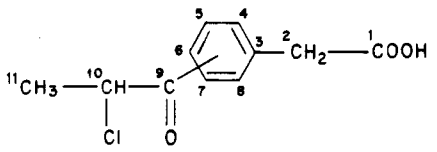
Table II. Significative Values of Long-Range Coupling Constants $^{2,3}J$(C-H) (Hz) of Aromatic Carbons for Isomers 3b-c[a]



	3b	3c
C_3	$J_{C_3-H_5}$ 7.3	$J_{C_3-H_{5,7}}$ 7.8
C_4	*b*	$J_{C_4-H_2}$ 6.3; $J_{C_4-H_8}$ 6.9
C_5		$J_{C_5-H_7}$ 6.5
C_6	*b*	$J_{C_6-H_{5,7}}$ 6.7; $J_{C_6-H_{4,8}}$ 7.8; $J_{C_6-H_{10}}$ 1.5
C_7	$J_{C_7-H_8}$ 6(6.5)[c]; $J_{C_7-H_6}$ 6.5(6)[c]; $J_{C_7-H_5}$ 7.8; $J_{C_7-H_{10}}$ 1.4	$J_{C_7-H_5}$ 6.5
C_8	*b*	$J_{C_8-H_2}$ 6.3; $J_{C_8-H_4}$ 6.9

[a] An iterative computer analysis with LAOCOON 3 Program confirmed these coupling constant values. [b] Broad signal. [c] The values can be exchanged.

then extracted from chloroform with saturated sodium bicarbonate solution (3 × 50 mL). The pH of the sodium bicarbonate solution was brought to 1.5–2.0 with 6 N HCl under ice-bath cooling, and the product was back-extracted with chloroform (4 × 50 mL). The organic phase was dried over anhydrous sodium sulfate, filtered, and evaporated under vacuum to give **3b** or **3c**.

3b: ^{1}H NMR (Me_2SO-d_6) δ 1.68 (d, 3 H), 3.76 (s, 2 H), 5.79 (q, 1 H), 7.45–8.00 (m, 4 H).

3c: ^{1}H NMR (Me_2SO-d_6) δ 1.68 (d, 3 H), 3.76 (s, 2 H), 5.79 (q, 1 H), 7.55–8.20 (AA'BB', 4 H).

The ^{13}C NMR chemical shifts and the long-range ^nJ(C–H) values[12,13] available from ^{13}C coupled spectra for acids (**3b,c**) are reported in Tables I and II, respectively.

Preparation of 2-Bromopropiophenone. 2-Bromopropionyl chloride (19.9 g, 0.116 mol) was added dropwise into a suspension of aluminum chloride (16 g, 0.12 mol) in 1,1,2,2-tetrachloroethane. The mixture was heated to 50 °C for 20 min and benzene (7.8 g, 0.1 mol) was added at a rate such that the temperature did not exceed 50 °C. The reaction mixture was kept at the same temperature for 4 h, then worked up as described above for the preparation of compounds **2a–c**. Distillation of the reaction crude gives the 2-bromopropiophenone (identified by comparison with an authentic sample purchased from Aldrich) as an oil, bp 109–111 °C (5 mmHg) (19 g; 0.89 mol) 89% yield.

Competitive Reaction between the Methyl Ester of Phenylacetic Acid and Benzene with 2-Bromopropionyl Chloride in the Presence of Aluminum Chloride. (a) 2-Bromopropionyl chloride (3.85 g, 0.023 mol) was added dropwise into a suspension of aluminum chloride (6.65 g 0.05 mol) in 1,1,2,2-tetrachloroethane (20 mL). The mixture was heated to 50 °C for 20 min, and a mixture of methyl ester of phenylacetic acid (3.75 g, 0.025 mol) and benzene (1.95 g, 0.025 mol) was added at a rate such that the temperature did not exceed 50 °C. The reaction mixture was kept at the same temperature for 4 h and worked up as described above for the preparation of compounds **2a–c**.

Quantitative GC analysis of the reaction crude showed a mixture of the methyl ester of phenylacetic acid (2.55 g, 0.017 mol), (2-bromopropiophenone (3.29 g, 0.015 mol), and a mixture of ortho, meta, and para methyl esters of [(2-bromopropionyl)-phenyl]acetic acid (2.08 g, 0.007 mol) in the ratio **2a:2b:2c** = 6:46:48.

