Nucleophilic Addition of Amines to Benzo-Substituted Oxetenes. Formation of 6-Amino-2,4-cyclohexadienones and Their Ring Expansion

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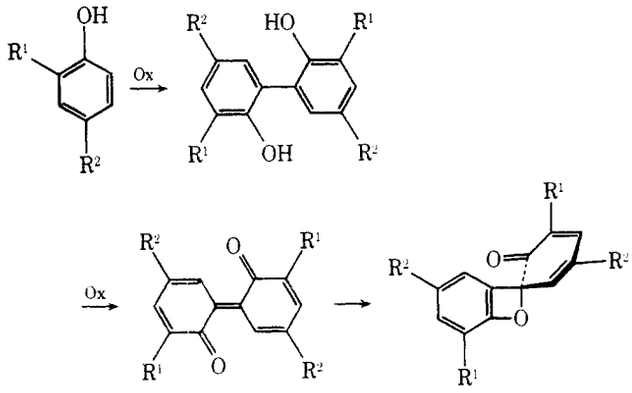
Benzo-substituted oxetenes have been found to react with primary and secondary amines to give 7-aryl-1,3-dihydro-2*H*-azepin-2-ones **3** and 6-amino-substituted 2,4-cyclohexadienones **10**, respectively. Upon direct irradiation through Pyrex, azepinones **3** and their oxidation products, benzofurano-annelated azepinones **4**, undergo isomerization to acetamido-substituted cyclobutenes.

The oxidative coupling of sterically hindered 2,4-substituted phenols smoothly leads to spiroquinol ethers[1] whose remarkable stability was first described in 1961 by Müller and his co-workers.[1]



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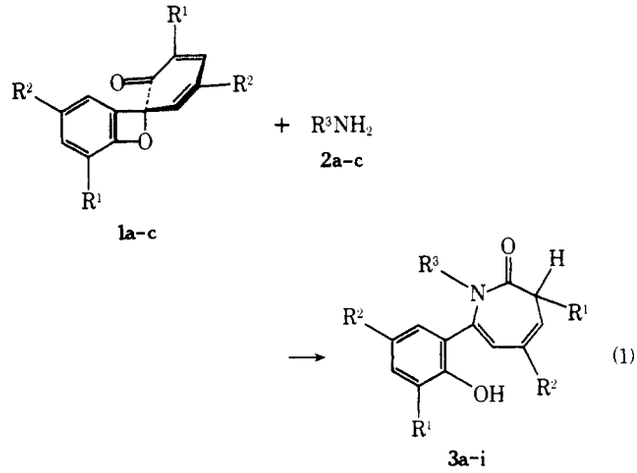
Outside the field of phenol oxidation, these spiroquinol ethers have attracted little attention and, consequently, their potential oxetene reactivity toward nucleophiles has not been investigated.[2] We deemed it worthwhile to consider spiroquinol ethers of structure **1** as easily available benzo-substituted representatives of otherwise hardly known oxetenes[3] and study their displacement reactions with amines. The present paper describes the formation of arylated azepinones by nucleophilic addition of primary amines to benzoxetes **1**.[4]

Results and Discussion

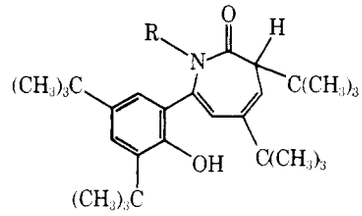
Benzoxetes **1a–c**, when suspended in methanol, readily react with primary amines **2a–c** to give colorless, crystalline 7-aryl-1,3-dihydro-2*H*-azepin-2-ones **3a–i** in good to excellent yields (reaction 1; see Table I). Depending on the degree of solubility of **1**, the reaction may be carried out at ambient or elevated temperature. As exemplified for **3a**, the azepinone structure is supported by the following data and reactions.



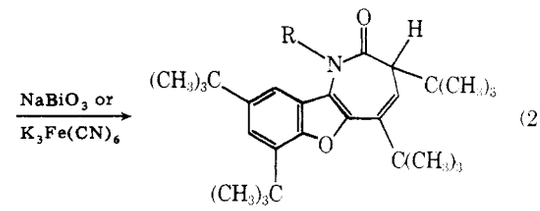
1a–c + R^3NH_2 **2a–c** → **3a–i** (1)

The mass spectrum of compound **3a** confirms the molecular weight of a 1:1 addition product by its molecular ion (M^+· 439).[5] The infrared spectrum of **3a** shows absorptions at 1680, 1655, and 1625 cm^{-1}, attributed to the seven-membered cyclic enamide structure. The phenolic hydroxyl gives rise to a sharp band at 3320 cm^{-1}. In its ^1H NMR spectrum, **3a** shows its aromatic hydrogens at 7.38 and 7.03 ppm (J = 2.5 Hz), and the hydrogens at the 3, 4, and 7 positions of the azepinone ring at 2.31, 5.62, and 6.43 ppm, respectively ($J_{3,4}$ = 6.5; $J_{3,6}$ = 1 Hz). In analogy to **3a**, the ^1H NMR spectra of azepinones **3b–i** exhibit the expected similar features of the cyclic enamide moiety (see Table II). Characteristically, H-3 and H-6 show long-range coupling ($J \leq 1$ Hz); however, coupling between H-4 and H-6 was not observed.[6]

In agreement with its hindered phenol structure, **3a** was found to undergo oxidation by potassium ferricyanide in alkaline solution to give a deep green colored radical which was slowly converted into the colorless benzofurano-annelated azepinone **4a** (reaction 2). As the ring closure resembles that



3a



4a (2)

of an electrophilic substitution,[7] the phenoxy radical conceivably is transformed, either by bimolecular disproportionation or by direct oxidation, into the phenoxonium ion. Under more stringent oxidation conditions, namely, by oxidation with sodium bismuthate in refluxing toluene, the conversion of **3** into **4** proceeds rapidly and in excellent yield.

Spectroscopic data of **4a** (and **4b,c**) are in agreement with the proposed structure (see Experimental Section). In particular, the ^1H NMR spectrum of **4a**, in general strikingly similar to that of **3a**, shows the disappearance of H-6 and, of

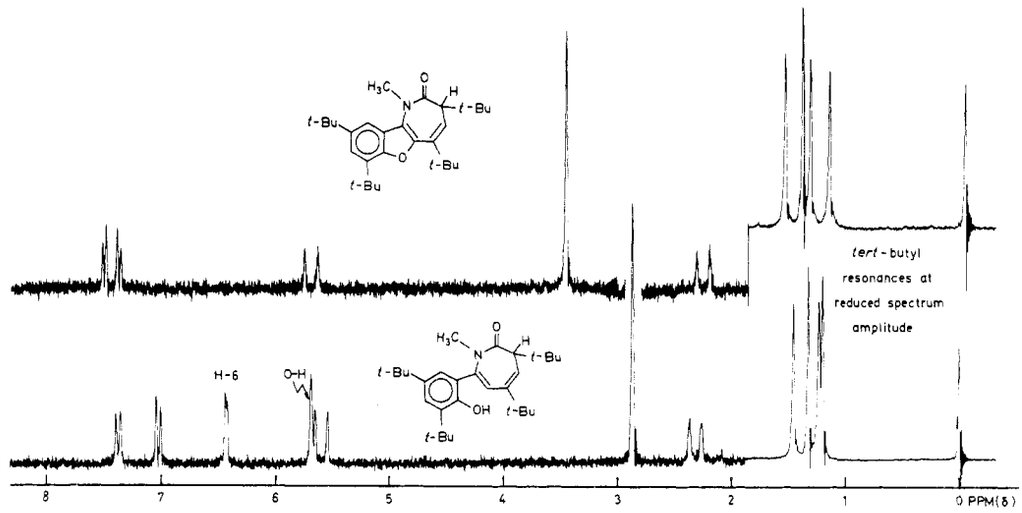


Figure 1. ^{1}H NMR spectra of azepinones **3a** and **4a**.

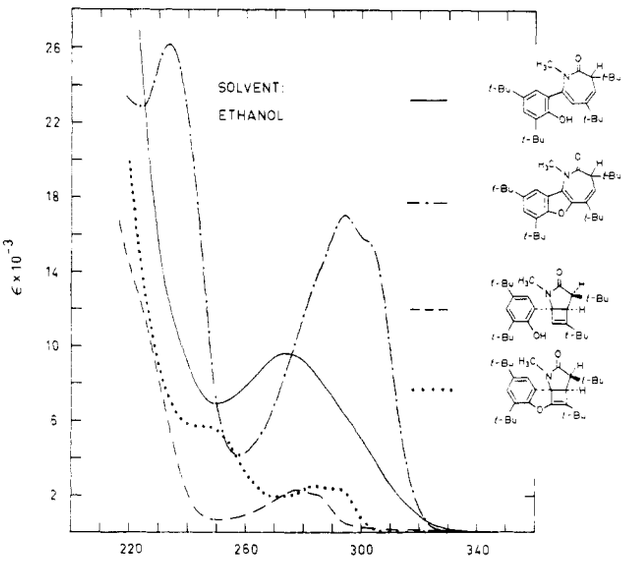


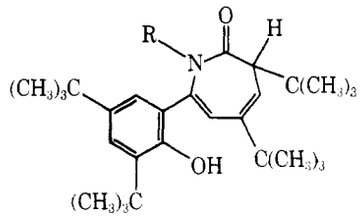
Figure 2. Electronic absorption spectra of azepinones **3a** and **4a**, and their photoproducts **5a** and **6a**.

