Table I. Solid-Solid-Liquid Substitution Reactions Catalyzed by TMAX on Silica[a]

substrate	solid reagent	catalyst loading weight %	catalyst amount molar %	product	temp, °C	time, h	yield,[b] %, GC
benzyl chloride	HCO_2K	10	5	benzyl formate	120	12	99
		25	5			11	99
		50	5			12	21
(without solvent)		25	5		150	2	100[c]
1-chlorodecane	HCO_2K	10	7.5	decyl formate	120	120	86
					150	2	14
						20	52
						72	64
		25	7.5		150	20	7
1-bromooctane	CH_3CO_2K	10	7.5	octyl acetate	120	80	99
					150	9	100
1-bromooctane	NaI	10	7.5	1-iodooctane	120	80	97
					150	25	99
		25	7.5		120	40	1

[a] 10 mL of a solution of the substrate (1 M) in *p*-xylene (for reactions at 120 °C) or *o*-chlorotoluene (for reactions at 150 °C) was magnetically stirred with the inorganic reagent (15 mmol) and the catalyst. [b] Yields are determined by GC calibrated with pure reference substances. [c] The product was isolated in 97% yield.

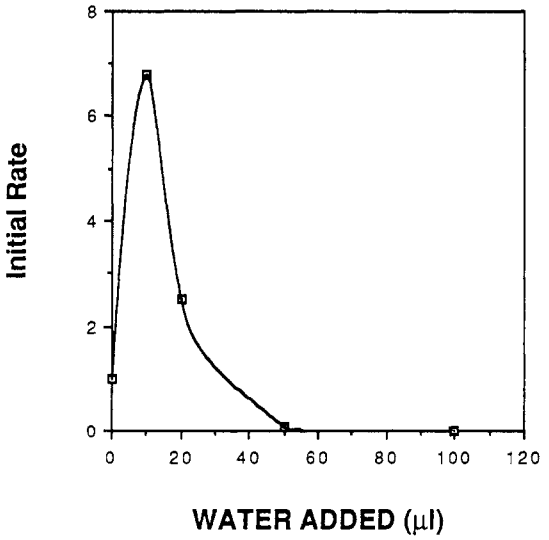

Figure 1. Effect of water on the esterification rate of benzyl chloride. Reaction conditions: Benzyl chloride (10 mmol) in *p*-xylene (10 mL) was magnetically stirred with potassium formate (15 mmol) and 0.22 g (25%) TMACl/Silica D22 at 120 °C. The reactions were followed by GC. When no water was added the reaction system contained approximately 2 μL of water (Karl Fisher). The initial rates were determined between 0 and 25% conversion. They are expressed in units of 10^5 M s^{-1}.

oven at 120 °C, 1 mmHg. The following catalyst supports were used: Silica SIPERNAT® D22 (Degussa Co., W. Germany, precipitated colloidal silica, not surface treated, particle size 180 Å, BET surface area 190 m^2/g, spray dried agglomerates of 40–200 μm); Silica SIPERNAT D17 (Degussa Co., sililated with alkylchlorosilane, particle size 280 Å, BET surface area 110 m^2/g; silica gel 60 (Merck Catl. No. 7733, Particle size 0.2–0.5 mm, average pore diameter 60 Å); Polystyrene Amberlite XAD-4 (Rohm and Haas Co.); aluminiumoxide S neutral, active (Riedel De Haen Co., W. Germany, Catl. No. 31164).

Catalytic Preparation. All catalysts were prepared according to the procedure described for the preparation of 25% TMACl/Silica D22: 2.5 g of tetramethylammonium chloride were dissolved in about 25 mL of methanol, in a round-bottom flask; 7.5 g of Silica D22 were added, and the suspension was stirred at room temperature for 1 h. The solvent was evaporated, and the catalyst was dried. The catalysts are strongly hygroscopic. To prevent the adsorbtion of water, they were kept in tightly closed flasks, which were opened always for a few seconds only.

General Reaction Conditions. Ten milliliters of a solution of the substrate (1 M) in *p*-xylene (for reactions at 120 °C) or *o*-chlorotoluene (for reactions at 150 °C), the inorganic reagent (15 mmol), and the catalyst were placed in a vial (Thomas Scientific 9710 D61) equipped with a 15 × 7 mm magnetic bar. In some cases (Figure 1) water was added with a syringe. The vial was closed with a Teflon-lined screw cap, placed in an oil bath, and stirred vigorously. Small samples were taken at appropriate time intervals, filtered through cotton wool, and analyzed by GC (calibrated with authentic samples) on a 10% SP 2100 on Chromosorb P column.

