Table II. Crystallographic Data of 8 and 9

	8	9
formula	$C_{20}H_{18}N_2O_3 \cdot xCH_3OH$	$C_{20}H_{18}N_2O_3$
radiation used	Mo Kα (0.7107 Å)	Mo Kα (0.7107 Å)
maximum θ, deg	20	20
space group	$P2_1/c$	$Pbca$
a, Å	12.372 (4)	12.879 (4)
b, Å	18.660 (6)	24.923 (8)
c, Å	9.254 (3)	10.962 (4)
β, deg	111.75 (5)	
Z	4	8
no. of refl measured	1964	1537
observed refl ($I > \sigma(I)$)	1129	749
R_w	13.0%	8.3%

the intensity measurements. A correction for this effect (maximum 10%) was applied. The structures were solved by direct methods (MULTAN 78)[16] and refined by the full-matrix least-squares method (ORFLS).[17] Parameters refined were positional and anisotropic thermal parameters of all nonhydrogen atoms. A final-difference Fourier synthesis for compound 8 revealed two peaks with a distance of 1.5 Å. These peaks were ascribed to methanol, from which compound 8 was recrystallized. Subsequent refinements with inclusion of the carbon and oxygen atoms of the methanol molecule gave rather high temperature factors for both atoms. Therefore a partial occupancy (75%) of the methanol sites was supposed. The refinements now gave reasonable temperature factors, but the C–O distance found (1.7 Å) is too long. Our conclusion is that there is methanol in the crystal lattice, but the quality of our data does not allow us to draw more definite conclusions. A low-temperature X-ray structure determination may resolve the problems. Tables of atomic coordinates, thermal parameters, bond distances, and bond angles have been deposited as supplementary material. The perspective drawings of the structures were made by the ORTEP program.[18]

Registry No. 1, 75420-78-9; 2, 54494-80-3; 6a, 75420-79-0; 6b, 75420-80-3; 8, 75420-81-4; 9, 75420-82-5; 11, 75420-83-6; benzofuran, 271-89-6; 1-chloro-2-phenylacetylene, 1483-82-5; 1-pyrrolidinyllithium, 4439-90-1.

Supplementary Material Available: Tables of atomic coordinates, thermal parameters, bond distances, and bond angles and stereoscopic view of 8·MeOH (5 pages). Ordering information is given on any current masthead page.

(16) G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect. B*, **26**, 274 (1970); P. Main, "Recent Developments in MULTAN" in "Computing in Crystallography", H. Schenk, Ed., Delft University Press, The Netherlands, 1978.
(17) W. R. Busing, K. O. Martin, and H. A. Levy, ORFLS, Oak Ridge National Laboratory, Report ORNL-TM-305, 1962.
(18) C. K. Johnson, ORTEP, Oak Ridge National Laboratory, Report ORNL-3794, 1965.

Thermolysis of *N*-Alkyl-Substituted Phthalamic Acids. Steric Inhibition of Imide Formation

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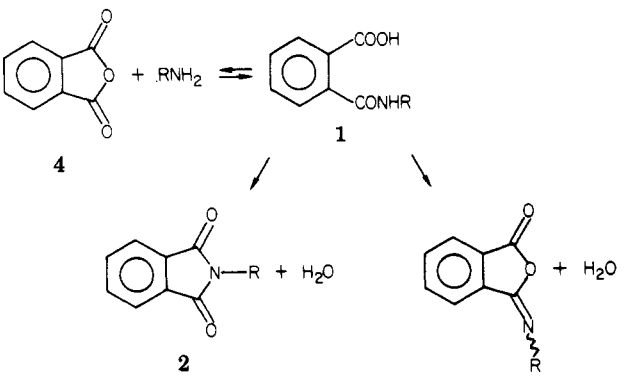
The dehydration of amic acids, derived from the reaction of cyclic anhydrides with primary amines, to yield imides is a general method for the preparation of this important class of heterocyclic compounds and is of major commercial significance in the conversion of polyamic acids to polyimides.[1] In principle, the thermal ring closure of amic acids can lead to the formation of imides, isoimides, or anhydrides (Scheme I). Numerous reagents have been employed to effect the dehydration of amic acids[2] to imides and isoimides and the partitioning of products between these isomers has been found to depend strongly upon the specific dehydrating agent used as well as on the nature of the amic acid itself.[3-10] In contrast, no detailed study of the relationship between the structure of the amic acid and the initial product distribution obtained in the thermal ring-closure reactions of amic acids has been reported. Furthermore, we have observed that in the reaction of phthalic anhydride with primary aliphatic amines to yield imides in refluxing acetic acid, the amount of excess amine required to optimize the yield of imide is strongly dependent upon the steric bulk of the amine employed. For these reasons, we have undertaken a study of the primary product distribution obtained in the vacuum thermolysis at 200 °C of a series of *N*-alkyl-substituted phthalamic acids in which the steric bulk of the *N*-alkyl substituents has been systematically varied.