Table I. Formation of Azepinones 3 from Benzoxetes 1

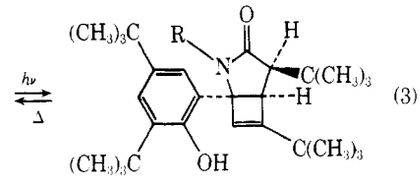
3a–i	R^1	R^2	R^3	Yield, %
a	*tert*-Butyl	*tert*-Butyl	Methyl	87
b	*tert*-Butyl	*tert*-Butyl	*n*-Propyl	76
c	*tert*-Butyl	*tert*-Butyl	Cyclohexyl	75
d	*tert*-Pentyl	*tert*-Pentyl	Methyl	72
e	*tert*-Pentyl	*tert*-Pentyl	*n*-Propyl	81
f	*tert*-Pentyl	*tert*-Pentyl	Cyclohexyl	41
g	*tert*-Butyl	Trityl	Methyl	83
h	*tert*-Butyl	Trityl	*n*-Propyl	90
i	*tert*-Butyl	Trityl	Cyclohexyl	86

course, the phenolic hydroxyl hydrogen (see Figure 1). The differences in the electronic absorption spectra of **3a** and **4a** are significant and revealing. Thus, nonplanar and nonrigid **3a** exhibits its longest wavelength maximum at 274 nm (ϵ 9500). More favorable π-orbital overlap of the 2-vinylbenzofuran chromophore in **4a** is associated with a bathochromic shift and a drastic enhancement of absorption (λ_{max} 294 nm, ϵ 17 000) (see Figure 2).

Support for the conjugated diene moiety in structures **3** and **4** was obtained by photochemical means. Thus, in accordance with the well-documented excited state reactivity of other seven-membered rings containing a conjugated diene moiety,[8] irradiation of **3a** and **4a** gave the acetamido-annelated cyclobutenes **5a** and **6a**, respectively (reactions 3 and 4, respectively). As the absorption of azepinones **3** and **4** at 300 nm is considerable (ϵ 5000 and 16 000 for **3a** and **4a**, respectively), irradiation through Pyrex was found to be most convenient from a preparative point of view, particularly in conjunction with the decrease of absorption in the photoproducts **5** and **6** (see Figure 2).

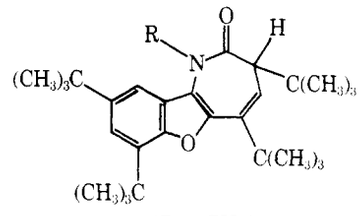


3a (R = CH_3)

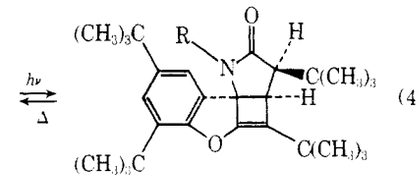


(3)

5a (R = CH_3)



4a (R = CH_3)



(4)

6a (R = CH_3)

Conceivable dimeric photoproducts[9] of **3** and **4** are excluded on the basis of an osmometric molecular weight determination and by the thermal reversibility of the photochemical isomerization.[10] In addition, oxidative cleavage of the cyclobutene

Table II. Chemical Shift Data of Azepinones 3a–i[a]

	3a	3b	3c	3d	3e	3f	3g	3h	3i
H-3	2.31	2.32	2.35	2.43	2.44	2.42	2.44	2.34	2.36
H-4	5.62	5.60	5.62	5.58	5.61	5.51	5.78	5.75	5.78
H-6	6.43	6.47	6.50	6.38	6.42	6.43	6.02	5.91	6.00
$J_{3,4}$	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5
$J_{3,6}$	1	<1	1	<1	<1	<1	<1	<1	<1

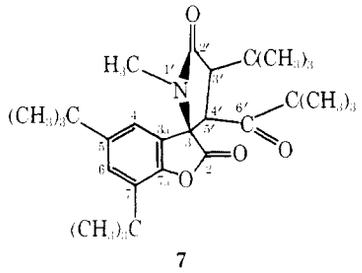
[a] Registry no.: **3a**, 62743-86-6; **3b**, 62778-07-8; **3c**, 62778-06-7; **3d**, 62778-05-6; **3e**, 62743-87-7; **3f**, 62743-88-8; **3g**, 62743-89-9; **3h**, 62743-90-2; **3i**, 62743-91-3.

Table III. ^{13}C Chemical Shifts of 7, 8a, 8b, and 8c[a,g]

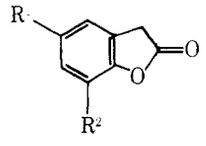
Carbon	7	8a	8b	8c
2	173.9[b]	174.0	173.5	174.1
3	69.8	32.5	33.5	32.7
3a	125.8[c]	123.3[b]	122.2	122.9[b]
4	117.7	122.4[b]	118.7	118.9
5	147.9	133.7[c]	147.1	146.8
5α	34.7[d]	21.0	34.4	34.6[c]
5β	31.3		31.5	31.5
6	125.0[c]	126.2	127.1	122.7[b]
7	134.3	133.1[c]	120.0	133.3
7α	34.2[d]	33.9	15.0	34.3[c]
7β	29.6[e]	29.4		29.6
7a	149.1	150.5	151.3	150.4
1′α	26.4			
2′	173.0[b]			
3′	56.5[f]			
3′α	34.0[d]			
3′β	29.3[e]			
4′	59.0[f]			
6′	212.8			
6′α	45.2			
6′β	25.7			

[a] In parts per million relative to internal Me_4Si. [b–f] Interchangeable assignments within any vertical column. [g] Registy no.: **7**, 60434-65-3; **8a**, 55510-86-6; **8b**, 62743-92-4; **8c**, 62743-93-5.

double bond in **6a** by potassium permanganate afforded the spiro-substituted benzofuranone **7**, exhibiting in its IR spectrum the characteristic[11] carbonyl absorption at about 1800 cm^{-1}. The presence of two strongly coupled hydrogens (J = 11 Hz) in the ^1H NMR spectrum of **7** is indicative of the cis arrangement of H-3′ and H-4′.[12] Comparison with the ^{13}C NMR spectra of model compounds **8a–c**, finally, facilitated



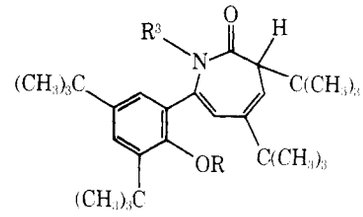
7



8a, $R^1 = CH_3$; $R^2 = C(CH_3)_3$
b, $R^1 = C(CH_3)_3$; $R^2 = CH_3$
c, $R^1 = R^2 = C(CH_3)_3$

complete assignment of the ^{13}C resonances in the NMR spectrum of **7** (see Table III).

In contrast to their excited state reactivity, azepinones **3** and **4** were found to be rather inert in ground state chemistry. Thus, anionic alkylation and acid-catalyzed acylation did not take place in the azepinone moiety but only affected the phenolic hydroxyl group. Thus, **3a** reacts with methylsulfinyl carbanion followed by treatment with methyl iodide to give methyl ether **9a**. Perchloric acid catalyzed reaction of acetic



9a, R = CH_3
b, R = $COCH_3$

anhydride with **3a** gave the acetate **9b**. Attempts to deuterate **9a** at C-3 by treatment with strong base and, subsequently, with deuterium oxide were unsuccessful. Likewise, azepinone **9a** was recovered unchanged after treatment with lithium aluminum hydride in refluxing ether. Attempts to hydrolyze the amido group in azepinones **3a**, **4a**, and **9a** failed. Thus, we have not been able to prove the presence of the amide function in **3** or **4** by chemical means.[14]

The formation of **3** from benzoxetes **1** and primary amines **2** can be rationalized by a nucleophilic displacement reaction leading to 6-amino-substituted 2,4-cyclohexadienones **10** (R^4 = H in Scheme I) which then spontaneously isomerize as

Scheme I

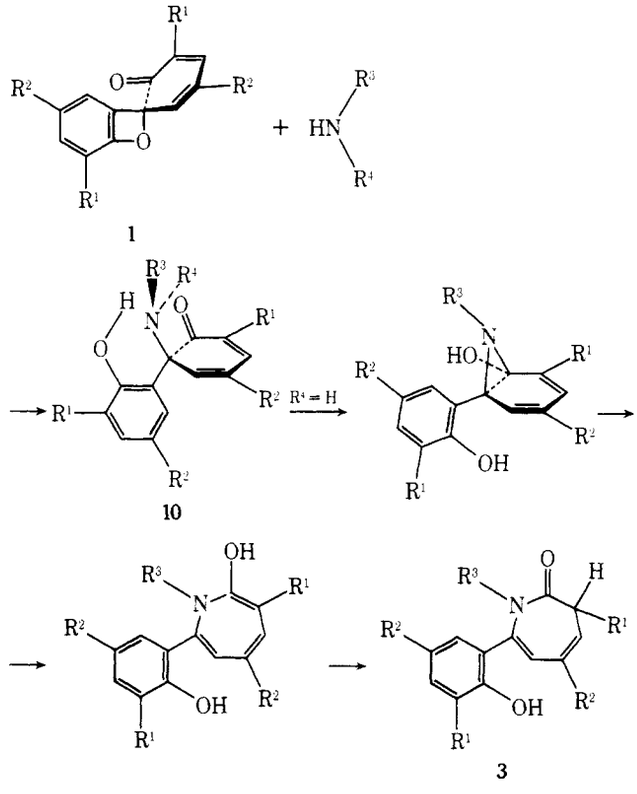


Table IV. Formation of 6-Amino-2,4-cyclohexadienones 10 from Benzoxetes 1

Registry no.	10a–f	R^1	R^2	R^3 R^4	Yield, %
62743-94-6	a	*tert*-Butyl	*tert*-Butyl	$-(CH_2)_2O(CH_2)_2-$	94
62743-95-7	b	*tert*-Butyl	*tert*-Butyl	$-(CH_2)_5-$	88
62743-96-8	c	*tert*-Pentyl	*tert*-Pentyl	$-(CH_2)_2O(CH_2)_2-$	80
62743-97-9	d	*tert*-Pentyl	*tert*-Pentyl	$-(CH_2)_5-$	91
62743-98-0	e	*tert*-Butyl	Trityl	$-(CH_2)_2O(CH_2)_2-$	97
62743-99-1	f	*tert*-Butyl	Trityl	$-(CH_2)_5-$	92

