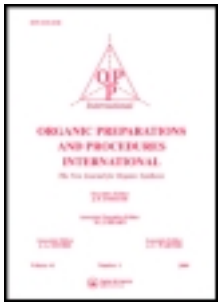

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EFFICIENT AND FACILE ROUTES TO NITRONES

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EFFICIENT AND FACILE ROUTES TO NITRONES

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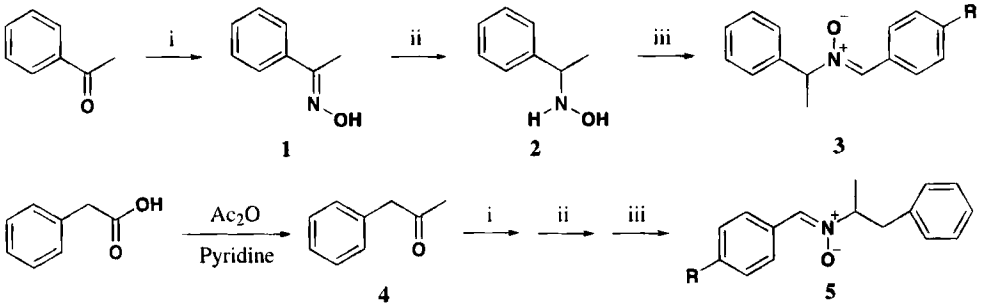
Azomethine *N*-oxides, commonly known as nitrones, have been extensively investigated[1,2] because of their utility as versatile synthetic intermediates and their relative stability compared with the analogous azomethine imines and azomethine ylides. [3] A nitrone is often viewed as an extended carbonyl group that should be subject to electrophilic attack at the oxygen and nucleophilic attack at the carbon. Nitrones are classic examples of octet-stabilized 1,3-dipoles lacking an orthogonal double bond.[4] As such, they participate in [3+2] cycloaddition reactions with a wide variety of dipolarophiles to provide numerous heterocyclic systems.[5a-c, 6a-b] Interest in nitrones also stems from their photochemical reactivity[7] as well as from their excellent radical spin-trapping capability leading to their use as antioxidants. [8]

Nitrones are normally synthesized *via* one of the following routes: i) Condensation of carbonyl compounds with hydroxylamines,[9] or oxidation of hydroxylamines[10] if the appropriate hydroxylamines are available. ii) Oxidation of a secondary amine by peroxide in the presence of sodium tungstate[11a-c] or selenium dioxide[12] catalyst (which is a good method for easily prepared secondary amines). iii) Oxidation of imines by treatment with potassium permanganate under phase-transfer conditions[13] (the imines are readily obtained;[14] however, if this reaction is not carefully controlled, the oxidation procedure is complicated and frequently leads to over-oxidation to amides and other by-products). iv) Peroxy acid oxidation of azomethines to the corresponding oxaziridines and then thermal rearrangement under carefully controlled conditions (to avoid subsequent nitrone to amide rearrangement) is a viable method for the general synthesis of nitrones,[9] but sometimes the rearrangement is complicated and difficult to control.[15] v) *N*-Alkylation of oximes by alkyl halides or sulfonates[14] (this method is useful only for activated alkyl halides such as α-halocarbonyl compounds).

In the context of other investigations, several nitrones with specific structures (**3**, **5**, **12**, and **15**) were required as model compounds. In fact, few such compounds have been previously described in the literature. Herein, we report two facile and practical routes to these target nitrones.

The condensation of *N*-substituted hydroxylamines with aromatic aldehydes offers the most direct approach to the preparation of nitrones and can be achieved smoothly at room temperature in a solvent such as ether or ethanol.[16a-b] The only limitation is the relative inaccessibility of the hydroxylamine starting materials. This disadvantage can be overcome by the *in situ* generation of the requisite hydroxylamine from more accessible precursors, *e.g.* nitro and oxime compounds. Based on this consideration, we designed the following route to synthesize the target molecules **3** and **5** (*Scheme 1*).



a) R = H b) R = OCH_3 c) R = CF_3 d) R = $NHCOCH_3$

i) EtOH/Pyridine (5/1), NH_2OH HCl ii) $NaCNBH_3$, AcOH/THF (2/1) iii) ArCHO, EtOH, r.t.