Scheme I



Results and Discussion

Phthalimides are known to undergo very slow ring opening in the presence of water or amines while the ring opening of anhydrides and the isomerization of isoimides to imides in the presence of these species are known to occur quite readily.[8,11] Therefore, the thermolysis had to be accomplished under conditions which provided for the rapid removal of water and amine as they formed, in order to avoid these secondary reactions. Although various combinations of temperature and pressure were adequate for this purpose, we found that conducting the thermolyses

(1) J. A. Kreuz, A. L. Endrey, F. P. Gay, and C. E. Sroog, *J. Polym. Sci., Part A*, 4, 2607 (1966), and references contained therein.
(2) Some of the more commonly used dehydrating agents include: acetyl chloride, thionyl chloride, phosphorous pentoxide, phosphorous oxychloride, trifluoroacetic anhydride–triethylamine, ethyl chloroformate–triethylamine, and *N,N'*-dicyclohexylcarbodiimide.
(3) A. E. Kretov and N. E. Kullchitskaya, *Zh. Obshch. Khim.*, **26**, 208 (1956).
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(5) W. H. Warren and R. A. Briggs, *Chem. Ber.*, **64**, 26 (1939); F. E. King and D. A. Kidd, *J. Chem. Soc.*, 3315 (1949).
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(7) K. C. Tsov, R. J. Varrnett, and A. M. Seligman, *J. Am. Chem. Soc.*, **77**, 4613 (1955).
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(11) The facile rearrangement of isoimides to imides has also been demonstrated by G. V. Boyd et al., *J. Chem. Soc., Perkin Trans. 1*, 1338 (1978).

0022-3263/81/1946-0175$01.00/0

Table I. Primary Product Distribution in the Vacuum Thermolysis of *N*-Alkyl-Substituted Phthalamic Acids at 200 °C[e] (1 → 2 + 4)

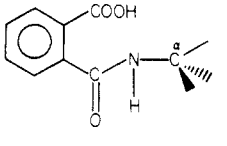
				elemental analysis[c]				% yield[d]	
				C		H			
compd	R	*n*[a]	mp, °C[b]	calcd	found	calcd	found	imide	anhydride
5	CH_3	0	122	60.29	60.09	5.02	5.21	100.0	0.0
6	*n*-C_3H_7	1	105	63.69	63.62	6.28	6.33	100.0	0.0
7	*n*-C_4H_9	1	103	65.15	65.14	6.78	6.87	100.0	0.0
8	*n*-C_5H_{11}	1	114.5	66.38	66.16	7.23	7.26	100.0	0.0
9	*i*-C_4H_9	1	122	65.15	65.04	6.78	6.82	98.9	1.1
10	neo-C_5H_{11}	1	129.5	66.38	66.18	7.23	7.38	97.6	2.4
11	c-C_6H_{11}	2	151.0	68.00	67.97	6.88	6.91	82.2	17.8
12	*i*-C_3H_7	2	133.5	63.69	63.56	6.28	6.28	66.3	33.7
13	*sec*-C_4H_9	2	123	65.15	65.18	6.78	6.83	65.3	34.7
14	*t*-C_4H_9	3	143.5	65.15	65.27	6.78	6.95	12.0	88.0
15	*t*-C_5H_{11}	3	110	66.38	66.58	7.23	7.20	0.0	100.0