outlined in Scheme I, analogous to a mechanism suggested by Paquette for the reaction of chloramine with phenolate ion.[15] In support of the involvement of the heretofore hypothetical intermediacy of **10**, we have found that secondary amines, such as morpholine and piperidine, smoothly react with **1** in the presence of methanol, even at room temperature, to give 6-amino-2,4-cyclohexadienones **10a–f** in excellent yields (see Table IV). Compounds **10a–d** had been obtained previously in the copper–amine catalyzed autoxidation of the corresponding phenols. However, other structures had been assigned to these products, and they were believed to be formed by oxidative coupling.[17,30] The presence of methanol in the nucleophilic displacement reaction is quite essential,[16] as no **10a** was formed when benzoxete **1a** ($R^1 = R^2 =$ *tert*-butyl) was treated with neat morpholine.[17] Significantly, methanol is known to catalyze the valence isomerization of *o*-diphenoquinones to benzoxetes.[18] Thus, we believe that the formation of 6-amino-2,4-cyclohexadienones **10** from benzoxetes **1** described in this paper does involve a displacement reaction rather than a conceivable 1,4-addition to *o*-diphenoquinones in equilibrium with their thermodynamically favored valence isomers.

Experimental Section

Melting points (uncorrected) were determined on a hot-stage microscope. Infrared spectra, in KBr disks, and electronic absorption spectra were taken on Beckman IR9 and Beckman DK2 instruments, respectively. ^1H NMR spectra were obtained on a Varian A-60 or Bruker WH 270 spectrometer, using chloroform-*d* as solvent with Me_4Si as internal standard. Chemical shifts are reported in parts per million (δ). ^{13}C NMR spectra (in chloroform-*d*) with chemical shifts relative to internal Me_4Si were recorded at 67.88 MHz using a Bruker WH 270 instrument. Mass spectra were obtained at 70 eV ionizing voltage on an AEI MS9 instrument. Elemental analyses were performed by NOVO Microanalytical Laboratory, Bagsvaerd, Denmark.

Recrystallization of products in all cases involved filtration through Celite in order to remove trace amounts of insoluble material.

Materials. 2-*tert*-Butyl-4-tritylphenol was prepared according to the following modification of Shulgin's method.[19] Sulfuric acid (10 mL) was added to a stirred solution of 2-*tert*-butylphenol (30 g, 0.2 mol) and triphenylcarbinol (52 g) in glacial acetic acid (500 mL) at 45–50 °C. After stirring for 20 h at room temperature the precipitate formed was filtered off, washed with acetic acid and water, and then dried. Recrystallization from petroleum ether (bp 80–110 °C) gave 64 g (81%) of colorless crystals: mp 181–183 °C (lit.[19] 173–174 °C); IR 3540 cm^{-1}; NMR 7.20 (s, 15 H), 7.03 (d, J = 2.5 Hz, 1 H), 6.87 (dd, J = 8 and 2.5 Hz, 1 H), 6.45 (d, J = 8 Hz, 1 H), 4.37 (s, 1 H), 1.25 ppm (s, 9 H).

Anal. Calcd for $C_{29}H_{28}O$ (392.54): C, 88.73; H, 7.19. Found: C, 88.85; H, 7.28.

Benzoxetes **1a** ($R^1 = R^2 =$ *tert*-butyl)[20] and **1b** ($R^1 = R^2 =$ *tert*-pentyl)[21] were prepared according to the literature.

Benzoxete 1c. 2′,6-Di-*tert*-butyl-4,4′-ditritylbenzoxete-2-spiro[6′-cyclohexa-2′,4′-dien-1′-one].[22] A solution of potassium hydroxide (2 g) in anhydrous methanol (80 mL) and a solution of 2-*tert*-butyl-4-tritylphenol (see above, 15.7 g, 40 mmol) in methylene chloride (120 mL) were added to a stirred suspension of dichlorobis(pyridine)copper(II)[23] (8.5 g) in anhydrous methanol (80 mL) containing molecular sieve (25 g, 3 A). Dry oxygen was passed through the solution at 30–35 °C for 4 h; the reaction mixture was then diluted with ether and filtered and the residue was repeatedly washed with ether. The combined filtrates were thoroughly washed with water and dried (magnesium sulfate) and the solvent was removed in vacuo to give a residue which was dissolved in methylene chloride. Addition of a 3:2 mixture (75 mL) of methanol and 1-propanol to the boiling solution gave a pale yellow precipitate which was filtered off and recrystallized by dissolving in methylene chloride and adding ethanol to give 11.2 g (64%) of colorless crystals (containing 1 molar equiv of methylene chloride): mp 211–214 °C;[24] IR 1655 (m), 1625 (m),[25] 1600 cm^{-1} (s); UV (isooctane) λ ($\epsilon \times 10^{-3}$) 274 (sh, 10.4), 284 (sh, 8.9), 322 nm (sh, 2.5); NMR 7.18 (m, 30 H), 6.90 (d, J = 2 Hz, 1 H), 6.86 (d, J = 2 Hz, 1 H), 6.25 (s, 1 H), 5.25 (s, 2 H, CH_2Cl_2), 5.05 (s, 1 H), 1.27 (s, 9 H), 1.01 ppm (s, 9 H).

Anal. Calcd for $C_{58}H_{52}O_2 \cdot CH_2Cl_2$ (865.99): C, 81.83; H, 6.29. Found: C, 81.84; H, 6.36.

3,5 - Di - *tert*-butyl-7-(3,5-di-*tert*-butyl-2-hydroxyphenyl)-1-methyl-1,3-dihydro-2*H*-azepin-2-one (3a). A suspension of benzoxete **1a** (4.08 g, 10 mmol) in a 1:1:1 mixture of methylene chloride, methanol, and methylamine (40% aqueous solution) was refluxed for 2 h under nitrogen blanketing. Partial vacuum evaporation of solvent followed by addition of aqueous ethanol to the warm mixture gave a colorless, crystalline precipitate. It was recrystallized from hot ethanol to give 3.82 g (87%) of colorless crystals: mp 153–155 °C; IR 3520 (m), 1680 (s), 1655 (s), 1625 cm^{-1} (m); UV (ethanol) λ ($\epsilon \times 10^{-3}$) 216 (33.4), 274 nm (9.5); NMR 7.38 (d, J = 2.5 Hz, 1 H), 7.03 (d, J = 2.5 Hz, 1 H), 6.43 (d, J = 1 Hz, 1 H), 5.68 (s, 1 H, OH), 5.62 (d, J = 6.5 Hz, 1 H), 2.87 (s, 3 H), 2.31 (d, J = 6.5 Hz, 1 H), 1.45 (s, 9 H), 1.32 (s, 9 H), 1.23 (s, 9 H), 1.19 ppm (s, 9 H); mass spectrum *m/e* 439 (3, $M^{+\cdot}$), 382 (100, M − 57), 354 (6, M − 57 − 28), 326 (7, M − 57 − 56), 242 (2, M − 57 − 56 − 84); ^{13}C NMR 167.9 (s), 148.9 (s), 145.8 (s), 142.0 (s), 139.0 (s), 135.6 (s), 124.1 (d), 123.7 (s), 123.1 (d), 120.0 (d), 120.0 (d), 53.8 (d), 34.5, 34.1, 33.6, 32.7, 31.2, 31.0, 29.5, 29.2, 27.4 ppm.

Anal. Calcd for $C_{29}H_{45}NO_2$ (439.68): C, 79.22; H, 10.32. Found: C, 79.33; H, 10.36.

3,5 - Di - *tert*-butyl-7-(3,5-di-*tert*-butyl-2-hydroxyphenyl)-1-*n*-propyl-1,3-dihydro-2*H*-azepin-2-one (3b). A suspension of benzoxete **1a** (4.08 g, 10 mmol) in methanol (25 mL) and *n*-propylamine (5 mL) was refluxed for 3 h under nitrogen blanketing. The precipitate obtained on cooling to room temperature was filtered off and recrystallized by precipitation with methanol from methylene chloride solution to give 3.55 g (76%) of colorless crystals: mp 162–164 °C; IR 3520 (m), 1675 (s), 1620 cm^{-1} (w); UV (ethanol) λ ($\epsilon \times 10^{-3}$) 216 (31.2), 273 nm (8.4); NMR 7.33 (d, J = 2 Hz, 1 H), 7.03 (d, J = 2 Hz, 1 H), 6.47 (s, 1 H), 5.68 (s, 1 H, OH), 5.60 (d, J = 6.5 Hz, 1 H), 4.16–3.46 (m, 1 H), 2.97–2.50 (m, 1 H), 2.32 (d, J = 6.5 Hz, 1 H), 1.67–0.90 ppm (m containing sharp peaks at 1.43, 1.33, and 1.22 ppm, 41 H).