Scheme 1

Acetophenone oxime (**1**) was prepared by the condensation of acetophenone and hydroxylamine hydrochloride in a mixture of ethanol and pyridine (ratio 5/1); the pyridine served as a base to neutralize the hydrochloride in the hydroxylamine and to remove the water produced during condensation. In this way, oxime (**1**) may be prepared on large scale (up to 100 g) in high yield (>95%). When NaOH was used as the base as in the procedure for the preparation of benzophenone oxime,[17] unreacted acetophenone was always recovered.

Oximes have been reported to be reduced by BH_3-THF[18] or $NaCNBH_3$.[19a-b] Our initial attempts using the borane-tetrahydrofuran method unfortunately only led to the recovery of the starting material. The use of sodium cyanoborohydride was successfully applied to reduce oxime **1** in acid medium (HOAc/THF: 2/1). The crude material **2** was sufficiently pure for the next step and was smoothly condensed with the appropriate aldehydes at room temperature to give the nitrones **3a-d**. Using α-phenylacetone (**4**) (obtained from phenylacetic acid by decarboxylative acylation with acetic anhydride in the presence of pyridine in 70% yield[20]) we obtained four additional nitrones **5a-d** through the same procedure as for **3**.

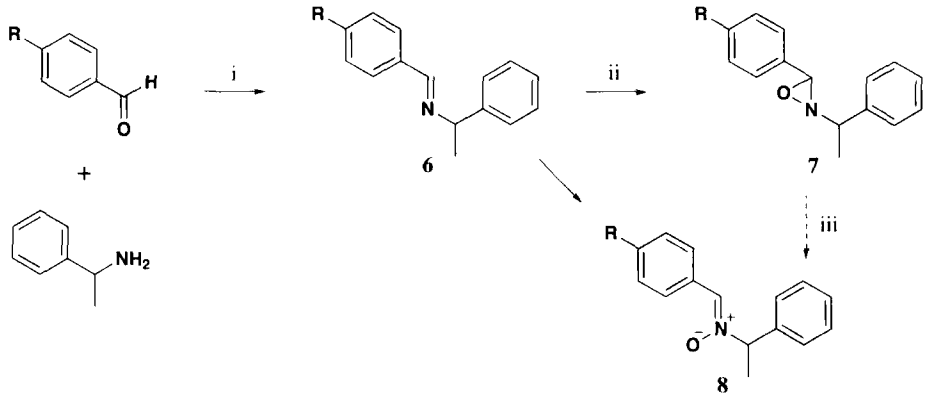
While oxime **1** is stable to storage for months without any change, the *N*-substituted hydroxylamine **2** is hygroscopic, and must be stored at low temperature and as free of solvent as possible. Although purification of the hydroxylamine **2** might be helpful in increasing the yield of nitrone, a preferable method to improve the yield is to change the conditions used for the reaction. We used several different conditions, which were dependent mainly on the solubility of the raw material aldehyde. The conditions listed in Table 1 typically provided excellent yields of nitrones. The progress of

the reaction can easily be monitored by TLC. It is useful to add 10-20% mole hydroxylamine after 24 hours of reflux if the reaction is not complete, which is usually the case when using electron-rich aldehydes.

TABLE 1. Condensation Conditions for the Preparation of Nitrones

Solvent	Catalyst	Conditions
Ethanol	HOAc	N_2, 25°C
Chloroform	molecular sieves, silica gel	N_2, 25°C
Methanol	HCl: For electron rich aldehydes, reflux, molecular sieves	N_2, 65°C
Benzene	*p*-TsOH, Dean-Stark trap	N_2, 80°C

The other two series of nitrones, **12** and **15**, could not be synthesized through the same route because of their α,α-disubstituted nature. Initially, the oxidation of imines **6** directly to nitrones was attempted (*Scheme 2*), because the imines are readily prepared in excellent yields from the condensation of aldehydes and α-methylbenzamine.