(b) 2-Bromopropionyl chloride (0.9 g, 0.0058 mol) was added dropwise into a suspension of aluminum chloride (4.78 g, 0.036 mol) in 1,1,2,2-tetrachloroethane (20 mL). The mixture was heated to 50 °C for 20 min, and a mixture of methyl phenylacetate (3.75 g, 0.025 mol) and benzene (1.95 g, 0.025 mol) was added at a rate such that the temperature did not exceed 50 °C. The reaction mixture was kept at the same temperature and worked up as described above for the preparation of compounds **2a–c**.

Quantitative GC analysis of the reaction crude showed a mixture of methyl phenylacetate (3.75 g, 0.025 mol) and 2-bromopropiophenone (1.23 g, 0.0058 mol).

Acknowledgment. We thank Prof. Minisci and Dr. A. Longo for helpful discussions and P. Ind. M. Paiocchi for technical assistance.

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N-(Trimethylsilyl)methylphenylsulfoximine: A Convenient Intermediate for the Preparation of Functionalized Sulfoximines

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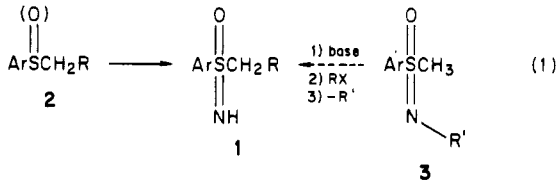
Because of their interesting chemical properties and biological activities,[1] heterocyclic sulfoximines[2] have recently attracted considerable attention. During a study aimed at the synthesis of such compounds, we required several functionalized free sulfoximines as intermediates. Although several methods are available for the preparation of free sulfoximines from di- and trivalent sulfur compounds (**2** → **1**, eq 1),[3] they are often of limited applica-



(1)

bility when the desired sulfoximines contain labile functional groups. An alternative approach of alkylating the readily generated anion derived from N-substituted methylsulfoximines (**3** → **1**, eq 1) has been studied in some cases,[4] but preparation of the desired *free* sulfoximines is again difficult and limited. Furthermore, alkylation chemistry of N-protected sulfoximines has not been studied in a systematic way.

We now report that carbon–carbon bond formation between *N*-(trimethylsilyl)(lithiomethyl)phenylsulfoximine and various electrophiles, followed by ready desilylation, provides simple access to a variety of free sulfoximines that

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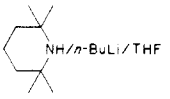
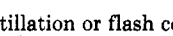
(3) (a) From sulfoxides and NaN_3/H_2SO_4: J. K. Whitehead and H. R. Pentley, *J. Chem. Soc.*, 1572 (1952); (b) From sulfoxides and mesitylenesulfonylhydroxylamine; Y. Tamura, K. Sumoto, J. Minamikawa, and M. Ikeda, *Tetrahedron Lett.*, 4137 (1972); C. R. Johnson, R. A. Kirchhoff, and H. G. Corkins, *J. Org. Chem.*, **39**, 2458 (1974); (c) From sulfide and via indirect routes; references cited in review articles.

(4) C. R. Johnson and C. J. Stark, Jr., *J. Org. Chem.*, **47**, 1193 (1981) and references cited therein.

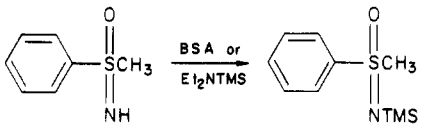
0022-3263/86/1951-0099$01.50/0

Table I

	R	conditions	yield,[a] %
6a	$CH_2CH(OCH_3)_2$	1) 1 equiv of BuLi/THF 2) $BrCH_2CH(OCH_3)_2$/HMPA/THF (−78–20 °C/16 h)	63
6b	$C(=O)CH_3$	1) 2.1 equiv of $(p\text{-}Pr)_2NH/n$-BuLi/THF 2) $CH_3CO_2C_2H_5$	76
6c	CO_2CH_3	1) 2.1 equiv of  2) $ClCO_2Me$ (−78–0 °C/1 h)	80
6d	CH_2CH_2OH	1) 1 equiv of BuLi/THF 2) 	75

[a] Yields were obtained after distillation or flash column chromatography and are not optimized. [b] Use of LDA gave 68% yield. [c] Due to instability, **6d** was not purified but directly converted to **7d**, whose yield is given.