Preparation of Benzyl Formate. Benzyl chloride (200 mmol, 25.3 g), potassium formate (220 mmol, 18.5 g), and 25% TMACl/Silica D22 (10 mmol, 4.38 g) were stirred mechanically at 150 °C for 2 h. The reaction mixture was filtered, and the solids were washed thorougly with chloroform. After evaporation of the chloroform, 99.6% benzyl formate was obtained in a yield of about 97% (the product contained 0.4% benzyl alcohol; residual benzyl chloride was not detected by GC).

Alkylation of Benzyl Cyanide. Benzyl cyanide (5 mmol), 1-chlorobutane (20 mmol, solvent), sodium hydroxide (20 mmol, partially crushed), and 25% TMACl/Silica D 22 (0.25 mmol, 0.110 g) were stirred overnight (18 h) at room temperature. GC analysis indicated a quantitative conversion to α-butylbenzyl cyanide (78%) and α,α-dibutylbenzyl cyanide (22%).

Alkylation of Phenoxide. The reactions were carried out as described before.[27] Sodium phenoxide was prepared from phenol and sodium hydroxide;[22] 10 mL of a 0.2 M solution of benzyl bromide in toluene was stirred with sodium phenoxide (3.2 mmol) and the catalyst at 55 °C as described above. The reactions were followed by GC.

Registry No. TMABr, 64-20-0; TMAC, 75-57-0; NaOPh, 139-02-6; HCO_2K, 590-29-4; CH_3CO_2K, 127-08-2; NaI, 7681-82-5; benzyl chloride, 100-44-7; 1-chlorodecane, 1002-69-3; 1-bromooctane, 111-83-1; benzyl formate, 104-57-4; decyl formate, 5451-52-5; octyl acetate, 112-14-1; 1-iodooctane, 629-27-6.

A Facile One-Step Synthesis of *C*-Arylnitrones Using Dimethyldioxirane[1]

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Nitrones are versatile organic compounds that are used widely in organic synthesis.[2-9] Of more recent but equal

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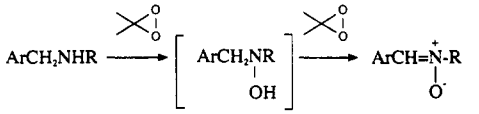
importance is the use of nitrones to trap and identify reactive free radicals,[10,11] particularly in the biomedical area. The literature contains a number of methods for synthesizing nitrones. The most commonly used methods are the condensation of aldehydes with hydroxylamines and the oxidation of the corresponding hydroxylamines.[2-7] The synthesis of hydroxylamines is not a trivial matter. We have recently reported,[12] however, that these intermediates in nitrone synthesis can be prepared in high yield by oxidizing secondary amines with dimethyldioxirane (1). Nitrones are also synthesized by oxidizing secondary amines with a variety of oxidizing agents.[6,7,9,13-17] Reactions of nitrosobenzene with phenylhydrazones also give[18] the corresponding nitrones in reasonably good yields. A recent report[19] describes the synthesis of nitrones by oxidizing imines with aqueous permanganate under phase-transfer conditions. Imines can also be oxidized by peracids[20-23] to give nitrones via the rearrangement of intermediate oxaziridines.[24] Photolysis of cyclic hydroxylamines in the presence of the electron acceptor 1,4-dicyanonaphthalene gives[25] good yields of cyclic nitrones. An improved preparation[26] (55–70% yield) of α,*N*-diphenylnitrones by direct oxidation of secondary anilines using *m*-chloroperbenzoic acid in dry acetone has been reported recently. A very nice synthesis of the important spin trap phenyl-*tert*-butylnitrone has been reported by Cherry and Huie.[27] This method involves the in situ production of a hydroxylamine by the metallic Zn reduction of 2-methyl-2-nitropropane and the subsequent condensation of the hydroxylamine with aldehydes to give the nitrones. Janzen and co-workers[28] have extended this method to the synthesis of 5,5-dimethyl-1-pyrroline *N*-oxide (DMPO) type spin traps. Nitrones have also been obtained[29] by the oxidation of secondary amines with 2-(phenylsulfonyl)-3-aryloxaziridines (Davis reagents).

