The Direct Alkylation of π-Rich, Acid-Sensitive Heterocyclic Compounds *via* Essentially Free Carbocations[1]

Ron W. Darbeau* and Emil H. White

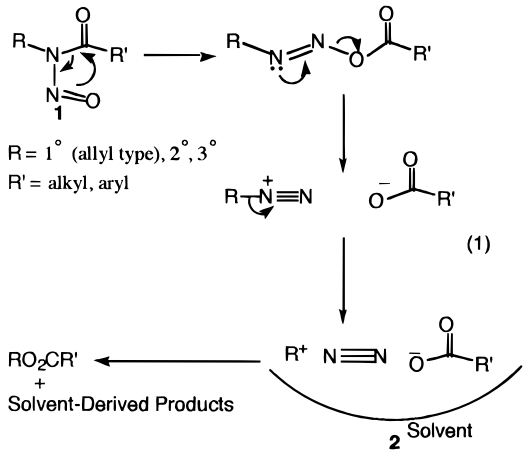
Department of Chemistry, McNeese State University, Lake Charles, Louisiana 70609 and Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218

Received June 16, 1997[⊗]

Alkylation of π-rich heteroaromatics such as pyrroles and furans by the standard Friedel−Crafts approach is impractical because the acid catalysts employed (Brønsted or Lewis) induce polyalkylation, ring opening, and polymerization. The present study describes the facile benzylation of π-excessive heteroaromatics using the nitrosoamide approach, which generates nitrogen-separated carbocation−counterion ion-pairs as the alkylating agent with no catalyst being required. *N*-Nitrosoamides are favorable sources of carbocations because of the following variables: mildness of the conditions required to generate cations, high reactivity of the unsolvated carbocations formed, solubility of the precursors in a wide range of solvents, homogeneity of the reactions, wide range of decomposition temperatures possible, straightforward chemistry, and excellent product balance. The majority of the cations that are generated in pyrrole (80%) are intercepted by the solvent, and only 20% are intercepted by the counterion; this result provides support for the intermediacy of nitrogen-separated ion-pairs in deamination. A nucleophilicity scale is presented for reactions of selected nucleophiles with essentially free carbocations.

Introduction

Carbocations are reaction intermediates in the thermal decomposition of *N*-alkyl-*N*-nitrosoamides (eq 1);[2] they are generated in the form of nitrogen-separated ion-pairs. Carbocations formed in this way are little solvated and thus highly reactive;[2] they are probably the "freest" type of carbocations that can be readily prepared in liquid solution. The nitrogen molecule, through its screening



action with respect to the counterion, provides the carbocation with time to interact with molecules comprising the solvent cage. Thus, the overall reaction is one in which the carbocations are scavenged in competing processes: by nucleophiles in the solvent cage and by the counterion (after diffusion of the nitrogen molecule from its blocking position) (eq 1).[3] Neutral conditions in nonpolar solvents can be used,[2,4b] and since catalysts are not used, the reaction constitutes a particularly useful way of investigating the intrinsic reactions of essentially free carbocations introduced by a unimolecular process[6] into essentially any medium.[3b] The nitrosoamide approach has been used in alkylation of compounds ranging from hydrocarbons (e.g. benzene, toluene)[4] to carboxylic acids.[6b] Several related reactions lead to analogous intermediates,[7] and through their use, a wide range of temperatures[4] can be employed for the generation and study of carbocations.

Heterocyclic compounds such as furan and pyrrole are "π-rich" or "π-excessive," because resonance involving lone-pair electrons on the heteroatom result in an enhanced electron density on the carbon atoms of the ring.[8] Consequently, these heteroaromatics are as reactive as anilines and phenols in undergoing electrophilic substitutions.[8] Mono C-alkylation of pyrrole cannot be achieved through direct reaction with simple alkyl halides, either alone or with Lewis-acid catalysts, because

⊗ Abstract published in *Advance ACS Abstracts,* October 15, 1997.