[a] *n* = number of carbon branches on the carbon attached to nitrogen. [b] Phthalamic acids undergo ring-closure reactions above their melting point. [c] Satisfactory ^1H NMR, ^{13}C NMR, IR, and UV spectra were obtained for each compound listed. [d] Material balance was quantitative in all cases. [e] Thermolyses were accomplished under a vacuum of 0.3 mmHg.

at 200 °C and a pressure of 0.3 mmHg provided the most satisfactory removal of water and amine without the loss of phthalic anhydride by sublimation. The results of the thermolysis of a series of 11 *N*-alkyl-substituted phthalamic acids under these conditions are shown in Table I. The efficient removal of water and amine from the system was verified by the observation that the product distribution was unchanged when the thermolyses were conducted in the absence or presence of 1 molar equiv of phthalic anhydride.

Although we found no evidence for the formation of phthalisoimides **3** in any of our thermolyses, control experiments indicated that phthalisoimides rearrange rapidly to phthalimides during the thermolysis of phthalamic acids under our conditions. Thus, if phthalisoimides were formed during thermolysis, they were rapidly converted to the corresponding phthalimides.

Examination of the relative yields of imide and anhydride in Table I shows that the product distribution obtained in the thermolysis of phthalamic acids undergoes a total reversal in going from *N*-methylphthalamic acid **5** to *N*-*tert*-amylphthalamic acid **15**. The acid **5** yields only imide while **15** yields only anhydride. From the data there is a clear trend toward reduced imide formation as the steric bulk of the alkyl substituent in the phthalamic acid increases. Specifically, the yield of imide appears to depend upon the number and type of branching structures at the α-carbon of the alkyl substituent in the phthalamic acids **16**.



16

The effect of the number of branches on the α-carbon (n) on the product distribution is shown in Table I. The effect of the type of branching on product distribution can be seen by the substantial increase in imide formation in going from *N*-isopropylphthalamic acid (**12**) to *N*-cyclohexylphthalamic acid (**11**) in which the two branching carbons are "tied-back" in the cyclohexane ring. This effect is also shown by the total inhibition of imide formation in the thermolysis of **15** which results from the replacement of one of the methyl groups in **14** by an ethyl group. Since all of the phthalamic acids studied here were derived from amines of nearly identical basicity ($K_b \simeq (3\text{–}5) \times 10^{-4}$), it seems unlikely that the significant differences observed in the product distributions arising from the thermolysis of compounds **5** through **15** could reflect electronic differences among these compounds.

Thus it is clear that the results reported here are consistent with a steric inhibition to imide formation in the thermal ring-closure reactions of *N*-alkyl-substituted phthalamic acids. The mechanistic implications of this rather dramatic steric effect are currently under investigation in our laboratory.

Experimental Section

Melting points were determined on a Melt-Temp apparatus and are uncorrected. Chromatographic analysis were performed with a Waters Associates HP liquid chromatograph equipped with a fixed UV detector at 254 nm, using a solvent mixture of 5% tetrahydrofuran in isooctane and a Waters Associates μBondapak CN column. Yields were determined by using a benzophenone internal standard and product identification was accomplished by comparison with retention volumes for authentic samples.

Materials. Authentic samples of the *N*-alkylphthalimides were prepared by refluxing a solution of 4 molar equiv of the primary alkyl amine with phthalic anhydride in glacial acetic acid according to the method of Vanags and Veinsbergs.[12] Phthalic anhydride was sublimed under reduced pressure prior to use and the primary alkylamines were used as obtained commercially without further purification.