Table I. Synthesis of Nitrones with Dimethyldioxirane

nitrone	yield,[a] %	mp, °C (lit. mp, °C)
N-(phenylmethylene)-2-methyl-2-propanamine *N*-oxide	96	74–75 (75–76[40])
N-[(4-chlorophenyl)methylene]-2-methyl-2-propanamine *N*-oxide	99	70–72 (69–71[16])
N-[(4-methoxyphenyl)-methylene]-2-methyl-2-propanamine *N*-oxide	98	97–99 (96–98[41])
N-[(4-(trifluoromethyl)phenyl)-methylene]-2-methyl-2-propanamine *N*-oxide	98	85–87
N-[(4-nitrophenyl)methylene]-2-methyl-2-propanamine *N*-oxide	95	147–148 (134–135[40])
N-(phenylmethylene)-benzenamine *N*-oxide	98	112–114 (112–114[42])
N-(phenylmethylene)benzene-methanamine *N*-oxide	96	83–84 (82–83[13])
N-[(4-chlorophenyl)methylene]-benzenamine *N*-oxide	96	156–158 (153–154[43])
N-(phenylmethylene)tricyclo-[3.3.1.1^{3,7}]decan-1-amine *N*-oxide	99	118–119 (118–120[44])
N-[(4-fluorophenyl)methylene]-2-methyl-2-propanamine *N*-oxide	99	82–84
N,*N*′-1,2-ethanediylidenebis-(benzenamine) *N*,*N*′-dioxide	57	183–187 (182–183[45])
N-[(4-methylphenyl)methylene]-2-methyl-2-propanamine *N*-oxide	99	70–73 (68–70[40])
N-[(4-(1,1-dimethylethyl)phenyl)methylene]-2-methyl-2-propanamine *N*-oxide	99	160–163 (159–161[46])

[a] Isolated yield.

In the procedure reported here secondary amines containing benzylic hydrogens[30] are oxidized cleanly, rapidly, and in high yield to nitrones by dimethyldioxirane (Table I). The general method involves treating an acetone solution of the required amine with exactly 2 equiv of 1 at 0 °C for 10 min. Removal of the solvent usually gives the solid nitrone, which is easily purified. Use of excess 1 leads to further reaction of the nitrone and should be avoided when the nitrone is the desired product. Oxidation of *N*-methylaniline by 1 leads to the formation of a dinitrone.[31]



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(30) Preliminary experiments using amines not containing benzylic hydrogens indicate that these reactions are complicated by side reactions and lower yields.
(31) While the mechanism of formation of the dinitrone is not clear, it is likely that one molecule of the mononitrone condenses with another via a canonical form bearing a negative charge on the methylene group. When more than 2 equiv of 1 is used to oxidize *N*-methylaniline, then new products are formed. One of these products distills over during solvent removal and has been identified as nitrosobenzene. The other products have not been identified.

Dioxiranes are a relatively new class of peroxides having a very rich chemistry.[32-36] The current results are the latest to be reported in a continuing program involving the oxidation of nitrogen-containing compounds by 1. We earlier reported[37,38] that 1 can be used to efficiently convert primary amines to nitro compounds. Secondary amines can be converted to hydroxylamines.[12] Hydroxylamines containing no α hydrogens are readily converted to stable nitroxides.[39] As indicated in this report hydroxylamines with α hydrogens react with 1 to give nitrones.

Experimental Section

Materials and Methods. Acetone (Fisher) was fractionally distilled over anhydrous potassium carbonate. Benzene (Fisher), toluene (Fisher), petroleum ether (Fisher), ethyl ether (Fisher), and ligroin (MCB) were purified by distillation before use. Dibenzylamine (Aldrich), methylbenzylamine (Aldrich), ethylbenzylamine (Kodak), and phenylbenzylamine (Kodak) were fractionally distilled under reduced pressure before use. *tert*-Butyl(4-nitrobenzyl)amine, *tert*-butyl(4-fluorobenzyl)amine, *tert*-butyl(4-chlorobenzyl)amine, *tert*-butyl(4-methoxybenzyl)amine, *tert*-butyl(trifluoromethyl)benzylamine, phenyl(4-chlorobenzyl)amine, adamantylbenzylamine, *tert*-butyl(4-methylbenzyl)amine, and *tert*-butyl(4-*tert*-butylbenzyl)amine were prepared by the reduction of the corresponding imines with sodium borohydride in methanol.[16,47] The amines were isolated and purified by distillation and characterized by ^1H, ^{13}C, and mass spectra. Oxone (Du Pont), $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$, was obtained from Aldrich and used as such. Anhydrous K_2CO_3 (Aldrich), anhydrous sodium sulfate (Aldrich), and anhydrous magnesium sulfate (Fisher) were used as such. Acetone solutions of dimethyldioxirane were prepared by the literature method.[48]