(1) Publication no. 56 in a series on alkane diazonium ion-pairs and deamination. Preceding publication: White, E. H. *et al. J. Org. Chem.* **1996**, *61*, 7986.

(2) (a) White, E. H.; Field, K. W.; Hendrickson, W. H.; Dzadzic, P.; Roswell, D. F.; Paik, S.; Mullen, P. W. *J. Am. Chem. Soc.* **1992**, *114*, 8023. (b) White, E. H.; DePinto, J. T.; Polito, A. J.; Bauer, I.; Roswell, D. F. *J. Am. Chem. Soc.* **1988**, *110*, 3708. (c) White, E. H.; McGirk, R. H.; Aufdermarsh, C. A.; Jr.; Tiwari, H. P.; Todd, M. J. *J. Am. Chem. Soc.* **1973**, *95*, 8107. (d) White, E. H.; Tiwari, H. P.; Todd, M. J. *J. Am. Chem. Soc.* **1968**, *90*, 4734. (e) White, E. H.; Field, K. W. *J. Am. Chem. Soc.* **1975**, *97*, 2148.

(3) (a) The decomposition products (∼98%) in a reactive solvent are the corresponding ester and the solvent-derived products (SDP).[4b] (b) The yields of solvent-derived products (SDP) increase[4b,5] with the reactivity of the cation,[2c,4b] with the nucleophilicity of the solvent, and inversely with the nucleophilicity of the counterion.[2b,4b]

(4) (a) White, E. H.; Woodcock, D. J. In *The Chemistry of the Amino Group*; Patai, S., Ed.; John Wiley and Sons, Inc.: New York, 1968; Chapter 8. (b) From the Ph.D. Thesis of Ron W. Darbeau, The Johns Hopkins University, Baltimore, Maryland, 1996.

(5) The yield of SDP also increases, but to a lesser extent, as the inert molecule is varied from N_2 to N_2O[4b] and by performing the reactions at lower temperatures.[4b]

(6) (a) Huisgen, Rüchardt, C. *Justus Liebigs Ann. Chem.* **1956**, *601*, 1. (b) White, E. H.; Dolak, L. A. *J. Am. Chem. Soc.* **1966**, *88*, 3790.

(7) (a) White, E. H.; Ribi, M. A.; Cho, L. K.; Egger, N.; Dzadzic, P. M.; Todd, M. D. *J. Org. Chem.* **1984**, *49*, 4866. (b) White, E. H. *J. Am. Chem. Soc.* **1955**, *77*, 6014. (c) White, E. H.; Maskill, H.; Woodcock, D. J.; Schroeder, M. A. *Tetrahedron Lett.* **1969**, 1713. (d) White, E. H.; Lewis, C. P.; Ribi, M. A.; Ryan, T. J. *J. Org. Chem.* **1981**, *46*, 552. (e) Müller, H.; Haiss, H. *Chem. Ber.* **1963**, *96*, 570. (f) Olah, G. A.; Friedman, N.; Bollinger, J. M.; Lukas, J. *J. Am. Chem. Soc.* **1966**, *88*, 5328. (g) Schmid, H.; Sami, A. F. *Monatsh. Chem.* **1955**, *86*, 904. (h) Soll, H. *Methoden der Organischen Chemie*; Muller, E., Ed., (Houben-Weyl), Georg Thieme Verlag: Stuttgart, 1958; Vol. 11, Part 2, p 133.

S0022-3263(97)01081-5 CCC: $14.00

Table 1. Benzylation of Heterocyclic Compounds with *N*-Benzyl-*N*-nitrosobenzamide (1a)[a]

solvent	temp (°C)	% yields: ester **3**	% yields: alkylated heteroaromatics **4** + **5**	isomer distribution (%): 2-isomer **4**	isomer distribution (%): 3-isomer **5**
pyrrole	40	20	80	62	38
equimolar pyrrole/$CDCl_3$	40	41	59	64	36
N-methylpyrrole	40	32	68	49	51
furan	25	77	23	88	12