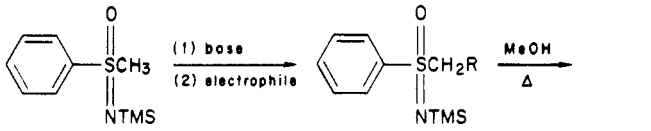
are not readily prepared by other methods. The key reagent, *N*-(trimethylsilyl)methylphenylsulfoximine (**5**),



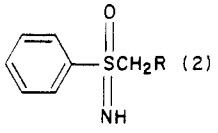
4 **5**

was obtained in almost quantitative yield by treating **4**[5] with either bis(trimethylsilyl)acetamide (BSA) or (trimethylsilyl)diethylamine, followed by distillation. The latter is more convenient to use because it produces volatile diethylamine as a byproduct. Compound **5** is a colorless liquid and is stable when protected from moisture. (No sign of decomposition after 6 months under N_2 in a refrigerator.)

The anion of compound **5**, which can be generated in various ways, was treated with alkyl halides, esters, methyl chloroformate, and epoxides to give corresponding products **6** in good yield (eq 2). The results are summarized



5 **6**



7

in Table I. The compounds **6** are all stable to aqueous workup and distillation and can be converted to the free sulfoximines **7** in over 95% yield simply by heating at reflux in methanol for 3–4 h (eq 2). Alternatively, addition of a catalytic amount (10–20 mol %) of cesium fluoride remarkably accelerates methanolysis of the silyl group, permitting deprotection within 10–20 mm.

The power of this methodology is illustrated by the fact that attempted prepartion of compounds **7b–7d** was completely unsuccessful from the corresponding sulfoxides by the standard procedures (both NaN_3/H_2SO_4 and MSH[3]).

(5) C. R. Johnson, M. Haake, and C. W. Schroeck, *J. Am. Chem. Soc.*, **92**, 6594 (1970).

In conclusion, it has been shown that carbon–carbon bond formation between the anion of *N*-silyl-protected sulfoximine **5** and various electrophiles can be successfully carried out to give *N*-silyl-protected functionalized sulfoximines **6**, which are readily convertible to their free sulfoximines **7**.

Experimental Section

Proton nuclear magnetic resonance spectra were recorded on either a Varian EM 360L or Bruker 360 instrument using tetramethylsilane (Me_4Si) as an internal standard, and spectral data are reported as follows: chemical shifts in parts per million downfield from Me_4Si (multiplicity, coupling constants, number of protons). Gas chromatography was carried out on a Hewlett-Packard 5790 spectrometer with Fl detector using OV101(5%) on WHP (80/100 mesh). Instrument conditions were as follows: temperature program 150–300 °C at a rate of 15°/min; initial time 0 min; injector temperature 180 °C; detector temperature 300 °C; carrier gas nitrogen. Analytical thin-layer chromatography (TLC) was performed on precoated silica gel $60F_{254}$ (E. Merck) glass supported plates. All chromatographic separations were performed on Merck silica gel (Kieselgel 60, 230–400 mesh ASTM). All solvents were used as received (Aldrich gold label for THF, Fisher AR grades for other solvents). Elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, GA.

***S*-Methyl-*S*-phenyl-*N*-(trimethylsilyl)sulfoximine (5). Method A.** To a solution of sulfoximine **4** (38 g, 0.245 mol) in acetonitrile (60 mL) was added bis(trimethylsilyl)acetamide (51 g, 0.250 mol) over 1 min at 25 °C with stirring. The reaction mixture was stirred at 60 °C for 10 min and then concentrated under reduced pressure. The residue was subjected to vacuum distillation with a short-path distillation head. After a discarded forerun (up to 80 °C (0.1 mmHg), mostly *N*-trimethylsilylacetamide), 54 g (97% yield) of pure product was collected as a colorless liquid: bp 82–84 °C (0.1 mmHg); R_t = 3.13 min; ^1H NMR ($CDCl_3$) δ 0.07 (9 H, s), 2.93 (3 H, s), 750 (m, 3 H), 7.85 (m, 2 H). Anal. Calcd for $C_{10}H_{17}N_1O_1S_1Si_1$: C, 52.82; H, 7.54. Found: C, 52.89; H, 7.58.