Instrumentation. ^1H and ^{13}C NMR spectra were obtained in $CDCl_3$ solution at 300 and 75 MHz, respectively. Mass spectra were recorded at 70 eV. Melting points were measured on either a hot-stage apparatus or a capillary melting point apparatus and are uncorrected.

***N*-(Phenylmethylene)-2-methyl-2-propanamine *N*-Oxide (PBN) (General Procedure).** To a cold (0 °C), magnetically stirred solution of *tert*-butylbenzylamine (0.244 g, 1.49 mmol) in acetone (5 mL) was added a solution of 1 in acetone (63.7 mL, 2.99 mmol). The reaction mixture was stirred at 0 °C for 10 min. Evaporation of the solvent on a rotary evaporator gave a white crystalline solid (0.256 g). This solid was dissolved in a 20:80 ethyl acetate–petroleum ether (35–60 °C) mixture and flash chromatographed over silica gel. Elution with the same solvent mixture gave the pure nitrone as white needles (0.256 g, 96% yield), mp 74–75 °C (lit.[40] mp 75–76 °C). IR (KBr, cm^{-1}): 1580, 1560, 1365, 1195, 1125, 1118, 905, 835, 710, 695. ^1H NMR: δ 1.62 (s, 9 H, $C(CH_3)_3$), 7.36–7.46 (m, 3 H, aromatic), 7.54 (s, 1 H, CH=N), 8.24–8.34 (m, 2 H, aromatic). ^{13}C NMR: δ 28.24 ($C(CH_3)_3$), 70.70 ($C(CH_3)_3$), 128.33 (C-3), 128.68 (C-2), 129.75 (HC=N), 130.01 (C-4), 130.92 (C-1).

***N*-[(4-Chlorophenyl)methylene]-2-methyl-2-propanamine *N*-Oxide.** The general procedure was used with 0.367 g of *tert*-butyl(4-chlorobenzyl)amine. Removal of the solvent gave white shiny plates of the nitrone, which was homogeneous in TLC analysis. This solid was dissolved in CH_2Cl_2. Drying with Na_2SO_4 and evaporation of the solvent gave white shiny flakes (0.392 g). IR (KBr, cm^{-1}): 1590, 1572, 1552 (C=N), 1490, 1415, 1392, 1368, 1255, 1202 (NO), 1132, 1015, 915, 835, 515. ^1H NMR: δ 1.61 (s, 9 H, $C(CH_3)_3$), 7.38 (d, 2 H, J = 8.6 Hz, aromatic), 7.53 (s, 1 H, HC=N), 8.25 (d, 2 H, J = 8.5 Hz, aromatic). ^{13}C NMR: δ 28.24 ($C(CH_3)_3$), 71.02 ($C(CH_3)_3$), 128.60, 128.74, 129.44, 129.89, 135.36. Mass spectrum (EI, 70 eV): m/z 211 (M^+, 37), 57 (base peak), Calcd for $C_{11}H_{14}ClNO$: 211.68.

***N*-[(4-Methoxyphenyl)methylene]-2-methyl-2-propanamine *N*-Oxide.** Oxidation of 0.382 g of *tert*-butyl(4-methoxybenzyl)amine gave a colorless, viscous liquid that was homogeneous in TLC analysis. This liquid was dissolved in CH_2Cl_2 and dried (Na_2SO_4). Removal of the solvent and recrystallization from hexane gave white needles (0.404 g, 98%). IR (KBr, cm^{-1}): 1605, 1580, 1565 (C=N), 1510, 1362, 1310, 1260, 1245, 1182, 1130, 1110, 1030, 860, 545. ^1H NMR: δ 1.60 (s, 9 H, $C(CH_3)_3$), 3.85 (s, 3 H, CH_3O), 6.93 (d, 2 H, J = 9 Hz, aromatic), 7.47 (s, 1 H, CH=N), 8.29 (d, 2 H, J = 9 Hz, aromatic). ^{13}C NMR: δ 28.25 ($C(CH_3)_3$), 55.27 (CH_3O, 70.01 ($C(CH_3)_3$), 113.66, 123.98, 129.41, 130.66, 160.73 (C-4). Mass spectrum (EI, 70 eV): m/z 207 (M^+), 57 (base peak). Calcd for $C_{12}H_{17}NO_2$: 207.26.