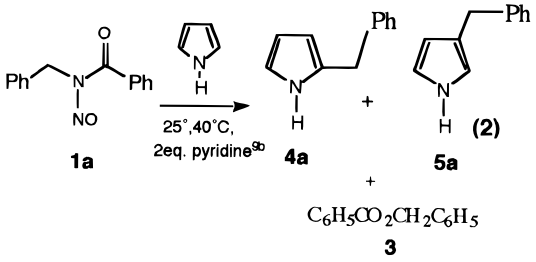
[a] [Nitrosoamide] ≈ 0.05 M. The data are averages of two or more runs; standard deviation for yields and for isomer distributions ≤0.4.

pyrroles are polymerized by strong acids.[8] Similarly, traditional Friedel−Crafts alkylation is not practical with furan because of catalyst-promoted polymerization and polyalkylation.[8]

The present study demonstrates that mono C-benzylated, π-rich heteroaromatics can be readiliy prepared *via* the nitrosoamide route.

Results and Discussion

Direct Benzylation of Pyrrole Using the Nitrosoamide Approach. *N*-Benzyl-*N*-nitrosobenzamide (**1a**) was decomposed in pyrrole (eq 2) at 25 °C and at 40 °C; the half-lives of these decompositions were ∼2 days at 25 °C and ∼7 h at 40 °C.[9a,b]



From the reaction in neat pyrrole, the yield of C-benzylpyrroles (**4a** + **5a**) was 80% (Table 1) with a 2-benzylpyrrole/3-benzylpyrrole ratio (**4a/5a**) of 62/38. The latter ratio is consistent with the larger nucleophilicity at the C_2 center vs that at C_3.[8a,b] Interestingly, no *N*-benzylpyrrole was observed which may appear a little surprising given the high reactivity of the deaminatively formed benzyl cation.[2,4,7] It has been proposed, however, that five-membered heteroaromatics do not react with electrophiles (alkyl groups, protons, etc.) at the heteroatom[8a,b] because reaction at this position would lead to a substantial loss of resonance stabilization.[8c]

In equimolar pyrrole/$CDCl_3$, although the isomer distribution was virtually unchanged (Table 1), the yield of benzylpyrroles was 59% (*vide infra*). Deuteriomethylbenzene was not observed in decompositions of **1a** in 10:1, 1:1, or 1:10 mixtures (vol/vol) of either pyrrole/$CDCl_3$ or of hexane/$CDCl_3$;[4b] since alkyl radicals are known to abstract hydrogen from chloroform,[10] it appears that free-radical pathways are absent in these reactions.

Benzylation of *N*-Methylpyrrole *via* the Nitrosoamide Approach. Compound **1a** was decomposed in *N*-methylpyrrole at 40 °C (the half-life of the decomposition was also ∼7 h at 40 °C as above[9a,b]). In the present case, the yield of solvent-derived products (SDP) (**4** + **5**) was 68% (Table 1), and the isomer distribution (**4**:**5**) was roughly 1:1 (Table 1). *N*-Methylpyrrole ($pK_a = -2.9$)[8a] is more basic than pyrrole ($pK_a = -3.8$),[8a] but from the larger yield of SDP in the latter case (80% vs 68%) (Table 1) it would appear that pyrrole competes better for the carbocation than does *N*-methylpyrrole. Further, the relative yield of 2-benzylpyrrole, **4a** (62%) (Table 1), is larger than that of 2-benzyl-1-methylpyrrole (49%) (Table 1). The steric effect of the *N*-methyl group may be responsible for these observations by decreasing the rate of alkylation at the adjacent 2-position of the pyrrole nucleus.

The results shown in Table 1 indicate that the nitrosoamide approach allows for direct syntheses of mono C-benzylpyrroles in good to excellent yields under mild conditions.