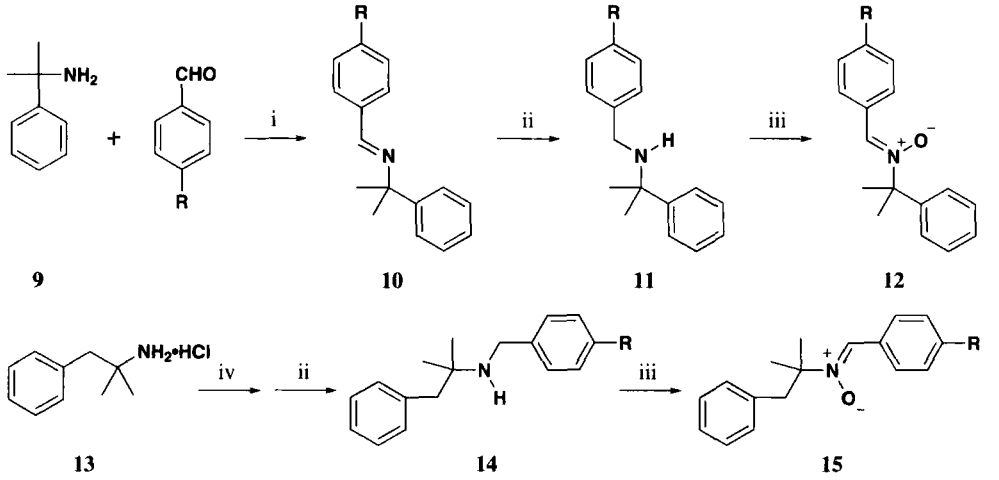
i) Toluene reflux ii) m-CPBA iii) H^+, MeCN or i-PrOH, reflux

Scheme 2

We obtained imine **6** in excellent yield. Attempts to oxidize these imines directly using H_2O_2 in THF or with sodium tungstate as a catalyst, failed. The use of a literature method[13] involving treatment of **6** with potassium permanganate under phase-transfer conditions (Bu_4NBr) was unfortunately too difficult to control and yielded the over-oxidized products acetophenone and benzoic acid.

The peroxy acid oxidation of an azomethine to the corresponding oxaziridine followed by the thermal rearrangement appeared to provide a viable alternative for the general synthesis of nitrones.[15] It was surprising to find that oxaziridine **7** (obtained smoothly from imine **6** by oxidation with *m*-chloroperoxybenzoic acid) had such a high thermal stability that it did not undergo thermal rearrangement as expected.[21] Heating oxaziridine **7** at reflux temperature for two days in different solvents (MeCN, *i*-PrOH) and with an acid catalyst let to the recovery of **7** in all cases.

We then utilized the method developed by Murahashi *et al.*[11c] and modified it by the reduction of imines to secondary amines using sodium borohydride, followed by the catalytic oxidation of the amines to nitrones to afford the remaining nitrones **12** and **15** as shown in (*Scheme 3*).



a) R = H b) R = OCH_3 c) R = CF_3 d) R = $NHCOCH_3$

i) Toluene, reflux ii) $NaBH_4$, MeOH, r.t. iii) $Na_2WO_4•2H_2O$, H_2O_2, MeOH
iv) $NaHCO_3$, Toluene, reflux

Scheme 3

The first two steps gave nearly quantitative yields. It was unnecessary to isolate the reaction intermediates, as the crude products were of sufficient purity for the next step of the reaction. The sodium tungstate catalyzed oxidation of secondary amines with hydrogen peroxide gave the nitrones as described. It should be noted that secondary amines **11** and **14** do not have α-protons on one side and thus the oxidation should give only the expected nitrones.

In summary, several approaches have been investigated, and two routes have been developed to produce nitrones. Both methods are suitable for the preparation of nitrones in multi-gram quantities and provide high yields (three steps ~60%) from commercially available chemicals.

EXPERIMENTAL SECTION

Melting points were determined with a Koefler hot-stage apparatus without correction. The NMR spectra were recorded on a Varian Gemini-300 in $CDCl_3$ (or DMSO-d_6) with tetramethylsilane as the internal standard for ^1H (300 MHz) or solvents as the internal standard for ^{13}C (75 MHz). The GC-MS spectra (EI, 70 ev) were obtained using a HP-5972 series mass selective detector coupled to a HP-5890 series II GC apparatus, which was equipped with a fused silica capillary column (L 30 m, ID 0.32 mm). Elemental analyses were carried out with a Carlo Erba 1106 instrument.