***N*-[(4-(Trifluoromethyl)phenyl)methylene]-2-methyl-2-propanamine *N*-Oxide.** Oxidation of 0.360 g of *tert*-butyl-[(4-(trifluoromethyl)benzyl]amine and removal of the solvent gave a white crystalline solid that was homogeneous in TLC analysis. This solid was dissolved in CH_2Cl_2 and dried (Na_2SO_4). Removal of the solvent gave 0.376 g of the nitrone as a white crystalline solid. IR (KBr, cm^{-1}): 1618, 1570, 1560, (C=N), 1485, 1422, 1365, 1330, (CF_3), 1205 (NO), 1175, 1070, 1020, 915, 870, 855, 675, 645, 602. ^1H NMR: δ 1.62 (s, 9 H, $C(CH_3)_3$), 7.62 (s, 1 H, CH=N), 7.65 (d, 2 H, J = 8.41 Hz, aromatic), 8.39 (d, 2 H, J = 8.05 Hz, aromatic). ^{13}C NMR: δ 28.25 ($C(CH_3)_3$), 71.60 ($C(CH_3)_3$), 123.8 (q, $^1J_{C-F}$ = 272.2 Hz, CF_3), 125.25 (q, $^3J_{C-F}$ = 3.7 Hz, C-3), 128.48 (C-1), 128.61 (C-2), 131.0 (q, $^2J_{C-F}$ = 32.4 Hz, C-4), 134.09 (CH=N). Mass spectrum (EI, 70 eV): m/z 246 (M + 1, 2.5), 245 (M^+, 19), 57 (base peak, 100). Calcd for $C_{12}H_{14}F_3NO$: 245.23.

Anal. Calcd for $C_{12}H_{14}F_3NO$: C, 58.76; H, 5.75; N, 5.71. Found: C, 58.81; H, 5.75; N, 5.71.

***N*-[(4-Nitrophenyl)methylene]-2-methyl-2-propanamine *N*-Oxide.** Oxidation of 0.420 g of *tert*-butyl(4-nitrobenzyl)amine and removal of the solvent after reaction gave 0.445 g of a yellow microcrystalline solid that was homogeneous in TLC analysis. Recrystallization of this solid from methylene chloride–petroleum ether gave 0.435 g of lemon yellow, reflecting needles. IR (KBr, cm^{-1}): 1600, 1560, 1520, 1510, 1490, 1460, 1425, 1400, 1388, 1355, 1345, 1322, 1255, 1200, 1178, 1140, 1110, 915, 865, 838, 790, 755, 745, 695, 665, 560, 510. ^1H NMR: δ 1.64 (s, 9 H, $C(CH_3)_3$), 7.70 (s, 1 H, CH=N), 8.25 (dd, 2 H, J = 9 Hz, aromatic), 8.45 (d, 2 H, J = 9 Hz, aromatic). ^{13}C NMR: δ 28.30 ($C(CH_3)_3$), 72.32 ($C(CH_3)_3$), 123.68, 127.87, 128.90, 136.68 (CH=N), 147.51 (4-N-O_2C). Mass spectrum (EI, 70 eV): m/z 222 (M^+), 57 (base peak).

***N*-(Phenylmethylene)benzenamine *N*-Oxide.** Oxidation of 0.371 g of phenylbenzylamine by the addition of 1 led to the immediate formation of a dark yellow color that disappeared quickly, leaving a pale yellow solution. Removal of the solvent gave a cream-colored mirocrystalline solid. This solid was recrystallized from acetone–petroleum ether to give 0.391 g of white crystalline needles. IR (KBr, cm^{-1}): 1595, 1575, 1550, 1485, 1462, 1445, 1398, 1325, 1300, 1195, 1085, 1070, 920, 890, 830, 775, 752, 685, 645, 585, 515. ^1H NMR: δ 7.43–7.55 (m, 6 H, aromatic), 7.74–7.82 (m, 2 H, aromatic), 7.93 (s, 1 H, CH=N), 8.36–8.46 (m, 2 H, aromatic). ^{13}C NMR: δ 121.67, 128.57, 128.95, 129.08, 129.85, 130.58, 130.86, 134.52, 149.0.