The high yield of benzylpyrroles formed (80%) (Table 1) indicates that even in the case of the relatively unreactive, resonance-stablized benzyl cation, the majority of the carbocations of the inert-molecule-separated ion-pair are interceptible by solvent molecules if the latter are sufficiently reactive. This fact provides further evidence for the initial presence of a nitrogen molecule between the cation and its counterion, since in its absence one would have expected that a facile carbocation−anion reaction would have produced principally the ester (**3**). The 80% yield of SDP is similar to values of 75−80% observed for the yields of acetate ester from decomposition in acetic acid,[2c] and for methyl alkyl ethers from decompositions in methanol.[4b] In general, it would appear that ∼80% is the maximum amount of solvent interception that is possible. This limit is set presumably by the high diffusion rate of nitrogen into the medium, which would allow a finite amount of ester formation through ion-pair collapse involving the cation and its counterion.

In the presence of equimolar $CDCl_3$ (an inert diluent for the benzyl cation),[4b,9d] the yield of SDP from the benzylation of pyrrole remains high (59%; Table 1). The fact that equimolar $CDCl_3$ reduces the solvent-capture yield only from 80% to 59% and not to 40%, the value expected on statistical grounds, suggests that not all abortive collisions of the benzyl cation with inert molecules will lead to ion-pair collapse (ester formation). Evidently carbocations which have undergone such collisions still have the ability to alkylate pyrrole.

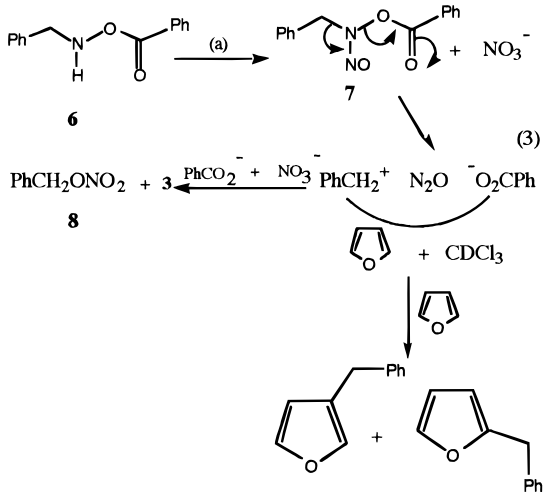
Benzylation of Furan. Furan was benzylated using nitrosoamide **1a** at 25 °C; a 23% yield of benzylfurans was observed (Table 1). The lower yield of SDP is consistent with furan being less nucleophilic than the pyrroles.[8a,b] The 2-isomer/3-isomer ratio was 88/12 (Table 1). A second approach to the benzylation was pursued in which ^{1}H NMR spectra were recorded at −80 °C to

(8) (a) Joule, J. A.; Mills, K.; Smith, G. F. *Heterocyclic Chemistry*, 3rd ed., Chapman and Hall: London, 1995; pp 231−232. (b) Schofield, K. *Hetero-Aromatic Nitrogen Compounds: Pyrroles and Pyridines*, Plenum Press: New York, 1967; p 3. (c) *N*-Alkylpyrroles, however, are readily prepared by reaction of pyrryl salts with iodoalkanes (Candy, C. F.; Jones, A. R. *J. Org. Chem.* **1971**, *36*, 3990 and Hobbs, C. F. et al. *J. Am. Chem. Soc.*, **1962**, *84*, 43).

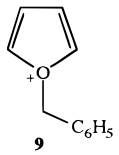
(9) (a) Half-lives were determined by measuring the changes in the integral of the benzyl signal as a function of time at a constant temperature in the NMR probe. (b) With bulkier nitrosoamides such as *N*-benzyl-*N*-nitrosopivalamide (which has a half-life of ∼30 min in ∼0.1 M solutions in benzene/toluene at 25 °C)[4b] benzylation would be faster. (c) No alkylpyridines were observed presumably because of the low concentration of the relatively unreactive pyridine. (d) No reaction between the benzyl cations and chloroform has been observed in that neither toluene nor hexachloroethane were detected by ^{1}H NMR or GC and by GC, respectively (see ref 2e for comparison).