Anal. Calcd for $C_{31}H_{49}NO_2$ (467.77): C, 79.60; H, 10.56. Found: C, 79.54; H, 10.80.

3,5-Di-*tert*-butyl-7-(3,5-*tert*-butyl-2-hydroxyphenyl)-1-cyclohexyl-1,3-dihydro-2*H*-azepin-2-one (3c). A suspension of benzoxete **1a** (4.08 g, 10 mmol) in methanol (25 mL) and cyclohexylamine (5 mL) was refluxed for 2 h under nitrogen. Addition of a few drops of water to the reaction mixture gave a precipitate which was filtered off and recrystallized by dissolving in methylene chloride and adding methanol: yield 3.80 g (75%) of colorless crystals, mp 209–211 °C; IR 3520 (m), 1675 (s), 1620 cm^{-1} (m); UV (ethanol) λ ($\epsilon \times 10^{-3}$) 216 (32.4), 274 nm (9.0); NMR 7.28 (d, J = 2.5 Hz, 1 H), 7.02 (d, J = 2.5 Hz, 1 H), 6.50 (d, J = 1 Hz, 1 H), 5.80 (s, 1 H, OH), 5.62 (d, J = 6.5 Hz, 1 H), 3.80–3.50 (br m, 1 H), 2.35 (dd, J = 6.5 and 1 Hz, 1 H), 1.80–1.00 ppm (m containing sharp peaks at 1.43, 1.32, 1.28, and 1.17 ppm, 46 H); mass spectrum *m/e* 507 (11, $M^{+\cdot}$), 450 (70, M − 57), 368 (100, M − 57 − 82), 312 (17, M − 57 − 82 − 56).

Anal. Calcd for $C_{34}H_{53}NO_2$ (507.80): C, 80.42; H, 10.52. Found: C, 80.69; H, 10.71.

1-Methyl-3,5-di-*tert*-pentyl-7-(2-hydroxy-3,5-di-*tert*-pentylphenyl)-1,3-dihydro-2*H*-azepin-2-one (3d) was prepared as described for **3a** using benzoxete **1b** (2.33 g, 5 mmol) and refluxing for 4 h. The reaction mixture was diluted with ethanol (25 mL) and then concentrated by partial vacuum evaporation of solvent. The precipitate thus obtained was filtered off, washed with methanol, and

recrystallized from hot ethanol giving 1.78 g (72%) of colorless crystals: mp 144–146 °C; IR 3535 (m), 1675 (s), 1630 cm^{-1} (m); UV (ethanol) λ (ε × 10^{-3}) 275 nm (8.9); NMR 7.25 (d, J = 2.5 Hz, 1 H), 6.93 (d, J = 2.5 Hz, 1 H), 6.38 (s, 1 H), 5.70 (s, 1 H, OH), 5.58 (d, J = 6.5 Hz, 1 H), 2.83 (s, 3 H), 2.43 (d, J = 6.5 Hz, 1 H), 2.20–0.55 ppm (br m, 44 H).

Anal. Calcd for $C_{33}H_{53}NO_2$ (495.79): C, 79.94; H, 10.78. Found: C, 79.86; H, 10.69.

3,5-Di-*tert*-pentyl-7-(2-hydroxy-3,5-di-*tert*-pentylphenyl)-1-*n*-propyl-1,3-dihydro-2*H*-azepin-2-one (3e) was prepared as described for **3b** using benzoxete **1b** (2.33 g, 5 mmol) and refluxing for 1 h. The colorless precipitate thus obtained was washed with methanol and recrystallized by dissolving in methylene chloride and adding methanol to the hot solution: yield 2.12 g (81%) of colorless crystals, mp 180–182 °C; IR 3530 (m), 1670 (s), 1625 cm^{-1} (m); UV (ethanol) λ (ε × 10^{-3}) 275 nm (8.3); NMR 7.26 (d, J = 2.5 Hz, 1 H), 6.98 (d, J = 2.5 Hz, 1 H), 6.42 (s, 1 H), 5.73 (br s, 1 H, OH), 5.61 (d, J = 6.5 Hz, 1 H), 4.10–3.60 (m, 1 H), 2.98–2.63 (m, 1 H), 2.44 (d, J = 6.5 Hz, 1 H), 1.98–1.15 (m, 34 H), 0.98–0.54 ppm (m, 15 H).

Anal. Calcd for $C_{35}H_{57}NO_2$ (523.85): C, 80.25; H, 10.97. Found: C, 80.10; H, 11.06.

1-Cyclohexyl-3,5-di-*tert*-pentyl-7-(2-hydroxy-3,5-di-*tert*-pentylphenyl)-1,3-dihydro-2*H*-azepin-2-one (3f) was prepared as described for **3c** using benzoxete **1b** (2.33 g, 5 mmol) and refluxing for 15 h. The reaction mixture was concentrated by vacuum evaporation of solvent. Addition of a few drops of water gave a crystalline precipitate which was recrystallized from hot ethanol to give 1.15 g (41%) of colorless crystals: mp 153–156 °C; IR 3520 (m), 1680 (s), 1620 cm^{-1} (m); UV (ethanol) λ (ε × 10^{-3}) 276 nm (8.1); NMR 7.24 (d, J = 2.5 Hz, 1 H), 6.98 (d, J = 2.5 Hz, 1 H), 6.43 (s, 1 H), 5.87 (S= [H, OH), 5.51 (d, J = 6.5 Hz, 1 H), 3.67 (br m, 1 H), 2.42 (d, J = 6.5 Hz, 1 H), 2.13–0.52 ppm (m, 54 H).

Anal. Calcd for $C_{38}H_{61}NO_2$ (563.91): C, 80.94; H, 10.90. Found: C, 80.75; H, 10.99.

3-*tert*-Butyl-7-(3-*tert*-butyl-2-hydroxy-5-tritylphenyl)-1-methyl-5-trityl-1,3-dihydro-2*H*-azepin-2-one (3g). A suspension of benzoxete **1c** (500 mg, 0.58 mmol), methylamine hydrochloride (0.5 g), and sodium carbonate (1 g) in methanol (10 mL) was kept in an autoclave at 90–100 °C under nitrogen for 45 min. The suspension was then diluted with methylene chloride and washed with water. The organic layer was dried (magnesium sulfate), and solvent was evaporated in vacuo to give an oily residue which was dissolved in a little methylene chloride to give, after addition of methanol, a colorless, crystalline precipitate. It was recrystallized by dissolving in methylene chloride and adding 2-propanol to the boiling solution. The colorless needles obtained in this way contained (according to NMR and elemental analysis) 2 molar equiv of 2-propanol. Solvent-free azepinone **3g** was obtained by dissolving this material in methanol whereupon the substance dissolved, then formed a new precipitate which was dried at 130 °C for 1 h: yield 390 mg (83%) of colorless crystals, mp 143–145 °C; IR 3510 (m), 1685 (s), 1630 (m), 1600 cm^{-1} (m); UV (*n*-heptane) λ (ε × 10^{-3}) 274 (sh, 10.2), 284 (10.5), 301 nm (sh, 7.6); NMR 7.35–7.10 (m containing sharp peaks at 7.24 and 7.18 ppm, 31 H), 6.49 (d, J = 2.5 Hz, 1 H), 6.02 (s, 1 H), 5.78 (d, J = 6.5 Hz, 1 H), 4.86 (br s, 1 H), 2.68 (s, 3 H), 2.44 (d, J = 6.5 Hz, 1 H), 1.17 and 1.08 ppm (two s, 18 H).

Anal. Calcd for $C_{59}H_{57}NO_2$ (812.11): C, 87.26; H, 7.07. Found: C, 87.14; H, 7.13.

3-*tert*-Butyl-7-(3-*tert*-butyl-2-hydroxy-5-tritylphenyl)-1-*n*-propyl-5-trityl-1,3-dihydro-2*H*-azepin-2-one (3h). A suspension of benzoxete **1c** (500 mg, 0.58 mmol) in methanol (7 mL) and *n*-propylamine (3 mL) was kept in an autoclave at 120–130 °C under nitrogen for 15 min. The suspension obtained on cooling was dissolved in methylene chloride and the solution was concentrated by vacuum evaporation of solvent. Addition of acetonitrile gave a precipitate which was recrystallized by dissolving in a little methylene chloride and adding acetonitrile: yield 440 mg (90%) of colorless crystals, mp 211–214 °C after drying at 130 °C for 1 h; IR 3500 (m), 1675 (s), 1655 (s), 1620 (m), 1600 cm^{-1} (m); UV (*n*-heptane) λ (ε × 10^{-3}) 274 (sh, 9.8), 286 nm (11.0); NMR 7.19 (apparent s, 31 H), 6.55 (d, J = 2.5 Hz, 1 H), 5.91 (s, 1 H), 5.75 (d, J = 6.5 Hz, 1 H), 5.03 (br s, 1 H), 3.75 (br m, 1 H), 2.70 (m, 1 H), 2.34 (d, J = 6.5 Hz, 1 H), 1.45–0.87 (m containing sharp peaks at 1.19 and 1.09 ppm, 20 H), 0.62 ppm (m, 3 H).