***N*-(Phenylmethylene)benzenemethanamine *N*-Oxide.** Oxidation of 0.263 g of *N*,*N*-dibenzylhydroxylamine and removal of the solvent gave a solid which was dissolved in acetone and the solution dried (Na_2SO_4). Evaporation of the solvent gave a white crystalline solid. Flash chromatography of this solid on silica gel and elution with 15:85 ethyl acetate–petroleum ether

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gave 0.252 g of the nitrone as a white crystalline solid. IR (KBr, cm^{-1}): 1590, 1585, 1500, 1460, 1455, 1385, 1355, 1320, 1315, 1302, 1215, 1202, 1155, 1030, 950, 760, 750, 715, 695, 580. ^1H NMR: δ 5.06 (s, 2 H, $CH_2C_6H_5$), 7.35–7.53 (m, 9 H, aromatic and vinyl protons), 8.16–8.26 (m, 2 H, aromatic). ^{13}C NMR: δ 71.22, 128.42, 128.57, 128.95, 129.21, 130.35, 130.44, 133.16, 134.23.

***N*-[(4-Chlorophenyl)methylene]benzenamine *N*-Oxide.** Oxidation of 0.236 g of phenyl(4-chlorobenzyl)amine and removal of the solvent gave a pale yellow microcrystalline solid. Recrystallization of this solid from ethyl acetate–petroleum ether gave 0.244 g of cream-colored, shiny needles. IR (KBr, cm^{-1}): 3065, 1595, 1572, 1555, 1490, 1460, 1408, 1390, 1305, 1290, 1200 (NO), 1178, 1098, 1078, 1020, 920, 900, 848, 820, 770, 710, 702, 692, 532, 510. ^1H NMR: δ 7.43–7.55 (m, 6 H, aromatic), 7.74–7.82 (m, 2 H, aromatic), 7.93 (s, 1 H, CH=N), 8.36–8.46 (m, 2 H, aromatic). ^{13}C NMR: δ 121.67, 128.57, 128.95, 129.08, 129.85, 130.58, 134.52, 149.0. Mass spectrum (EI, 70 eV): m/z 231 (M^+, 11), 91 (base peak).

***N*-(Phenylmethylene)tricyclo[3.3.1.1^{3,7}]decan-1-amine *N*-Oxide.** Oxidation of 0.437 g of (1-adamantyl)benzylamine and removal of the solvent gave a white, flaky solid that was homogeneous in TLC analysis. This solid was dissolved in CH_2Cl_2, the solution was dried with anhydrous Na_2SO_4, and the solvent was evaporated to give 0.456 g of the white, flaky nitrone. IR (KBr, cm^{-1}): 1578, 1558 (C=N), 1545, 1445, 1415, 1350, 1312, 1190, 1140, 1115, 1058, 930, 800, 748, 695, 580, 510. ^1H NMR: δ 1.6–2.5 (m, 15 H, adamantane ring H), 7.41 (m, 3 H, aromatic), 7.48 (s, 1 H, CH=N), 8.30 (m, 2 H, aromatic). ^{13}C NMR: δ 29.71 (C-3,5,7), 35.96 (C-4,6,10), 40.87 (C-2,8,9), 70.74 (C-1), 128.37, 128.83, 129.51, 129.97, 130.98 (CH=N). Mass spectrum (EI, 70 eV): m/z 256 (M + 1), 255 (M^+), 135 (base peak). Calcd for $C_{17}H_{21}NO$: 255.34.