(10) Fossey, J.; Lefort, D.; Sorba, J. *Free Radicals in Organic Chemistry*; John Wiley and Sons: New York, 1955; pp 202−203.

determine whether *O*-benzylfuranonium ion, **9**, was a reaction intermediate. To this end, furan in 30% furan/$CDCl_3$ (vol/vol) was benzylated using nitrosation of *N*-benzyl-*O*-benzoylhydroxylamine (**6**) at −80 °C as a source of benzyl cations (eq 3).[7a] With the exception of benzyl benzoate (**3**) and benzyl nitrate (**8**) (eq 3), no new



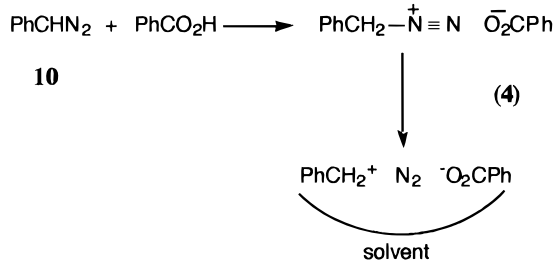
signals (^{1}H NMR) were observed between 5−7,[11,12] at −80 °C or on warming to 25 °C. The signals for the *C*-benzylpyrroles were already present in the first spectrum run at −80 °C (time from mixing ≈ 45 s). This observation indicates that either the *O*-benzylfuranonium ion (**9**) did not form or that it is too labile for detection at −80 °C. The yield of benzylfurans in this latter experiment



9

was ∼5%, consistent with the low mole fraction of furan in the medium.[4] The isomer distribution [90% (2-isomer)/10% (3-isomer)] was similar to that obtained in the nitrosoamide aproach.

A Nucleophilicity Scale for Substrates in Reactions with Highly Reactive Carbocations. Thermolyses of *N*-benzyl-*N*-nitrosoamides (eq 1) and acidification of phenyldiazomethane (**10**) (eq 4) lead to the formation of equivalent suites of particles: nitrogen-separated ion-pairs.[4b,17] These ion-pairs consist of essentially free benzyl carbocations that react with either the counterion or with solvent molecules.[4] Thus the yield



of solvent-derived products (SDP) (when different solvents, but a common cation/counterion pair are used) can be considered as a measure of the relative nucleophilicities of the solvents.

The data show (Table 2) that the nucleophilicities decrease in the order: pyrrole > methanol > *N*-methylpyrrole > acetone > furan ≈ acetonitrile > toluene > benzene > chloroform ≈ pentane.[14a,b] The present scale (Table 2) is more compressed than scales that are based on S_N2 reactions[15a] or on reactions of stable cations such as trityl with nucleophiles.[15b] This observation is consistent with the high reactivity of deaminatively generated carbocations.

Table 2. Yields[a] of Solvent-Derived Products (SDP) from the Reaction of Benzyl Cations Generated from *N*-Benzyl-*N*-nitrosobenzamides or from Phenyldiazomethane

solvent	pK_b	yield of SDP (%)	yield of SDP yield of ester	yield of SDP in solvent X yield of SDP in benzene
pyrrole	17.8[b]	80[c,d]	4.0	11.4
methanol	16[e]	76[f−h]	3.2	10.9
N-methylpyrrole	16.9[b]	68[c,d]	2.1	9.7
acetone	21.2[i]	41[g,j]	0.7	5.9
furan	27[b]	23[c,g]	0.3	3.3
acetonitrile	24[e]	23[g,k]	0.3	3.3
toluene	−	18[c,d]	0.2	2.6
benzene	−	7[c,d]	0.08	1.0
chloroform	−	0[c,d]	0.0	0.0
pentane	−	0[c,d]	0.0	0.0

[a] Yields independent of nitrosoamide or diazoalkane concentration over the range 0.05−0.5 M; all reactions were performed in the presence of 2 equiv of pyridine.[9c] [b] References 8a,b. [c] Compound **1a** was used. [d] Run temperature = 40 °C. [e] Reference 16a. [f] Compound **10** and benzoic acid were used.[17] [g] Run temperature = 25 °C. [h] Reference 15c. [i] Reference 16b. [j] Compound **10** and acetic acid were used.[17] [k] *N*-Benzyl-*N*-nitrosopivalamide was used.