Acetophenone Oxime (1).- A solution of acetophenone (32 mL, 0.28 mol), hydroxylamine hydrochloride (30 g, 0.43 mol) and pyridine (40 mL) in ethyl alcohol (200 mL) was heated to reflux temperature. After the disappearance of acetophenone as indicated by TLC, the reaction was

quenched with water (200 mL) and extracted with $CHCl_3$ (5 x 100 mL). The combined organic layers were dried over anhydrous Na_2SO_4. Removal of the solvent gave the crude product in greater than 95% purity (36 g, yield 95%) suitable for further transformations. A pure analytical sample was obtained by recrystallisation from methyl alcohol and then cyclohexanes, mp 58-59° (*lit.*[22] 59.1-59.7°). ^1H NMR ($CDCl_3$, 300 MHz): d 2.30 (s, 3H), 7.35-7.40 (m, 3H), 7.60-7.70 (m, 2H), 9.68 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): d 12.3, 126.0, 128.5, 129.2, 136.5, 156.0.

General Procedure for the Preparation of α'-Monomethyl Nitrones (3, 5).- Acetophenone oxime (**1**) was dissolved in the binary solvent AcOH (40 mL) and THF (20 mL). Then sodium cyanoborohydride (1.0 g, 16 mmol) was added in portions while cooling with an ice-water bath. After stirring at room temperature for 24 hours, the reaction was quenched with 2 N NaOH (100 mL) and extracted with $CHCl_3$ (5 x 60 mL). After drying and removal of the solvent, the crude product was condensed with the corresponding *p*-substituted benzaldehyde (11 mmol) as described in Table 1. After TLC indicated the completion of the reaction, the mixture was poured into water and extracted with $CHCl_3$. After drying and evaporating the solvent, the crude nitrone was obtained. The crude material may be further purified by silica gel column chromatography using hexanes and EtOAc as eluents.

***N*-(1-Phenylethyl)-α-phenylnitrone (3a)**: mp 86-87°. R_f = 0.35 (hexane/EtOAc: 5/1). 1H NMR ($CDCl_3$, 300 MHz): d 1.89 (d, *J* = 6.9 Hz, 3H), 5.18 (q, *J* = 6.9 Hz, 1H), 7.35-7.45 (m, 6H), 7.48-7.54 (m, 3H), 8.21-8.22 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): d 19.1, 75.1, 127.2, 128.1, 128.4, 128.6, 128.7, 129.9, 130.2, 130.5, 133.0, 138.5. MS (70 ev) m/e: 225 (M*).

Anal. Calcd. for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 80.13; H, 6.78; N, 6.30

***N*-(1-Phenylethyl)-α-(*p*-methoxyphenyl)nitrone (3b)**.- mp 120-122°. R_f = 0.40 (hexane/EtOAc: 3/1). ^1H NMR ($CDCl_3$, 300 MHz): d 1.87 (d, *J* = 6.8 Hz, 3H), 3.78 (s, 3H), 5.13 (q, *J* = 6.8 Hz, 1H), 6.89 (d, *J* = 8.8 Hz, 2H), 7.28-7.37 (m, 3H), 7.42 (s, 1H), 7.50-7.53 (m, 2H), 8.23 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): d 18.9, 55.1, 74.2, 113.6, 123.4, 127.0, 128.3, 128.5, 130.4, 132.3, 138.6, 160.7.

Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.26; H, 6.72; N, 5.49. Found: C, 75.11; H, 6.61; N, 5.50

***N*-(1-Phenylethyl)-α-(*p*-trifluoromethylphenyl)nitrone (3c)**.- mp 105-107°. R_f = 0.40 (hexane/EtOAc: 2/1). ^1H NMR ($CDCl_3$, 300 MHz): d 1.90 (d, *J* = 6.6 Hz, 3H), 5.22 (q, *J* = 6.6 Hz, 1H), 7.36-7.40 (m, 3H), 7.50-7.55 (m, 2H), 7.56 (s, 1H), 7.62 (d, *J* = 8.0 Hz, 2H), 8.32 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): d 19.0, 75.6, 125.3 (q, *J* = 15.0 Hz), 127.1, 128.4, 128.8, 128.9, 131.5, 133.6, 138.2.