General Procedure for Preparation of *N*-Alkyl-Substituted Phthalamic Acids 5–15. The primary alkylamine (1 equiv) was added slowly with stirring to a solution of 10.0 g (67.5 mmol) of phthalic anhydride in 100 mL of methylene chloride at 25 °C. After the mixture was stirred for 30 min, the precipitated phthalamic acid was suction filtered and washed with several portions of pentane. The products were then dried under reduced pressure at ambient temperature for 3–4 h and stored in sealed vials.

Vacuum Thermolysis Procedure. Thermolyses were carried out on 5.0-mg samples of the phthalamic acids which were placed in the bottom of a 10-mL pear-shaped flask attached to a short-path distillation head under a vacuum of 0.3 mmHg. The bottom tip of the flask containing the phthalamic acid was immersed in a hot oil bath held at 200 °C to just above the level of the solid. The flask was removed from the oil bath after the molten acid had been converted to solid imides and anhydrides which condensed on the walls of the flask just above the oil line. The time required for the completion of the thermolysis was generally 5–8 s after melting occurred. The solid residues were then taken up in a THF/isooctane solvent mixture and the benzophenone standard was added. The resulting solutions were then analyzed by high-pressure liquid chromatography as previously described.

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Acknowledgment. We thank Professor Samuel Danishefsky, Dr. D. M. White, and Dr. H. M. Relles for helpful discussions.

Registry No. 2 (R = CH_3), 550-44-7; **2** (R = n-C_3H_7), 5323-50-2; **2** (R = n-C_4H_9), 1515-72-6; **2** (R = n-C_5H_{11}), 71510-39-9; **2** (R = i-C_4H_9), 304-19-8; **2** (R = neo-C_5H_{11}), 61020-63-1; **2** (R = c-C_6H_{11}), 2133-65-5; **2** (R = i-C_3H_7), 304-17-6; **2** (R = sec-C_4H_9), 10108-61-9; **2** (R = t-C_4H_9), 2141-99-3; **4**, 85-44-9; **5**, 6843-36-3; **6**, 17332-34-2; **7**, 19357-01-8; **8**, 19357-03-0; **9**, 75476-64-1; **10**, 75476-65-2; **11**, 19357-06-3; **12**, 20320-33-6; **13**, 69338-48-3; **14**, 20320-35-8; **15**, 75476-66-3; methylamine, 74-89-5; propylamine, 107-10-8; butylamine, 109-73-9; pentylamine, 110-58-7; isobutylamine, 78-81-9; neopentylamine, 5813-64-9; cyclohexylamine, 108-91-8; isopropylamine, 75-31-0; sec-butylamine, 13952-84-6; $tert$-butylamine, 75-64-9; $tert$-pentylamine, 594-39-8.

Anodic Oxidation of Mixed Ethers of Hydroquinones. A Complementary Route to Benzoquinone Monoketals

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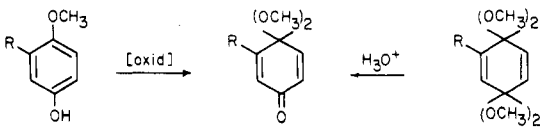
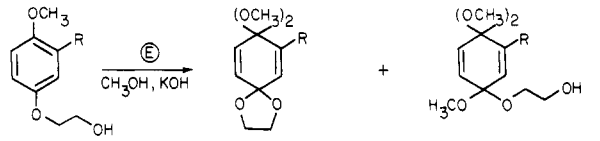
Quinone monoketals are of demonstrated utility in organic synthesis.[1] These compounds are prepared from oxidation of p-methoxyphenols[1,2] or by regioselective hydrolysis of quinone bisketals.[1,3] The former method is dependent upon the availability of the requisite phenol; the latter procedure affords the quinone monoketal wherein the less hindered quinone carbonyl is present as the free carbonyl group. We report here a technique for preparation of selected quinone monoketals wherein the more hindered carbonyl group of the quinone is unprotected.