Experimental Section

Materials and Methods. Dinitrogen tetraoxide was obtained from The Matheson Gas Co. The pyrroles and furan were distilled prior to use; all other commercial reagents were

(11) The chemical shifts (in $CDCl_3$) of the benzyl protons of the *N*-benzylacetonitrilium ion and of *N*-benzylpyridinium ion are, respectively, δ 5.3[8b] and 6.4 (Friedrich, E. C.; Vartanian, P. F. *J. Organomet. Chem.* **1976**, *110*, 159). Since oxygen is more electronegative than nitrogen it would be expected to deshield the benzylic protons to a greater extent than would nitrogen (Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. *Spectrometric Identification of Organic Compounds*, 4th ed.; John Wiley and Sons: New York, 1981; p 220).

(12) The absence of a signal between δ 5−7 which rose then fell with time also indicates that the *N*-benzyl-*N*-nitroso-*O*-benzoylhydroxylamine is too labile to be detected at −80 °C.[4a,13]

(13) White, E. H.; Lim, H. M. *J. Org. Chem.* **1987**, *52*, 2162.

(14) (a) Ideal data would be obtained by decomposing the same precursor (e.g., **1a**) at the same temperature in a medium comprised of the solvent under study dissolved in a large excess (∼90%) of an inert diluent. (b) Interestingly, with the more reactive 1-norbornyl cation, the yields of ester in ethanol and chloroform were 67% and 49%, respectively.[2c]

(15) (a) McManus, S. P.; Pittman, C. U., Jr. *Organic Reactive Intermediates*; McManus, S. P.; Ed., Academic Press: New York, 1973; Vol. 26, p 299. (b) McClelland, R. A.; Banait, N.; Steenken, S. *J. Am. Chem. Soc.* **1986**, *108*, 7023. (c) Interestingly, no methoxytoluenes were observed.[4b]

(16) (a) Gordon, A. J.; Ford, R. A. *The Chemists' Companion: A Handbook of Practical Data, Techniques and References*; Wiley-Interscience: New York, 1972; p 6063. (b) Streitweiser, A. Jr.; Heathcock, C. H. *Introduction to Organic Chemistry*, 3rd ed.; Macmillan Publishing Co.: New York, 1981; p 1155.

(17) Product distributions (% ester, % SDP) from thermolysis of compound **1a** in equimolar benzene/toluene are the same within experimental error as that from acidification of phenyldiazomethane (compound **10**) with benzoic acid in the same solvent.[4b] Thus it would appear that phenyldiazomethane on general acid protonation leads directly to the corresponding intimate ion-pair and eventually into the nitrogen-separated ion-pair (eqs 1 and 4) which is the active alkylating agent in these deaminations. Ion-pair formation is likely to be facilitated in more polar solvents such as acetone and methanol.

used without further purification. NMR spectra were recorded on a 300 MHz, FT instrument; FT-IR data are reported. TLC analyses were performed on UV-fluorescent silica gel plates.

***N*-Benzylbenzamide.** This compound was prepared by the procedure of Heyns and von Bebenburg.[18] mp 103−104°C (lit.[18] 104−105 °C); IR (Nujol) 3289, 1638, 1491 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.65 (d, 2H, J = 5.7 Hz), 6.55 (bs, 1H), 7.29−7.50 (m, 8H), 7.80 (d, 2H, J = 6.9 Hz).

***N*-Benzyl-*N*-nitrosobenzamide.** This compound was prepared by the method of White et al.[19] IR (Nujol) 1719, 1609, 1502, 1375, cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.14 (s, 2H), 7.36−7.60 (m, 10H).