Anal. Calcd. for $C_{16}H_{14}NOF_3$: C, 65.52; H, 4.81; N, 4.78. Found: C, 65.32; H, 4.74; N, 4.81

***N*-(1-Phenylethyl)-α-(*p*-acetamidophenyl)nitrone (3d)**.- mp 225-227° R_f = 0.50 (acetone/EtOAc: 1/1). ^1H NMR ($CDCl_3$, 300 MHz): d 1.71 (d, *J* = 6.8 Hz, 3H), 2.06 (s, 3H), 5.39 (q, *J* = 6.8 Hz, 1H), 7.29-7.38 (m, 3H), 7.53-7.57 (m, 2H), 7.66 (d, *J* = 8.8 Hz, 2H), 8.02 (s, 1H), 8.22 (d, *J* = 8.8 Hz, 2H), 10.12 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): d 18.5, 24.1, 72.6, 118.2, 125.9, 127.2, 128.1, 128.2, 128.9, 131.6, 139.5, 140.4, 168.5. *Anal.* Calcd. for $C_{17}H_{18}N_2O_2$: C, 72.32; H, 6.43; N, 9.92. Found: C, 71.92; H, 6.37; N, 9.77.

***N*-(1-Phenylpropan-2-yl)-α-phenylnitrone (5a)**.- mp 91-93°. R_f = 0.37 (hexane/EtOAc: 2/1). ^{1}H NMR ($CDCl_3$, 300 MHz): d 1.54 (d, J = 6.3 Hz, 3H), 2.89 (dd, J_1, J_2 = 5.2 Hz, 1H), 3.37 (dd, J_1, J_2 = 8.8 Hz, 1H), 4.10-4.15 (m, 1H), 7.07 (s, 1H), 7.20-7.25 (m, 5H), 7.30-7.37 (m, 3H), 8.10-8.17 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): d 18.8, 40.5, 73.8, 126.5, 128.2, 128.3, 128.5, 128.8, 129.9, 130.0, 130.2, 133.4, 137.6.

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.48; H, 7.23; N, 5.92

***N*-(1-Phenylpropan-2-yl)-α-(*p*-methoxyphenyl)nitrone (5b)**.- mp 71°. R_f = 0.30 (hexane/EtOAc: 1/1).^{1}H NMR ($CDCl_3$, 300 MHz): d 1.53 (d, J = 6.5 Hz, 3H), 2.89 (dd, J_1, J_2 = 5.2 Hz, 1H), 3.37 (dd, J_1, J_2 = 8.5 Hz, 1H), 3.77 (s, 3H), 4.08-4.15 (m, 1H), 6.88 (d, J = 8.8 Hz, 2H), 7.02 (s, 1H), 7.20-7.25 (m, 5H), 8.15 (d, J = 8.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): d 18.6, 40.3, 55.0, 73.1, 113.5, 122.9, 126.5, 128.2, 128.8, 130.7, 133.9, 137.6, 160.9. MS (70 ev): 269 (M*).

Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 75.80; H, 7.11; N, 5.20. Found: C, 75.93; H, 7.30; N, 5.21

***N*-(1-Phenylpropan-2-yl)-α-(*p*-trifluoromethylphenyl)nitrone (5c)**.- mp 123-125°. R_f = 0.67 (hexane/EtOAc: 2/1).^{1}H NMR ($CDCl_3$, 300 MHz): d 1.57 (d, J = 6.4 Hz, 3H), 2.91 (dd, J_1 = 4.6 J_2 = 4.4 Hz, 1H), 3.36 (dd, J_1 = 9.1 Hz J_2 = 9.3 Hz, 1H), 4.18-4.23 (m, 1H), 7.11 (s, 1H), 7.15-7.21 (m, 5H), 7.61 (d, J = 8.0 Hz, 2H), 8.24 (d, J = 8.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): d 19.0, 40.7, 74.6, 125.1, 125.1, 125.2, 126.8, 128.3, 128.5, 128.8, 131.9, 133.4, 137.5. MS (70 ev): 307 (M*).