Method B. To a stirred, prewarmed solution of sulfoximine **4** (62 g, 0.40 mol) in acetonitrile (30 mL) at 60–70 °C was added (trimethylsilyl)diethylamine (65.2 g, 0.45 mol) from a dropping funnel over 20 min. GC analysis immediately upon addition of silylating agent indicated reaction was complete. Evaporation of volatiles (CH_3CN, Et_3N, and some remaining Et_2NSiMe_3) afforded 92 g of practically pure **5** as a pale yellow liquid. Fractional vacuum distillation provided 88 g (98% yield) of pure product a colorless liquid.

***S*-(3,3-Dimethoxypropyl)-*N*-(trimethylsilyl)-6-phenylsulfoximine (6a).** A 250-mL, three-necked, round-bottom flask equipped with a magnetic stirbar and a rubber septum was charged with **5** (11.96 g, 52.68 mmol) and THF (50 mL). The reaction mixture was cooled to −78 °C, and to it was added *n*-butyllithium (2.58 M in hexane, 21 mL, 54 mmol) via syringe over 5 min under argon atmosphere. After addition was complete, the reaction mixture was stirred at −78 to −20 °C for 10 min and at 0 °C for 20 min, and then hexamethyl phosphoramide (17.9 g, 100 mmol) was added. The reaction mixture was cooled back to −30 °C followed by addition of bromoacetaldehyde dimethyl acetal (13.5 g, 80 mmol) over 2 min. After stirring at 25 °C for 19 h, the reaction mixture was concentrated in vacuo, taken up in ether (300 mL), washed with cold water (2 × 60 mL) and brine (1 × 60 mL), and then filtered through $MgSO_4$. The filtrate was concentrated in vacuo to leave a brown liquid (20 g), which was subjected to Kugelrohr distillation to afford pure product **6a** (10.5 g, 63% yield) as a light yellow liquid: bp 105 °C (0.1 mmHg); R_t = 6.43 min; ^1H NMR ($CDCl_3$) δ 0.09 (s, 9 H), 1.85 (m, 2 H), 2.90 (m, 2 H), 3.00 (s, 6 H), 4.15 (t, J = 7.0 Hz, 1 H), 7.10–7.67 (m, 5 H). Anal. Calcd for $C_{14}H_{25}N_1O_3S_1Si$: C, 53.33; H, 7.93. Found: C, 53.51; H, 7.76.

1-[*S*-Phenyl-*N*-(trimethylsilyl)sulfonimidoyl]-2-propanone (6b). To a pregenerated lithium diisopropylamide (0.21 mol) solution in THF (100 mL) was added a solution of **5** (22.7 g, 0.10 mol) in THF (200 mL) over 10 min at −78 °C under argon. After addition of **5** was complete, the reaction mixture was allowed to warm to 0 °C, stirred at 0 °C for 0.5 h, and cooled

back to -78 °C, and then ethyl acetate (18.4 g, 0.21 mol) was added to the enolate solution over 15 min. The reaction mixture was kept at -78 °C for 10 min and at -78 to -20 °C for 0.5 h, quenched with pH 6.4 buffer (4 mL), and then concentrated in vacuo. The concentrate was diluted with ether (300 mL), washed with cold water (2 × 50 mL), filtered through $MgSO_4$, and evaporated to leave 27.1 g of faint yellow liquid, which was subjected to Kugelrohr distillation to give pure product **6b** (20.4 g, 75.8% yield), after ca. 3 g of impure forerun: bp 120 °C (0.2 mmHg) (Kugelrohr); R_t = 4.74 min; ^{1}H NMR ($CDCl_3$) 0.09 (s, 9 H), 2.33 (s, 3 H), 3.97 (s, 2 H), 7.40-7.94 (m, 5 H). Anal. Calcd for $C_{12}H_{19}N_1O_2S_1Si_1$: C, 53.49; H, 7.10. Found: C, 53.49; H, 7.06.

