues has been studied with respect to substituents on C-3 of the 1-aza diene. The 1-aza-Cope rearrangement was unsuccessful with an electron-donating methoxy substitution at C-3 of the aza diene. The origin of this effect is believed to be due to thermodynamic rather than kinetic factors; that is, the reactant 1-aza diene is more stable than the product. The electron-withdrawing methoxycarbonyl group on C-3 of the aza diene accelerates the 1-aza-Cope rearrangement. Both an electron-donating group (OCH_3) at C-4 and an electron-withdrawing group (CO_2CH_3) at C-3 result in an extremely reactive substrate for the 1-aza-Cope rearrangement. All of the results to date on the 1-aza-Cope rearrangement are consistent with the dipolar transition state depicted in Scheme III.

The 1-aza-Cope rearrangement (Scheme I) is unknown as a general transformation in organic chemistry.[2] The primary reason for this situation is probably due to thermodynamic rather than kinetic factors. Compared to carbon–carbon bonds, the carbon–nitrogen π-bond is relatively strong whereas the carbon–nitrogen σ-bond is relatively weak.[3] Thus, the imine reactants are usually more stable than the enamine product. For this reason there are a number of examples known of the 3-aza-Cope rearrangement.[4]

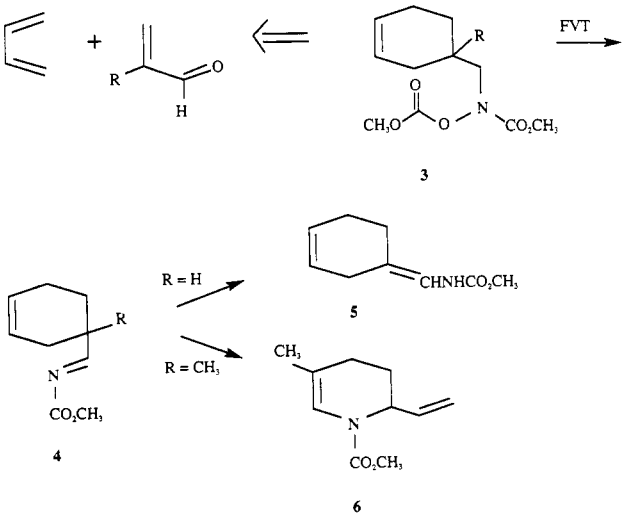
We have recently observed examples of the 1-aza-Cope rearrangement when an acyl function is present on the nitrogen atom of the imine.[5] The thermodynamic driving force for this reaction is presumably due to the resonance stabilization of the amide functionality present in the product. This scheme represents a new and potentially useful synthetic method. Its utility is further enhanced

Scheme I



1 2

Scheme II



3 4 5 6

(1) For part 1, see ref 5b.

(2) We apply the term 1-aza-Cope rearrangement to reactions where C-1 of the reacting 1,5-diene has been replaced by nitrogen. Although the term aza Claisen has also been used for the reverse of this process this designation is probably a misuse of the "replacement nomenclature". (*Nomenclature of Organic Compounds. Principles and Practice*; Fletcher, J. H., Cermer, O. C., Fox, R. B., Eds.; American Chemical Society: Washington, DC, 1974; Chapter 7. An aza Claisen rearrangement would be applied to those processes where one of the *carbon* atoms has been replaced by nitrogen. It is interesting to note that some aza Claisen rearrangements have also been called aza-Cope rearrangements. For example, see: (a) Mundy, B. P.; Bornmann, W. *Tetrahedron Lett.* **1978**, 957. (b) Lipkowitz, K. B.; Scarpone, S.; McCullouth, D.; Barney, C. *Tetrahedron Lett.* **1979**, 2241. (c) Kurth, M. J.; Soares, C. J. *Tetrahedron Lett.* **1987**, *28*, 1031.

(3) For example, the σ-bond strengths of CH_3–CH_3 and CH_3–NH_2 are 88 and 79 kcal/mol respectively, whereas the π-bond strengths for CH_2=CH_2 and CH_2=NH_2 have been calculated to be 59.4 and 74.3 kcal/mol respectively (*Handbook of Organic Chemistry*; Dean, J. A., Ed.; McGraw-Hill: New York, 1987; p 3–18, and *The Chemical of Double Bonded Functional Groups*; Shaw, R., Patai, S., Eds.; Wiley: New York, 1977; p 131). For a recent theoretical analysis of the relative strengths of these bonds, see: Schleyer, P.v.R.; Kost, D. *J. Am. Chem. Soc.* **1988**, *110*, 2105.

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