Anal. Calcd for $C_{61}H_{61}NO_2$ (840.16): C, 87.21; H, 7.31. Found: C, 86.82; H, 7.26.

3-*tert*-Butyl-7-(3-*tert*-butyl-2-hydroxy-5-tritylphenyl)-1-cyclohexyl-5-trityl-1,3-dihydro-2*H*-azepin-2-one (3i). A suspension of benzoxete **1c** (500 mg, 0.58 mmol) in methanol (7 mL) and cyclohexylamine (3 mL) was kept in an autoclave at 130–140 °C under nitrogen for 15 min. The reaction mixture was filtered and organic solvents were removed in vacuo from the filtrate to give an oily residue which formed a precipitate upon treatment with methanol. Recrystallization from acetonitrile gave colorless crystals which were dried at 130 °C: yield 435 mg (86%); mp 188–191 °C; IR 3500 (m), 1685 (s), 1600 cm^{-1} (m); UV (*n*-heptane) λ (ε × 10^{-3}) 275 (sh, 9.7), 286 nm (10.7); NMR 7.19 (apparent s, 31 H), 6.62 (s, 1 H), 6.00 (s, 1 H), 5.78 (d, J = 6.5 Hz, 1 H), 5.07 (br s, 1 H), 3.41 (br m, 1 H), 2.36 (br m, 1 H), 1.75–0.88 ppm (m containing sharp peaks at 1.20 and 1.08 ppm, 28 H).

Anal. Calcd for $C_{64}H_{65}NO_2$ (880.23): C, 87.33; H, 7.44. Found: C, 87.46; H, 7.51.

3,5,7,9-Tetra-*tert*-butyl-1-methyl-1,3-dihydro-2*H*-benzofuro[2,3-*f*]azepin-2-one (4a). Method A. Oxidation of 3a with Potassium Ferricyanide. Azepinone **3a** (2.20 g, 5 mmol) in ether (100 mL) was oxidized with a solution of potassium ferricyanide (20 g) in water (100 mL) containing potassium hydroxide (4 g) under nitrogen for 20 h. The pale green organic layer was then washed with water and dried (magnesium sulfate) and ether was removed in vacuo to give an oil which crystallized upon treatment with methanol. Recrystallization from hot ethanol gave 1.25 g (57%) of colorless crystals: mp 167–168 or 182–183 °C (depending on the rate of crystallization);[26] IR 1675 cm^{-1} (s); UV (ethanol) λ (ε × 10^{-3}) 234 (26.1), 294 (17.0), 301 nm (sh, 15.7); NMR 7.55 (d, J = 2 Hz, 1 H), 7.43 (d, J = 2 Hz, 1 H), 5.73 (d, J = 7 Hz, 1 H), 3.50 (s, 3 H), 2.30 (d, J = 7 Hz, 1 H), 1.58 (s, 9 H), 1.43 (s, 9 H), 1.36 (s, 9 H), 1.19 ppm (s, 9 H); mass spectrum *m/e* 437 (6, $M^{+\cdot}$), 380 (100, M − 57), 324 (39, M − 57 − 56); ^{13}C NMR 168.1 (s), 149.5 (s), 146.9 (s), 145.9 (s), 140.2 (s), 134.4 (s), 124.9 (s), 123.1 (s), 122.5 (d), 120.1 (d), 113.5 (d), 53.2 (d), 35.1, 34.9, 34.4, 34.2, 32.0, 30.4, 29.9, 29.9, 27.9 ppm.

Anal. Calcd for $C_{29}H_{43}NO_2$ (437.67): C, 79.58; H, 9.90. Found: C, 79.54; H, 9.85.

Method B. Oxidation of 3a with Sodium Bismuthate. A suspension of sodium bismuthate (10 g) and azepinone **3a** (4.40 g, 10 mmol) in toluene (130 mL) was refluxed for 2 h under nitrogen. The cooled reaction mixture was filtered and the inorganic residue was washed with ether. Vacuum evaporation of solvent left an oily residue which crystallized when treated with ethanol. Recrystallization from hot ethanol gave 3.45 g (79%) of colorless crystals, mp 167–168 or 182–183 °C (see note above).

3,5,7,9-Tetra-*tert*-butyl-1-*n*-propyl-1,3-dihydro-2*H*-benzofuro[2,3-*f*]azepin-2-one (4b). Method A. **4b** was prepared as described for **4a** (method A). Recrystallization by dissolving in methylene chloride and adding ethanol to the boiling solution gave 1.82 g (78%) of colorless crystals: mp 190–193 °C; IR 1675 (s), 1610 cm^{-1} (w); UV (ethanol) λ (ε × 10^{-3}) 234 (24.8), 294 (16.0), 301 nm (sh, 14.8); NMR 7.51 (d, J = 2 Hz, 1 H), 7.42 (d, J = 2 Hz, 1 H), 5.77 (d, J = 7 Hz, 1 H), 4.50–3.40 (br m, 2 H), 2.30 (d, J = 7 Hz, 1 H), 2.00–0.60 ppm (br m containing sharp peaks at 1.58, 1.43, 1.35, and 1.17 ppm, 41 H).

Anal. Calcd for $C_{31}H_{47}NO_2$ (465.72): C, 79.95; H, 10.17. Found: C, 80.17; H, 10.15.

Preparation of **4b** according to method B (reaction time 1 h) afforded **4b** in 82% yield.

3,5,7,9-Tetra-*tert*-butyl-1-cyclohexyl-1,3-dihydro-2*H*-benzofuro[2,3-*f*]azepin-2-one (4c) was prepared as described for **4a** (method A). Recrystallization by dissolving in methylene chloride and adding ethanol to the boiling solution gave 2.45 g (97%) of colorless crystals: mp 237–238 °C; IR 1670 (s), 1610 cm^{-1} (w); uv λ (ε × 10^{-3}) 234 (24.8), 294 (15.7), 301 nm (sh, 14.7); NMR 7.48 (d, J = 2 Hz, 1 H), 7.40 (d, J = 2 Hz, 1 H), 5.78 (d, J = 7 Hz, 1 H), 4.13–3.58 (m, 1 H), 2.92–1.00 ppm (m containing a d at 2.33, J = 7 Hz, and sharp peaks at 1.58, 1.44, 1.36, and 1.16 ppm, 47 H).

Anal. Calcd for $C_{34}H_{51}NO_2$ (505.79): C, 80.74; H, 10.16. Found: C, 80.44; H, 10.08.

Preparation of **4c** by oxidation with sodium bismuthate (cf. **4a**) afforded **4c** in 96% yield.

4,6-Di-*tert*-butyl-1-(3,5-di-*tert*-butyl-2-hydroxyphenyl)-2-methyl-2-azabicyclo[3.2.0]hept-6-en-3-one (5a). A solution of azepinone **3a** (2.20 g, 5 mmol) in benzene (180 mL) was irradiated (Pyrex immersion well apparatus, 450-W medium-pressure mercury lamp) at 20 °C under nitrogen for 2.5 h. Vacuum evaporation of solvent gave a crystalline residue which was recrystallized by dissolving in methylene chloride and adding ethanol: yield 1.45 g (66%) of colorless crystals, mp 130–143 °C dec; IR 3310 (m), 1665 (s), 1605 cm^{-1} (w); UV (ethanol) λ (ε × 10^{-3}) 222 (sh, 13.4), 279 (2.1), 284 nm (sh, 1.9); NMR 7.33 (d, J = 2.5 Hz, 1 H), 7.03 (d, J = 2.5 Hz, 1 H), 6.75 (s, 1 H), 6.23 (s, 1 H), 3.59 (d, J = 9 Hz, 1 H), 2.97 (d, J = 9 Hz, 1 H), 2.73 (s, 3 H), 1.42 (s, 9 H), 1.28 (s, 9 H), 1.24 ppm (s, 18 H); ^{13}C NMR 174.2 (s), 164.1 (s), 152.0 (s), 141.7 (s), 136.3 (s), 134.6 (d), 123.9 (d), 123.0 (s), 122.8 (d), 64.5 (s), 57.3 (d), 52.4 (d), 34.8, 34.8, 34.2, 34.2, 31.5, 30.2, 29.9, 29.2, 25.7 ppm.

Anal. Calcd for $C_{29}H_{45}NO_2$ (439.68): C, 79.22; H, 10.32. Found: C, 79.02; H, 10.31.

4,6-Di-*tert*-butyl-1-(3,5-di-*tert*-butyl-2-hydroxyphenyl)-2-*n*-propyl-2-azabicyclo[3.2.0]hept-6-en-3-one (5b) was prepared as described for **5a** using azepinone **3b** (1.50 g, 3.2 mmol). The crude product was recrystallized as dissolving in methylene chloride, adding ethanol, and evaporation of methylene chloride: yield 1.40 g (93%) of colorless crystals, mp 133–153 °C dec; IR 3310 (m), 1670 cm^{-1} (s); UV (ethanol) λ ($\epsilon \times 10^{-3}$) 223 (sh, 13.4), 279 (2.4), 284 nm (sh, 2.2); NMR 7.34 (d, J = 2.5 Hz, 1 H), 7.07 (d, J = 2.5 Hz, 1 H), 6.71 (s, 1 H), 5.94 (s, 1 H), 3.56 (d, J = 10 Hz, 1 H), 3.32–2.85 (m, 2 H), 1.75–0.70 ppm (br m containing sharp peaks at 1.42, 1.30, 1.25, and 1.22 ppm, 42 H).