***S*-(2-Methoxy-2-oxoethyl)-*S*-phenyl-*N*-(trimethylsilyl)-sulfoximine (6c).** To a 100-mL, three-necked flask equipped with a magnetic stirbar and a rubber septum was added tetramethylpiperidine (3.38 g, 24 mmol) and THF (10 mL). To this mixture was added *n*-butyllithium (2.7 M in hexane, 7.4 mL, 20 mmol) at 0 °C via syringe over 3 min. The resulting solution was stirred 10 min at 0 °C and then cooled to -78 °C, and to it was added dropwise via syringe a solution of compound **5** (2.27 g, 10 mmol) in THF (5 mL). The reaction mixture was stirred at -78 °C for 10 min and at -78 to -10 °C for 0.5 h and was then recooled to -78 °C followed by addition of methyl chloroformate (2.26 g, 24 mmol) over 5 min. The yellow mixture was kept at -78 °C for 1 h and at -78 to -10 °C for 10 min, quenched with aqueous NH_4Cl (1 mL), and then concentrated in vacuo. The residue was taken up in ether (100 mL), washed with cold water (2 × 15 mL) and brine (1 × 20 mL) filtered through $MgSO_4$, and evaporated to leave 3.70 g of crude compound. Kugelrohr distillation of the crude product gave pure **6c** (2.08 g, 80.0% yield) after ca. 1.5 g of impure forerun: bp 130 °C (0.1 mmHg) (Kugelrohr); R_t = 5.17 min; ^{1}H NMR ($CDCl_3$) δ 0.15 (s, 9 H), 3.67 (s, 3 H), 4.00 (s, 2 H), 7.61 (m, 3 H), 8.00 (m, 2 H); IR (NaCl, film) 1760 cm^{-1}. Anal. Calcd for $C_{12}H_{19}N_1O_3S_1Si_1$: C, 50.49; H, 6.70. Found: C, 51.16; H, 6.70. Inverse addition of the anion of **5** to a solution of methyl chloroformate gave the same result as reported here.

3-[*S*-Phenyl-*N*-(trimethylsilyl)sulfonimidoyl]-1-propanol (6d). The procedure is described in the preparation of **7d**.

1-(*S*-Phenylsulfonimidoyl)-2-propanone (7b). A solution of compound **6b** (9.6 g, 35.5 mmol) in methanol/water (10:1, 15 mL) was treated with cesium fluoride (0.5 g, 3.3 mmol) at 25 °C. The reaction mixture was heated at ca. 50 °C for 10 min. GC and TLC analysis after 10 min indicated reaction was complete. The reaction mixture was concentrated in vacuo, taken up in ethyl acetate (50 mL), and washed with water (1 × 20 mL). The water wash was extracted with CH_2Cl_2 (5 × 10 mL). The CH_2Cl_2 extracts were combined with the ethyl acetate solution, and the resulting mixture was dried ($MgSO_4$) and evaporated in vacuo to give crude product (7.2 g). Purification by flash column chromatography eluting with 60% EtOAc/hexane gave **7b** (6.9 g, 98.5% yield) as pale yellow liquid: R_t = 4.52 min; R_f (60% EtOAc/hexane) 0.33; ^{1}H NMR ($CDCl_3$) δ 2.33 (s, 3 H), 2.80 (br, 1 H), 4.09 (s, 2 H), 7.50-8.03 (m, 5 H). Anal. Calcd for $C_9H_{11}S_1N_1O_2$: C, 54.80; H, 5.62. Found: C, 54.70; H, 5.63.

(Phenylsulfonimidoyl)acetic Acid, Methyl Ester (7c). From the same procedure as for **7b**, **7c** was obtained in quantitative yield: R_t = 5.04 min; R_f (60% EtOAc/hexane) 0.40; ^{1}H NMR ($CDCl_3$) δ 3.47 (m, 1 H), 3.67 (s, 3 H), 4.15 (s, 2 H), 7.50-8.12 (m, 5 H). Anal. Calcd for $C_9H_{11}N_1O_2S_1$: C, 50.68; H, 5.20. Found: C, 49.65; H, 5.38.