Handling and Storage. *N*-Nitrosoamides are thermolabile and are also decomposed by acids, bases, and moisture. Dry, neutral *N*-benzyl-*N*-nitrosobenzamide (**1**) has been stored at −25 °C for ∼1 month before significant decomposition into ester was detected. Its half-life at 40 °C in ∼0.1 M solutions in benzene is ∼5 h. *N*-Benzyl-*O*-benzoylhydroxylamine (**6**) has been stored for months (dry and neutral) at −25 °C. These reagents and their reaction mixtures were handled in the dark. **Caution!** Nitrosoamides should be handled with care because of their possible mutagenicity[20a] and carcinogenicity[20b] (local and systemic). Efficient fume hoods and appropriate personal protection (chemical-resistant gloves, safety glasses, lab coat, etc.) are recommended when handling these compounds.

Decomposition of *N*-Benzyl-*N*-nitrosobenzamide in Pyrrole/$CDCl_3$. *N*-Benzyl-*N*-nitrosobenzamide (2.1 mg, 8.75 mmol) and pyridine (1.4 mL, 17.5 mmol, 2 equiv) were dissolved in equimolar pyrrole (freshly distilled, bp_{760} = 125−128 °C) (210 mL, 3 mmol) and $CDCl_3$ (240 mL, 3 mmol) in an NMR tube. The tube was cooled in liquid nitrogen and evacuated at oil pump pressure; it was sealed and incubated at 40 °C. Decomposition was complete in 3 days; the relative yields of products were 38% 2-benzylpyrrole (δ 3.74),[21a] 21% 3-benzylpyrrole (δ 3.71),[21a] and 41% benzyl benzoate (δ 5.22). The solution was divided into two parts, and one part was concentrated by evaporation of the solvent using a gentle stream of N_2 gas. Equimolar $CDCl_3$/pyrrole was added, and NMR integrals were retaken to ensure that this mode of evaporation did not affect the product distribution. The ratio of the 2- to 3-isomer was unchanged by the evaporations. The solvent was removed as before, and this time it was replaced by 9:1 $CCl_4/CDCl_3$ (vol/vol), and ^1H NMR spectra were retaken. The chemical shifts thus obtained agreed very well with the literature values for the 2- and 3-benzylpyrroles in CCl_4: δ_{obs} for 2-benzylpyrrole = 3.77 ($\delta_{lit.}$ = 3.78);[21a] δ_{obs} for 3-benzylpyrrole = 3.73 ($\delta_{lit.}$ = 3.70).[21a] No *N*-benzylpyrrole was observed (absence of signal at δ 4.87).[22]

The presence of benzyl benzoate was confirmed by (1) spiking the product solution with commercial benzyl benzoate; (2) a TLC of the product mixture on silica gel using 10% ether/hexane (vol/vol) gave a spot of R_f = 0.4 (the same value observed for commercial benzyl benzoate under the same conditions); (3) elution of the band at R_f = 0.4 from a preparative TLC plate [using the same conditions as in (2)] followed by evaporation of the solvent and redissolution of the residue in $CDCl_3$ gave a ^1H NMR spectrum which was identical with that of commercial benzyl benzoate.

Decompositions of *N*-Benzyl-*N*-nitrosobenzamide in Pyrrole and *N*-Methylpyrrole. *N*-Benzyl-*N*-nitrosobenzamide (5 mg, 20.8 mmol) and pyridine (3.3 mg, 41.6 mmol) were dissolved in 500 mL of pyrrole or *N*-methylpyrrole in an NMR tube containing ∼20 mg of Na_2SO_4. The tube was cooled, evacuated, and sealed and was incubated at 40 °C. After 4 days, the solvent was removed by a gentle stream of N_2, and the residue was dissolved in $CDCl_3$. ^1H NMR spectra revealed that the reactions were complete. The observed product distributions were as follows: In pyrrole: 20% benzyl benzoate (δ 5.23), 50% 2-benzylpyrrole (δ 3.74),[21a] and 30% 3-benzylpyrrole (δ 3.71)[21a] (Table 1). In *N*-methylpyrrole: 32% benzyl benzoate, 33% 2-benzyl-*N*-methylpyrrole (δ 3.88),[21b] and 35% 3-benzyl-*N*-methylpyrrole (δ 3.80).[21c]