Anal. Calcd for $C_{31}H_{49}NO_2$ (467.74): C, 79.60; H, 10.56. Found: C, 79.70; H, 10.56.

4,6-Di-*tert*-butyl-1-(3,5-di-*tert*-butyl-2-hydroxyphenyl)-2-cyclohexyl-2-azabicyclo[3.2.0]hept-6-en-3-one (5c) was prepared as described for **5a** using azepinone **3c** (2.54 g, 5 mmol). Recrystallization by dissolving in methylene chloride and adding ethanol gave 2.10 g (83%) of colorless crystals: mp 138–155 °C dec; IR 3200 (m), 1675 (s), 1650 cm^{-1} (s); UV (ethanol) λ ($\epsilon \times 10^{-3}$) 225 (sh, 12.6), 279 (2.2), 284 nm (sh, 1.9); NMR 7.32 (d, J = 2.5 Hz, 1 H), 7.02 (d, J = 2.5 Hz, 1 H), 6.72 (s, 1 H), 5.88 (s, 1 H), 3.85–3.33 (br m containing a d at 3.47 ppm, J = 10 Hz, 2 H), 2.97 (d, J = 10 Hz, 1 H), 2.00–0.70 ppm (br m containing sharp peaks at 1.43, 1.32, 1.25, and 1.22 ppm, 46 H).

Anal. Calcd for $C_{34}H_{53}NO_2$ (507.80): C, 80.42; H, 10.52. Found: C, 80.39; H, 10.44; mol wt, 565 (in benzene).

4,6,9,11-Tetra-*tert*-butyl-2-methylbenzofuro[2,3-*g*]-2-azabicyclo[3.2.0]hept-6-en-3-one[22] (6a) was prepared as described for **5a** using azepinone **4a** (2.20 g, 5 mmol). The crude product was recrystallized by dissolving in methylene chloride and adding ethanol: yield 1.90 g (86%); mp 203–205 °C dec; IR 1690 (s), 1655 (m), 1605 cm^{-1} (w); UV (ethanol) λ ($\epsilon \times 10^{-3}$) 246 (sh, 5.6), 285 (2.5), 291 nm (sh, 2.4); NMR 7.35 (d, J = 2 Hz, 1 H), 7.17 (d, J = 2 Hz, 1 H), 3.56 (d, J = 9 Hz, 1 H), 2.72 (d, J = 9 Hz, 1 H), 2.42 (s, 3 H), 1.42 (s, 9H), 1.30 (s, 18 H), 1.26 ppm (s, 9 H); ^{13}C NMR 173.8 (s), 160.4 (s), 155.5 (s), 145.5 (s), 137.4 (s), 133.8 (s), 124.4 (d), 124.1 (s), 120.8 (d), 64.9 (s), 55.0 (d), 43.6 (d), 34.6, 34.4, 34.4, 32.0, 31.5, 30.2, 29.5, 29.0, 26.1 ppm.

Anal. Calcd for $C_{29}H_{43}NO_2$ (437.67): C, 79.58; H, 9.90. Found: C, 79.60; H, 9.96.

4,6,9,11-Tetra-*tert*-butyl-2-*n*-propylbenzofuro[2,3-*g*]-2-azabicyclo[3.2.0]hept-6-en-3-one[22] (6b) was prepared as described for **5a** using azepinone **4b** (1.17 g, 2.5 mmol) in ether (180 mL) and irradiation for 1.5 h. The crude product was recrystallized by dissolving in methylene chloride and adding methanol: yield 0.83 g (71%) of colorless crystals; mp 136–138 °C dec; IR [69] (s), 1655 (m), 1605 cm^{-1} (w); UV (ethanol) λ ($\epsilon \times 10^{-3}$) 246 (sh, 5.6), 285 (2.4), 291 nm (sh, 2.3); NMR 7.35 (d, J = 2.5 Hz, 1 H), 7.18 (d, J = 2.5 Hz, 1 H), 3.68–3.32 (m, 4 H), 2.70 (d, J = 9 Hz, 1 H), 2.40–1.93 (m, 2 H), 1.60–0.60 ppm (m containing sharp peaks at 1.42, 1.32, and 1.27 ppm, 38 H).

Anal. Calcd for $C_{31}H_{47}NO_2$ (465.72): C, 79.95; H, 10.17. Found: C, 79.54; H, 10.09.

4,6,9,11-Tetra-*tert*-butyl-2-cyclohexylbenzofuro[2,3-*g*]-2-azabicyclo[3.2.0]hept-6-en-3-one[22] (6c) was prepared as described for **5a** using azepinone **4c** (1.26 g, 2.5 mmol) in ether (180 mL) and irradiation for 1.5 h. The crude product was recrystallized by dissolving in methylene chloride and adding methanol: yield 1.20 g (95%); mp 181–183 °C dec; IR 1685 (s), 1650 (m), 1630 cm^{-1} (w); UV (ethanol) λ ($\epsilon \times 10^{-3}$) 246 (sh, 5.1), 285 (2.3), 291 nm (sh, 2.2); NMR 7.35 (d, J = 2.5 Hz, 1 H), 7.25 (d, J = 2.5 Hz, 1 H), 3.60–3.15 (br m containing a d at 3.45 ppm, J = 9 Hz, 2 H), 2.70 (d, J = 9 Hz, 1 H), 1.75–0.70 ppm (br m containing sharp peaks at 1.43, 1.32, and 1.26 ppm, 46 H).

Anal. Calcd for $C_{34}H_{51}NO_2$ (505.79); C, 80.74; H, 10.16. Found: C, 80.50; H, 10.19.

3′,5,7-Tri-*tert*-butyl-4′-(2,2-dimethylpropionyl)-1′-methyl-2(3*H*)-benzofuranone-3-spiro-5′-pyrrolidone(2′)[22] (7). Potassium permanganate (948 mg, 6 mmol) was added to a stirred solution of **6a** (1.31 g, 3 mmol) in acetone (300 mL) giving an immediate precipitation of manganese dioxide. After 30 min the reaction mixture was filtered and solvent was removed in vacuo from the filtrate to give a crystalline residue. This was washed with methanol and recrystallized by dissolving in methylene chloride and adding methanol: yield 1.30 g (92%) of colorless crystals; mp 234–235 °C; IR 1818 (s), 1807 (sh, s), 1698 (sh, s), 1687 cm^{-1} (s); UV (ethanol) λ ($\epsilon \times 10^{-3}$) 285 nm (1.9); NMR 7.38 (d, J = 2 Hz, 1 H), 7.08 (d, J = 2 Hz, 1 H), 4.07 (d, J = 11 Hz, 1 H), 2.98 (d, J = 11 Hz, 1 H), 2.72 (s, 3 H), 1.40 (s, 9 H), 1.35 (s, 9 H), 1.17 (s, 9 H), 0.83 ppm (s, 9 H).

Anal. Calcd for $C_{29}H_{43}NO_4$ (469.67): C, 74.16; H, 9.23. Found: C, 73.89; H, 9.09.

Preparation of 5,7-Disubstituted 2(3*H*)-Benzofuranones. The compounds were prepared according to a procedure described in the literature[11c] for **7-*tert*-butyl-5-methyl-2(3*H*)-benzofuranone (8a).**

5-*tert*-Butyl-7-methyl-2(3*H*)-benzofuranone (8b). A mixture of 4-*tert*-butyl-2-methylphenol (16.5 g, 0.1 mol), glyoxal (7.5 g, 0.05 mol of 40% aqueous solution), and concentrated hydrochloric acid (1 mL) in glacial acetic acid (50 mL) was refluxed for 16 h. The organic layer was washed with water and dried (magnesium sulfate) and solvent was vacuum evaporated giving an oily residue. This was dissolved in methanol and upon cooling (in dry ice–ethanol) a colorless, crystalline precipitate formed which was recrystallized from *n*-pentane to give 3.10 g (15%)[27] of **8b:** mp 101–102 °C; IR 1800 cm^{-1} (s); NMR 7.22 (s, 2 H), 3.73 (s, 2 H), 2.35 (s, 3 H), 1.35 ppm (s, 9 H).

Anal. Calcd for $C_{13}H_{16}O_2$ (204.27): C, 76.44; H, 7.90. Found: C, 76.41; H, 7.90.

5,7-Di-*tert*-butyl-2(3*H*)-benzofuranone (8c) was prepared from 2,4-di-*tert*-butylphenol as described for **8b.** The oily residue obtained after evaporation of methylene chloride crystallized when treated with cold methanol. Recrystallization by dissolving in *n*-hexane and cooling (in dry ice–ethanol) gave 4.85 g (20%)[27] of colorless crystals: mp 87–89 °C; IR 1795 cm^{-1} (s); NMR 7.33 (s, 1 H), 7.23 (s, 1 H), 3.72 (s, 2 H), 1.42 (s, 9 H), 1.33 ppm (s, 9 H).

Anal. Calcd for $C_{16}H_{22}O_2$ (246.35): C, 78.01; H, 9.00. Found: C, 77.77; H, 9.01.