***N*,*N*′-1,2-Ethanediylidenebis(benzenamine) *N*,*N*′-Dioxide.** The general procedure was followed using 0.172 g of *N*-methylaniline. The reaction mixture turned yellow immediately upon addition of the solution of 1. After 5 min the reaction solution had turned dark orange. Removal of the solvent gave a dark orange crystalline solid (0.188 g). This solid was recrystallized from ethanol–petroleum ether to give orange needles. The needles were filtered off, washed with petroleum ether, and dried (0.110 g, 57% yield). IR (KBr, cm^{-1}): 3140, 3055, 1590, 1505, 1470, 1405, 1335, 1300, 1185, 1090, 1025, 1002, 815, 793, 772, 695, 660, 640, 635. ^1H NMR: δ 7.45–7.55 (m, 2 × 3 H, aromatic), 7.80–7.88 (m, 2 × 2 H, aromatic), 8.65 (s, 2 × 1 H, N=CHCH=N). ^{13}C NMR: δ 121.13, 128.04, 129.27, 130.94, 147.08. Mass spectrum (EI, 70 eV): 240 (M^+, 33), 242 (M + 2, 2), 241 (M + 1, 6).

***N*-[(4-Fluorophenyl)methylene]-2-methyl-2-propanamine *N*-Oxide.** Oxidation of 0.398 g of *tert*-butyl(4-fluorobenzyl)amine and removal of the solvent gave a white crystalline solid that was homogeneous in TLC analysis. The solid was dissolved in hexane and dried with anhydrous Na_2SO_4. Evaporation of the solvent gave 0.421 g of white needles. IR (KBr, cm^{-1}): 1605, 1595, 1565 (C=N), 1505, 1420, 1395, 1365, 1312, 1298, 1225, 1195, 1162, 1125, 1100, 1020, 915, 845, 815, 765, 715, 668, 525. ^1H NMR: δ 1.61 (s, 9 H, $C(CH_3)_3$), 7.10 (t, 2 H, J = 8.79 Hz, aromatic), 7.53 (s, 1 H, CH=N), 8.34 (dd, 2 H, J = 9.04, 9.03 Hz, aromatic). ^{13}C NMR: δ 28.23 ($C(CH_3)_3$), 70.70 ($C(CH_3)_3$), 115.42 (d, $^2J_{C-F}$ = 21.5 Hz, C-3), 127.37 (d, $^4J_{C-F}$ = 3.3 Hz, C-1), 128.70 (CH=N), 130.89 (d, $^3J_{C-F}$ = 8.0 Hz, C-2), 163.11 (d, $^1J_{C-F}$ = 251.4 Hz, C-4). Mass spectrum (EI, 70 eV): m/z 196 (M + 1, 1.5), 195 (M^+, 12.5), 57 (base peak).

Anal. Calcd for $C_{11}H_{14}FNO$: C, 67.67; H, 7.22; N, 7.17. Found: C, 67.92; H, 7.34; N, 7.25.

***N*-[(Methylphenyl)methylene]-2-methyl-2-propanamine *N*-Oxide.** Oxidation of 0.358 g of *tert*-butyl(4-methylbenzyl)-amine and removal of the solvent gave a colorless, viscous liquid that was homogeneous in TLC analysis. The liquid was dissolved in CH_2Cl_2 and the solution was dried with anhydrous Na_2SO_4. Evaporation of the solvent on the rotary evaporator gave a colorless, viscous liquid that solidified upon addition of hexane. The solid obtained (0.328 g) was recrystallized from hexane to give white cubes. IR (KBr, cm^{-1}): 1605, 1568 (C=N), 1560, 1510, 1480, 1455, 1415, 1362, 1325, 1302, 1255, 1238, 1202, 1186, 1125, 1115, 910, 846, 718, 665, 642, 525. ^1H NMR: δ 1.60 (s, 9 H, $C(CH_3)_3$), 2.37 (s, 3 H, 4-CH_3), 7.22 (d, 2 H, J = Hz, aromatic), 7.50 (s, 1 H, CH=N), 8.19 (d, 2 H, J = 8.49 Hz, aromatic). ^{13}C NMR: δ 21.57 (4-CH_3), 28.26 ($C(CH_3)_3$), 70.38 ($C(CH_3)_3$), 128.27, 128.76, 129.06, 129.85, 140.44 (C-4). Mass spectrum (EI, 70 eV): m/z 192 (M + 1, 3), 191 (M^+, 26), 57 (base peak). Calcd for $C_{12}H_{17}NO$: 191.26.