1 2 3a, R = CH_3; b, R = Br

A key aspect of the work was the finding that mixed aromatic ethers (i.e., **4**) undergo anodic oxidation to give predominantly **5**.[4] The lesser amount of **6** formed in the reaction is readily separated by chromatography on neutral alumina. The products **5** and **6** showed spectroscopic (IR, NMR) properties in agreement with the assigned structures.

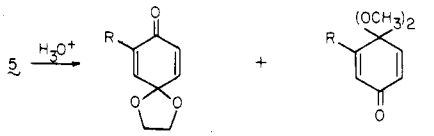


4g, R = H; b, R = CH_3; c, R = Br; d, R = OCH_3

5g, 66%; b, 83%; c, 81%; d, 86%

6g, 15%; b, 7%; c, 13%

The monohydrolysis of bisketals **5a–c** gave monoketals **7a–c** in the indicated yields after recrystallization or molecular distillation. In the case of **5d**, two products were formed in ca. 7:1 ratio. The major product, **8d**, was obtained by direct recrystallization in 68% yield. The minor product (presumably **7d**) was difficultly separable from **8d** by chromatography and was not rigorously characterized.



7g, 94%; b, 93%; c, 78%; d, --[5]

8g, --; b, --; c, --[5]; d, 68%

These results most reasonably arise from the slower rate of hydrolysis of the ethylene glycol ketal relative to the dimethyl ketal. For the dimethyl ketal a trans-periplanar arrangement between the departing methoxy group and the electron pair on the oxygen of the remaining methoxy group is possible (i.e., **9**), whereas for an ethylene glycol ketal this most favorable situation is not available (i.e., **10**) (Figure 1).[6] While the change in direction of ketal hydrolysis in going from the bisketals such as **3a** and **3b** to **5b** and **5c** was anticipated, the high selectivity of the hydrolysis in the latter two systems would not be expected from literature rate data.[7] The rate difference for hydrolysis of an ethylene glycol ketal vs. a dimethyl ketal is a factor of ~20. In the monohydrolysis of the bis(dimethoxy ketals) **3a** and **3b**, the regioselectivity of the hydrolysis is 85:15 and 95:5, respectively, in favor of the monoketal **2**.[3b] Assuming a rate retardation of 20 upon replacement of a dimethyl ketal by an ethylene glycol ketal, some regioselectivity of hydrolysis for **5b** and **5c** would have been predicted. The highly selective hydrolysis for **5b** and **5c** suggests there must be a small rate alteration in these systems upon replacement of a dimethyl ketal by an ethylene glycol ketal. In the case of **5d**, the stabilization of the carbonium ion formed in the hydrolysis by the methoxy group outweighs other considerations, and the major monoketal formed is **8d**, the same product obtained from the bis(dimethoxy ketal) **3d** (R = OCH_3).

As noted earlier conventional preparation of quinone monoketals often gives access to only one of the regioisomers. These results demonstrate that both benzoquinone monoketal regioisomers can be obtained from common intermediates—the p-methoxyphenol or the bisketal—provided good carbonium ion stabilizing groups are not substituted on the bisketal.

(1) For leading references, see: Henton, D. R.; Anderson, D. K.; Manning, M. J.; Swenton, J. S. *J. Org. Chem.* **1980**, *45*, 3422–3433.

(2) (a) McKillip, A.; Perry, D. H.; Edwards, M.; Antus, S.; Farkas, L.; Nogradi, M.; Taylor, E. C. *J. Org Chem.* **1976**, *41*, 282–287. (b) Büchi, G.; Chu, P.; Hoppmann, A.; Mak, C.; Pearce, A. *Ibid.* **1978**, *43*, 3983–3985. (c) Crouse, D. J.; Wheeler, D. M. S. *Tetrahedron Lett.* **1979**, 4797–4798. (d) Hart, W.; Scheinmann, F. *Ibid.* **1980**, *21*, 2295–2296.

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(4) The anodic oxidation of the 1,4-bis(2-hydroxyethoxy)benzene has been reported: Margaretha, P.; Tissot, P. *Helv. Chim. Acta* **1975**, *58*, 933–936.

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