3,5-Di-*tert*-butyl-7-(3,5-di-*tert*-butyl-2-methoxyphenyl)-1-methyl-1,3-dihydro-2*H*-azepin-2-one (9a). A solution of methylsulfinyl carbanion[28] (7.5 mL, ca. 12 mmol) was added to a stirred solution of azepinone **3a** (4.40 g, 10 mmol) in dimethyl sulfoxide (75 mL distilled from calcium hydride) under nitrogen. Methyl iodide (2 mL) was added and the resulting mixture was stirred for 20 min and then diluted with water. The precipitate thus obtained was washed with water and dried. Recrystallization from hot nitromethane gave 4.35 g (96%) of colorless crystals: mp 162–165 °C; IR 1670 (s), 1625 cm^{-1} (m); NMR 7.41 (d, J = 2.5 Hz, 1 H), 7.09 (d, J = 2.5 Hz, 1 H), 6.75 (d, J = 1 Hz, 1 H), 5.54 (d, J = 6.5 Hz, 1 H), 3.80 (s, 3 H), 2.93 (s, 3 H), 2.33 (d, J = 6.5 Hz, 1 H), 1.44 (s, 9 H), 1.33 (s, 9 H), 1.23 ppm (s, 18 H).

Anal. Calcd for $C_{30}H_{47}NO_2$ (453.71): C, 79.42; H, 10.44. Found: C, 79.20; H, 10.33.

3,5-Di-*tert*-butyl-7-(2-acetoxy-3,5-di-*tert*-butylphenyl)-1-methyl-1,3-dihydro-2*H*-azepin-2-one (9b). Azepinone **3a** (500 mg, 1.1 mmol) was dissolved in an acetic anhydride solution in ethyl acetate–perchloric acid[29] (20 mL). After stirring for 30 min the reaction mixture was poured into methanol (10 mL) and then concentrated by vacuum evaporation of solvent. Addition of methanol and a few drops of water gave a crystalline precipitate. It was recrystallized from ethanol to give 510 mg (93%) of colorless crystals: mp 187–190 °C; IR 1770 (s), 1675 (s), 1630 cm^{-1} (m); NMR 7.50 (d, J = 2.5 Hz, 1 H), 7.25 (br m, 1 H), 6.53 (s, 1 H), 5.54 (d, J = 6.5 Hz, 1 H), 2.88 (s, 3 H), 2.32 (s, 3 H), 2.22 (d, J = 6.5 Hz, 1 H), 1.40 (s, 9 H), 1.34 (s, 9 H), 1.22 (s, 9 H), 1.18 ppm (s, 9 H).

Anal. Calcd for $C_{31}H_{47}NO_3$ (481.72): C, 77.29; H, 9.84. Found: C, 77.20; H, 9.81.

2,4-Di-*tert*-butyl-6-(3,5-di-*tert*-butyl-2-hydroxyphenyl)-6-morpholino-2,4-cyclohexadien-1-one (10a). A suspension of benzoxete **1a** (4.08 g, 10 mmol) in methanol (50 mL) and morpholine (5 mL) was refluxed for 5 min. The yellow, crystalline precipitate obtained on cooling was filtered off, washed with methanol, and dried: yield 4.65 g (94%) of **10a;** mp 153–154 °C (lit.[30] 151–152 °C); IR 3400–2500 (m), 1675 (s), 1650 cm^{-1} (m); UV (methanol) λ ($\epsilon \times 10^{-3}$) 278 (3.7), 322 (2.5), 372 nm (sh, 1.5); NMR 11.25 (s, 1 H, OH), 7.25 (d, J = 2.5 Hz, 1 H), 6.98 (d, J = 2.5 Hz, 1 H), 6.65 (d, J = 2.5 Hz, 1 H), 6.25 (d, J = 2.5 Hz, 1 H), 3.88 (m, 4 H), 2.70 (m, 4 H), 1.38 (s, 9 H), 1.25 (s, 9 H), 1.20 (s, 9 H), 0.93 ppm (s, 9 H).

Anal. Calcd for $C_{32}H_{49}NO_3$ (495.75): C, 77.53; H, 9.96. Found: C, 77.26; H, 9.76.

2,4-Di-*tert*-butyl-6-(3,5-di-*tert*-butyl-2-hydroxyphenyl)-6-piperidino-2,4-cyclohexadien-1-one (10b) was prepared as described for **10a** using piperidine (5 mL) and refluxing for 10 min: yield 4.35 g (88%) of yellow crystals; mp 144–145 °C (lit.[30] 137–138 °C); IR 3400–2500 (m), 1675 (s), 1650 cm^{-1} (m); UV (ethanol) λ ($\epsilon \times 10^{-3}$) 280 (3.8), 321 (2.4), 370 nm (sh, 1.5); NMR 11.85 (s, 1 H, OH), 7.20 (d, J = 2.5 Hz, 1 H), 6.93 (d, J = 2.5 Hz, 1 H), 6.63 (d, J = 2.5 Hz, 1 H), 6.25 (d, J = 2.5 Hz, 1 H), 3.28–2.77 (m, 2 H), 2.63–1.56 (m, 8 H), 1.43 (s, 9 H), 1.33 (s, 9 H), 1.30 (s, 9 H), 1.05 ppm (s, 9 H).

Anal. Calcd for $C_{33}H_{51}NO_2$ (493.76): C, 80.27; H, 10.41. Found: C, 79.86; H, 10.93.

6-Morpholino-2,4-di-*tert*-pentyl-6-(2-hydroxy-3,5-*tert*-pentylphenyl)-2,4-cyclohexadien-1-one (10c). A suspension of benz-

oxete **1b** (1.17 g, 2.5 mmol) in methanol (25 mL) and morpholine (3 mL) was refluxed for 10 min. The yellow, crystalline precipitate obtained on cooling was filtered off, washed with methanol, and recrystallized from ethanol: yield 1.05 g (80%) of yellow crystals; mp 118–120 °C (lit.[30] 109–110 °C); IR 3300–2600 (m), 1675 cm^{-1} (s); UV (ethanol) λ (ε × 10^{-3}) 278 (3.4), 322 (2.2), 390 nm (2.0); NMR (11.15 (s, 1 H, OH), 7.10 (d, J = 2.5 Hz, 1 H), 6.90 (d, J = 2.5 Hz, 1 H), 6.59 (d, J = 2.5 Hz, 1 H), 6.18 (d, J = 2.5 Hz, 1 H), 3.90–3.70 (m, 4 H), 2.75–2.45 (m, 4 H), 2.10–0.20 ppm (m, 44 H).

Anal. Calcd for $C_{36}H_{57}NO_3$ (551.86): C, 78.35; H, 10.41. Found: C, 78.25; H, 10.37.

2,4-Di-*tert*-pentyl-6-(2-hydroxy-3,5-di-*tert*-pentylphenyl)-6-piperidino-2,4-cyclohexadien-1-one (10d) was prepared as described for **10c** using piperidine (3 mL). Recrystallization from ethanol gave 1.25 g (91%) of yellow crystals: mp 124–128 °C (lit.[30] 126–127 °C); IR 3300–2600 (m), 1680 cm^{-1} (s); UV (ethanol) λ (ε × 10^{-3}) 279 (4.4), 320 (2.5), 390 nm (2.0); NMR 11.70 (s, 1 H, OH), 7.06 (d, J = 2 Hz, 1 H), 6.85 (d, J = 2 Hz, 1 H), 6.58 (d, J = 2 Hz, 1 H), 6.18 (d, J = 2 Hz, 1 H), 3.10–2.70 (m, 5 H), 2.60–0.20 ppm (m, 49 H).

Anal. Calcd for $C_{37}H_{59}NO_2$ (549.88): C, 80.82; H, 10.82. Found: C, 80.73; H, 10.73.

2-*tert*-Butyl-6-(3-*tert*-butyl-2-hydroxy-5-tritylphenyl)-6-morpholino-4-trityl-2,4-cyclohexadien-1-one (10e). A suspension of benzoxete **1c** (500 mg, 0.59 mmol) in methanol (7 mL) and morpholine (3 mL) was kept in an autoclave at 140–150 °C under nitrogen for 10 min. After cooling the resulting suspension was dissolved in methylene chloride and filtered. The filtrate was concentrated by partial vacuum evaporation of solvent. Addition of methanol gave a yellowish precipitate which was recrystallized by dissolving in methylene chloride and addition of nitromethane followed by partial evaporation of methylene chloride: yield 485 mg (97%) of yellow crystals; mp 203–208 °C; IR 3100–2600 (m), 1675 cm^{-1} (s); UV (chloroform) λ (ε × 10^{-3}) 273 (sh, 7.9), 320 (2.7), 378 nm (sh, 1.8); NMR 11.13 (s, 1 H, OH), 7.25–6.85 (m, 32 H), 6.20 (d, J = 2 Hz, 1 H), 5.95 (d, J = 2 Hz, 1 H), 3.80–3.70 (m, 4 H), 2.80–1.95 (m, 4 H), 1.22 (s, 9 H), 0.92 ppm (s, 9 H).

Anal. Calcd for $C_{62}H_{61}NO_3$ (868.17): C, 85.78; H, 7.08. Found: C, 85.63; H, 7.02.