Decomposition of *N*-Benzyl-*N*-nitrosobenzamide in Furan. *N*-Benzyl-*N*-nitrosobenzamide (5 mg, 20.8 mmol) and pyridine (3.3 mg, 41.6 mmol) were dissolved in 500 mL of furan in an NMR tube with ∼20 mg of Na_2SO_4. The tube was sealed and set aside at 25 °C in the dark. After 14 days, the solvent was removed by a gentle stream of N_2, and the residue was dissolved in $CDCl_3$; ^1H NMR analysis revealed 70% decomposition had occurred to form 76% benzyl benzoate (δ 5.37), 21% 2-benzylfuran (δ 3.97),[23] and 3% 3-benzylfuran (δ 3.61)[24] (Table 1). The chemical shifts of the products agreed with the literature values.[23,24]

Nitrosation of *N*-Benzyl-*O*-benzoylhydroxylamine (6)[7a] in 30% Furan/$CDCl_3$ (vol/vol) at −80 °C. *N*-Benzyl-*O*-benzoylhydroxylamine (5 mg, 22 mmol) and pyridine (3.6 mL, 44 mmol) were dissolved in a mixture of furan (150 mL) and $CDCl_3$ (350 mL) in an NMR tube. The solution was cooled to −80 °C in the NMR probe. Using a jet of dry N_2, the tube was raised to the top of the probe into a plastic bag filled with dry N_2. N_2O_4 (0.27 cm^3, 11 mmol) was injected quickly ∼0.5 cm above the liquid surface through a serum stopper the inner surface of which was lined with Teflon tape. The tube was shaken quickly and was allowed to descend back into the cooled probe. The total time out of the cooled probe was ∼5 s. ^1H NMR spectra were taken immediately and after 5 min and 10 min. The temperature was raised in 10° intervals (∼5 min per interval), and spectra were recorded at the end of each interval. All the spectra had approximately the same appearance. The product distribution: 92% benzyl benzoate (δ 5.41), 3% benzyl nitrate (δ 5.25), 4.5% 2-benzylfuran (δ 4.01),[23] and 0.5% 3-benzylfuran (δ 3.68)[24] did not change with time or temperature. There was no evidence of the intermediacy of *O*-benzylfuranonium ions (absence of signal at δ ∼6).[11]

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the D. Mead Johnson Foundation for support of this research. The authors also thank Mr. Fenhong Song for the results in acetone (Table 2).

JO971081T

(18) Heyns, K.; v. Bebenburg, W. *Chem. Ber.* **1953**, *86*, 278.
(19) White, E. H.; Aufdermarsh, C. A., Jr. *J. Am. Chem. Soc.* **1961**, *83*, 1174.
(20) (a) Lee, K.; Gold, B.; Mirvish, S. *Mutat. Res.* **1977**, *48*, 131. (b) Preussman, R.; Stewart, B. W. *Chemical Carcinogenesis*; Searle, C., Ed., ACS Monograph No. 182, American Chemical Society, Washington, DC, 1984; pp 643−828.
(21) (a) Patterson, J. M.; Burka, L. T. *Tetrahedron Lett.* **1969**, *27*, 2215. (b) Logan, N. J.; Davies, C. S. *J. Organomet. Chem.* **1972**, *39*, 129 (c) Groves, J. K.; Anderson, H. J.; Nagy, H. *Can. J. Chem.* **1971**, *49*, 2427.
(22) Katritzky, A. R.; Lang, H.; Lan, X. *Tetrahedron* **1993**, *49*, 2829.
(23) Pelter, A.; Rowlands, M.; Clements, G. *Synthesis* **1987**, *(1)*, 51.
(24) Kotake, H.; Inomata, K.; Aoyama, S.; Kinoshita, H. *Chem. Lett.* **1977**, *(1)*, 73.