***N*-[(4-(1,1-Dimethylethyl)phenyl)methylene]-2-methyl-2-propanamine *N*-Oxide.** Oxidation of 0.422 g of *tert*-butyl-(4-*tert*-butylbenzyl)amine and removal of the solvent gave a white crystalline solid that was homogeneous in TLC analysis. The solid was dissolved in hexane, the solution was dried with anhydrous Na_2SO_4, and the solvent was evaporated to give 0.445 g of white needles. IR (KBr, cm^{-1}): 1610, 1578 (C=N), 1555, 1510, 1420, 1365, 1325, 1275, 1195, 1130, 1120, 1020, 915, 862, 565. ^1H NMR: δ 1.32 (s, 9 H, 4-$(CH_3)_3C$), 1.60 (s, 9 H, $NC(CH_3)_3$), 7.43 (d, 2 H, J = 8.68 Hz, aromatic), 7.51 (s, 1 H, CH=N), 8.22 (d, 2 H, J = 8.79 Hz, aromatic). ^{13}C NMR: δ 28.32 ($NC(CH_3)_3$), 31.11 (4-(C-$H_3)_3C$), 34.9 (4-$(CH_3)_3C$), 70.4 ($NC(CH_3)_3$), 125.31, 128.27, 128.63, 129.66, 153.52. Mass spectrum (EI, 70 eV): m/z 234 (M + 1, 3), (M^+, 17), 57 (base peak). Calcd for $C_{15}H_{23}NO$: 233.34.

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Registry No. 1, 74087-85-7; *N*-(phenylmethylene)-2-methyl-2-propanamine *N*-oxide, 3376-24-7; *tert*-butylbenzylamine, 3378-72-1; *N*-[(4-chlorophenyl)methylene]-2-methyl-2-propanamine *N*-oxide, 40117-30-4; *tert*-butyl(4-chlorobenzyl)amine, 46234-01-9; *N*-[(4-methoxyphenyl)methylene]-2-methyl-2-propanamine *N*-oxide, 40117-28-0; *tert*-butyl(4-methoxybenzyl)amine, 22675-83-8; *N*-[(4-nitrophenyl)methylene]-2-methyl-2-propanamine *N*-oxide, 3585-88-4; *tert*-butyl(4-nitrobenzyl)amine, 3489-67-6; *N*-(phenylmethylene)benzenamine *N*-oxide, 1137-96-8; phenylbenzylamine, 103-32-2; *N*-(phenylmethylene)benzenemethanamine *N*-oxide, 3376-26-9; *N*,*N*-dibenzylhydroxylamine, 621-07-8; *N*-[(4-chlorophenyl)-methylene]benzenamine *N*-oxide, 5909-74-0; phenyl(4-chlorobenzyl)amine, 4750-61-2; *N*-(phenylmethylene)tricyclo-[3.3.1.1^{3,7}]decan-1-amine, 31463-28-2; (1-adamantyl)benzylamine, 3717-60-0; *N*,*N*′-1,2-ethanediylidenebis(benzenamine) *N*,*N*′-dioxide, 13532-81-5; *N*-methylaniline, 100-61-8; *N*-[(4-fluorophenyl)methylene]-2-methyl-2-propanamine *N*-oxide, 85623-70-7; *tert*-butyl (4-fluorobenzyl)amine, 125640-89-3; *N*-[(4-methylphenyl)methylene]-2-methyl-2-propanamine *N*-oxide, 40117-29-1; *tert*-butyl(4-methylbenzyl)amine, 55980-45-5; *N*-[(4-(1,1-dimethylethyl)phenyl)methylene]-2-methyl-2-propanamine *N*-oxide, 88888-33-9; *tert*-butyl(4-*tert*-butylbenzyl)amine, 125640-90-6; nitrosobenzene, 586-96-9.

Synthesis of Novel 6β,14-Epoxy-Bridged Opiates

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During the course of our research directed toward the development of selective opioid receptor antagonists, we discovered a novel opiate cyclization that makes the opiate C-ring rigid in a manner similar to the oripavines **1**.[1] These new compounds (**2a**, **2b**) have a 6,14β-epoxy linkage in place of the 6,14β-ethano bridge of Bently's[1] extremely potent thebaine-derived oripavines **1**. This was accomplished by an intramolecular ether-forming reaction of the relatively flexible C ring of 6α-(mesyloxy)opiates **4a** and **4b**, converting them into the rigid 1,4-epoxycyclohexane derivatives **2a** and **2b**.

(1) Bently, K. W.; Hardy, D. G. *Proc. Chem. Soc.* **1963**, 220.

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