2-*tert*-Butyl-6-(3-*tert*-butyl-2-hydroxy-5-tritylphenyl)-6-piperidino-4-trityl-2,4-cyclohexadien-1-one (10f) was prepared as described for **10e** at 115–120 °C using piperidine (3 mL). The crude product was recrystallized by dissolving in methylene chloride and adding acetonitrile followed by partial evaporation of methylene chloride: yield 460 mg (92%); mp 195–197 °C; IR 3100–2600 (m), 1670 cm^{-1} (s); UV (chloroform) λ (ε × 10^{-3}) 280 (sh, 7.5), 320 (2.9), 382 nm (1.6); NMR 11.73 (s, 1 H, OH), 7.20–6.80 (m, 32 H), 6.18 (d, J = 2 Hz, 1 H), 5.91 (d, J = 2 Hz, 1 H), 3.00–2.50 (m, 2 H), 2.15–1.35 (m, 8 H), 1.21 (s, 9 H), 0.90 ppm (s, 9 H).

Anal. Calcd for $C_{63}H_{63}NO_2$ (866.20): C, 87.36; H, 7.33. Found: C, 86.97; H, 7.25.

Attempted Base-Catalyzed Deuterium Exchange of Azepinone 9a. Potassium *tert*-butoxide (600 mg) was added to a solution of azepinone **9a** (454 mg, 1 mmol) in hexamethylphosphoric triamide (15 mL, distilled from lithium aluminum hydride) under nitrogen. The deep purple suspension thus obtained was stirred for 30 min at room temperature and, in order to remove *tert*-butyl alcohol, it was then kept at 0.5 mmHg and 30 °C for 2 h. Addition of deuterium oxide (10 mL) under dry nitrogen gave a colorless, crystalline precipitate. It was dissolved in deuteriochloroform which then was washed with deuterium oxide. The organic layer was dried (magnesium sulfate) and solvent was vacuum evaporated to give an oily residue whose NMR spectrum was identical with that of the starting material and showed no incorporation of deuterium.

Attempted Reduction of Azepinone 9a with Lithium Aluminum Hydride. A solution of azepinone **9a** (454 mg, 1 mmol) in anhydrous ether (40 mL) was added to a suspension of lithium aluminum hydride (100 mg, 2.6 mmol) in anhydrous ether (20 mL) under nitrogen. The mixture was refluxed for 5 h and cooled in ice–water and excess lithium aluminum hydride was destroyed by dropwise addition of ethanol and water. The organic layer was washed with a saturated aqueous solution of ammonium chloride and, subsequently, with water. It was dried (magnesium sulfate) and solvent was removed in vacuo to give an oily residue which crystallized after addition of nitromethane, yield 440 mg (97%) of starting material as shown by melting point, TLC, and NMR.

Attempted Hydrolyses of Azepinones 3a, 4a, and 9a. A. A suspension of azepinone **3a** (200 mg) in methanol (15 mL) and concentrated hydrochloric acid (2 mL) was refluxed for 15 h. The crystalline precipitate obtained on cooling was filtered off, washed with water, and dried, yield 120 mg (60%), mp 153–155 °C (mixture melting point with starting material 153–155 °C). Likewise, no reaction was detectable (TLC) after keeping the reaction mixture at 150–160 °C (autoclave) for 60 min.

B. The sodium peroxide procedure of Vaughn and Robbins[31] was followed for hydrolysis of **4a.** The only detectable compound after 24 h was starting material (TLC and NMR).

C. Attempted hydrolysis of **9a** was performed using potassium *tert*-butoxide (6 equiv) and water (2 equiv) in refluxing tetrahydrofuran according to ref 32. Starting material (90%) was recovered after 40 h at reflux temperature.

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Registry No.—1a, 20026-75-9; **1b,** 20026-74-8; **1c,** 62778-04-5; **2a,** 74-89-5; **2a** HCl, 593-51-1; **2b,** 107-10-8; **2c,** 108-91-8; **4a,** 60434-67-5; **4b,** 60434-68-6; **4c,** 60434-69-7; **5a,** 60434-60-8; **5b,** 60434-61-9; **5c,** 60434-62-0; **6a,** 60434-70-0; **6b,** 60434-63-1; **6c,** 60434-64-2; **9a,** 62744-00-7; **9b,** 62744-01-8; 2-*tert*-butylphenol, 88-18-6; triphenylcarbinol, 76-84-6; 2-*tert*-butyl-4-tritylphenol, 60043-12-1; 4-*tert*-butyl-2-methylphenol, 98-27-1; glyoxal, 107-22-2; 2,4-di-*tert*-butylphenol, 96-76-4; morpholine, 110-91-8; piperidine, 110-89-4.

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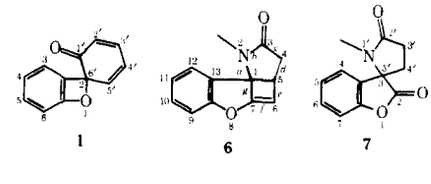

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(26) The high-melting modification can be obtained from the low-melting modification by melting and resolidification.
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Anodic Cyanation of Tertiary Aliphatic and Heterocyclic Amines

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Electrochemical cyanation of tertiary aliphatic and heterocyclic amines in sodium cyanide–aqueous methanol solution using platinum electrodes was studied. Cyanation occurred at the carbon α to the nitrogen atom in each case to form corresponding α-cyano amines in reasonable yields. Some of the unsymmetrical aliphatic and heterocyclic amines gave two isomers. From the relative amounts of the isomers, it was found that the order of ease of the cyanation at the α position of the alkyl group is $(CH_2)_4 > (CH_2)_5 > CH_3 > C_2H_5 > n\text{-}C_3H_7 > i\text{-}C_3H_7$, and that the substitution occurs at the α-carbon situated in positions easily accessible to the electrode.

Electrochemical cyanation of organic compounds has been studied by various investigators,[1-3] but there are only a few reports on the anodic cyanation of amines. Previously, Andreades and Zahnow[4] found that the anodic oxidation of *N,N*-dialkylanilines and benzylamines gave rise to cyanation at the alkyl carbon atom α to the amino nitrogen. Yoshida and Fueno[5] pointed out that the anodic oxidation of diphenylamines in methanol containing sodium cyanide gave *p*-cyanodiphenylamines in good yields. However, no systematic reports are available on the cyanation of tertiary aliphatic amines. We have now studied anodic cyanation of tertiary aliphatic and heterocyclic amines in aqueous methanol containing sodium cyanide at a platinum electrode, and have examined whether this reaction could be used for the preparation of α-cyano amines on a macro scale.

Results

Prior to the preparative studies, current–potential measurements were carried out with triethylamine and α-diethylaminopropionitrile in 0.5 M sodium cyanide–aqueous methanol solution at a platinum anode.

As shown in Figure 1, triethylamine initiated a discharge at approximately 0.7 V (SCE) and then the current rose steeply at 0.9 V or over, whereas α-diethylaminopropionitrile was oxidized at about 0.3 V more anodic than triethylamine. Generally, oxidation potentials of the cyanated products are substantially higher than the values for the corresponding amines. In aqueous methanolic sodium cyanide without triethylamine, a deviation from the ohmic current was observed in the vicinity of 1.0 V, and the electrolytic current gradually increased through the potential of 1.7 V.[6-8] Despite the high concentration of cyanide ion, the degree of increase in the current was very low. Therefore, in the presence of amine, the oxidation of amine itself would be insignificantly affected below 1.4 V.

According to controlled potential electrolyses of triethylamine in 2.0 M sodium cyanide solution, the number of electrons, n, involved in the overall electrode reaction amounted to ca. 2 at 1.2 V.

In a similar manner, relative discharge potentials of other amines were read from the current–potential curves. Each amine employed, except for diisopropylmethylamine and *N-tert*-butylpyrrolidine, was significantly oxidized in a potential range from 0.97 to 1.05 V.

On the basis of the data, preparative constant current electrolyses were carried out under such conditions as to maintain the potential at a convenient range.

In Table I, representative results of anodic cyanation of several kinds of tertiary amines on a macro scale are summarized.

In each case, cyanation occurred exclusively at the carbon atom α to the nitrogen atom and the corresponding α-cyano amines were produced in reasonable yields. Unsymmetrical tertiary aliphatic amines with the methyl group were mainly cyanated at the methyl group, and the amount of cyanation at the methylene group decreased as the length of the alkyl group increased. No cyanated products at the methine group were obtained from dimethylisopropylamine and diisopropylmethylamine.

On the other hand, some of the *N*-alkylpiperidine and pyrrolidine derivatives gave two isomers, one of which was a product substituted at the ring and the other was a product cyanated at the side chain, and it was ascertained that the former product invariably formed in preference to the latter. For example, *N*-methylpiperidine gave *N*-methyl-2-cyanopiperidine in a yield of 41% and α-piperidineacetonitrile in a 25% yield according to GLC analysis (62:38). In the case of *N*-ethylpiperidine, the ratio of cyanation at the ring to the side chain was 78:22, and in *N*-isopropylpiperidine, no side chain substituted product was detected. A similar tendency was observed for *N*-alkylpyrrolidine derivatives, although the substitution showed more precedence to the ring α position than the corresponding piperidine derivatives. Apparently, the order of ease of the cyanation at the α position of the alkyl group is as follows: $(CH_2)_4 > (CH_2)_5 > CH_3 > C_2H_5 > n\text{-}C_3H_7 > i\text{-}C_3H_7 = 0$. This order is compatible with that of steric hindrance around the nitrogen atom of amine.

Table II shows the results of the constant potential electrolysis of *N*-methylpiperidine at various anode potentials.

The current efficiency for the formation of the cyanated products was about 95% even at a potential of 1.4 V. In addition, the relative amount of the isomers was hardly affected by the potentials.