3-(*S*-Phenylsulfonimidoyl)-1-propanol (7d). To a solution of **5** (22.7 g, 0.10 mol) in THF (100 mL) was added *n*-butyllithium (2.58 M in hexane, 29.5 mL, 0.10 mol) over a 5 min at -78 °C under argon atmosphere. The reaction mixture was stirred at -78 to -20 °C for 15 min and at 0 °C for 20 min and recooled to -78 °C. Ethylene oxide (4.84 g, 0.11 mol), dried over sodium hydride, was bubbled through the reaction mixture, which was then allowed to warm to 20 °C. After stirring for 0.5 h at 20 °C, the reaction mixture was quenched with saturated NH_4Cl solution (3 mL), concentrated in vacuo, diluted with ether (200 mL), and washed with cold water (2 × 30 mL). The aqueous washings were further extracted with ether (1 × 20 mL). The combined ether solution was dried ($MgSO_4$) and evaporated to afford **6d** (30.0 g) as a colorless liquid, R_t = 6.51 min. Without purification, compound **6d** was desilylated by the same procedure as described for the preparation of **7b**. Purification of the crude product by flash column chromatography, eluting with ethyl acetate, gave free sulfoximine **7d** (14.8 g, 74.4% overall yield) as a white powder: mp 61.0-61.5 °C; R_t = 6.01 min; R_f (EtOAc) 0.21; ^{1}H NMR ($CDCl_3$) δ 1.96 (m, 2 H), 3.24 (br t, 4 H, including OH and =NH), 3.67 (t, J = 7.0 Hz, 2 H), 7.67 (m, 3 H), 7.94 (m, 2 H). Anal. Calcd for $Cl9H_{13}N_1O_2Si$: C, 54.24; H, 6.58. Found: C, 54.19; H, 6.62.

Acknowledgment. I thank Dr. E. W. Logusch for his helpful suggestions during the preparation of the paper.

Registry No. **4**, 4381-25-3; **5**, 89902-44-3; **6a**, 99531-75-6; **6b**, 99531-76-7; **6c**, 99531-77-8; **6d**, 99531-78-9; **7b**, 99531-79-0; **7c**, 99531-80-3; **7d**, 99531-81-4; bromoacetaldehyde dimethyl acetal, 7252-83-7; ethyl acetate, 141-78-6; methyl chloroformate, 79-22-1; ethylene oxide, 75-21-8.

Unusual "Hydrolysis" of 2-Nitrosopyridines: Formation of 1-(2-Pyridyl)-2(1*H*)-pyridones[1]

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Received September 11, 1985

We have recently described[2] a simple procedure for the conversion of primary heterocyclic (and aromatic) amino groups to nitroso groups by *m*-chloroperbenzoic acid oxidation of intermediate *S*,*S*-dimethylsulfilimines. During an investigation of the chemistry of these new nitroso-substituted heterocycles, it was observed that 2-nitrosopyridine (**1a**) and its 3-(**1b**) and 4-methyl (**1c**) derivatives were irreversibly transformed into new, colorless compounds in high yield upon heating with water. We describe in this paper the structures of these hydrolysis products and comment upon their possible mechanism of formation.

Stirring a suspension of powdered 2-nitrosopyridine (**1a**) in water at room temperature resulted in gradual dissolution and a change in the color of the solution from pale green to light yellow. TLC showed that the starting 2-nitrosopyridine had been completely consumed and that only one major product had been formed. The aqueous solution was extracted with methylene chloride, and the extracts were dried and evaporated to give a colorless crystalline solid, mp 55.5-56 °C, which was shown by microanalysis and by mass spectroscopy to have the empirical formula $C_{10}H_8N_2O$. The product contained one carbonyl group (IR 1667 cm^{-1}), which was confirmed by its ^{13}C NMR spectrum (see the Experimental Section). This compound was positively identified as 1-(2-pyridyl)-2(1*H*)-pyridone (**2a**) by comparison with an authentic sample prepared by the reaction of 2-pyridone with 2-bromopyridine in the presence of copper.[3]

Since the conversion of **1a** to **2a** by stirring in water accelerated with time, and the aqueous reaction solution became acidic over time, it was apparent that the reaction was probably acid catalyzed. This was confirmed by the observation that addition of one drop of concentrated sulfuric acid to a 25% dioxane/water solution of **1a** led to complete conversion to **2a** within $2^1/_2$ h; this contrasts with the 27-30 h required, in the same solvent mixture, in the absence of added acid. No reaction whatsoever took

(1) We are indebted to the National Institutes of Health (Grant No. R01 GM27983) for support of this work.

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