Anal. Calcd. for $C_{17}H_{16}NOF_3$: C, 66.44; H, 5.25; N, 4.56. Found: C, 66.53; H, 5.42; N, 4.64

***N*-(1-Phenylpropan-2-yl)-α-(*p*-acetamidophenyl)nitrone (5d)**.- mp 161-163°. Rf = 0.55 (Acetone/EtOAc: 2/3). ^{1}H NMR ($CDCl_3$, 300 MHz): d 1.52 (d, J = 6.3 Hz, 3H), 2.12 (s, 3H), 2.90 (dd, J_1, J_2 = 4.9 Hz, 1H), 3.34 (dd, J_1, J_2 = 8.6 Hz, 1H), 4.10-4.15 (m, 1H), 7.06 (s, 1H), 7.13-7.19 (m, 5H), 7.59 (d, J = 7.7 Hz, 2H), 8.08 (d, J = 7.7 Hz, 2H), 8.96 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): d 18.8, 24.4, 40.5, 73.4, 119.2, 125.6, 126.7, 128.4, 128.8, 129.6, 133.5, 137.5, 140.1, 169.2.

Anal. Calcd. for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80; N, 9.45. Found: C, 72.94; H, 6.93; N, 9.43

General Procedure for the Preparation of α',α'-Dimethyl nitrones (12, 15).- The preparation of *N*-(2-phenylpropan-2-yl)-α-phenylnitrone (**12a**) provides a typical example. Benzaldehyde (1.1 g, 10 mmol) and cumylamine (1.35 g, 10 mmol) were dissolved in toluene (50 mL) and heated to reflux for 20 hours. After evaporation of the solvent, the imine (2.1 g, purity > 95%) was directly used in the next reaction. To the stirred solution of the imine (1.9 g, 8.5 mmol) in methanol (40 mL), sodium borohydride (0.5 g, 13.2 mmol) was added slowly while cooling with ice. The reaction mixture was stirred at room temperature. After TLC indicated the completion of the reaction, the reaction mixture was quenched with 20 mL of water, extracted with chloroform, dried over anhydrous Na_2SO_4, and evaporated to give the amine intermediate (1.70 g).

In a 50 mL flask were placed: the above amine (1.67 g, 7.4 mmol), Na_2WO_4•$2H_2O$ (0.1 g, 0.3 mmol), and methanol (25 mL). 30% Aqueous hydrogen peroxide (2.6 g, 22.5 mmol) was added dropwise while cooling with an ice-water bath. After the addition was completed, the reaction mixture was warmed to room temperature overnight. Methanol was removed under reduced pressure. To the residue was added water (20 mL) and chloroform (30 mL). The organic layer was separated, washed

with saturated sodium chloride solution (3 x 10 mL), dried over anhydrous sodium sulfate, filtered, and evaporated. Column chromatography on silica gel (hexane/EtOAc: 5/1 as eluent) R_f = 0.35 gave the target nitrone **12a** (yield 1.3 g, 60%, three steps). mp 93-95°. ^{1}H NMR ($CDCl_3$, 300 MHz): d 1.98 (s, 6H), 7.29 (s, 1H), 7.30-7.49 (m, 8H), 8.18-8.21 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): d 28.0, 76.2, 125.8, 127.9, 128.2, 128.3, 128.6, 128.7, 130.0, 130.8, 132.4, 143.4.

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.26; H, 7.42; N, 5.89

***N*-(2-Phenylpropan-2-yl)-α-(*p*-methoxyphenyl)nitrone (12b)**.- mp 105°. R_f = 0.30 (Hexane/EtOAc: 1/1). ^{1}H NMR ($CDCl_3$, 300 MHz): d 1.94 (s, 6H) 3.79 (s, 3H), 6.90 (d, *J* = 8.7 Hz, 2H), 7.24 (s, 1H), 7.32-7.37 (m, 3H), 7.42-7.50 (m, 2H), 8.21 (d, *J* = 8.7 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): d 28.0, 55.1, 75.4, 113.6, 123.7, 125.7, 127.7, 128.6, 130.5, 131.9, 143.5, 160.7.

Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.89; H, 7.25; N, 5.22

***N*-(2-Phenylpropan-2-yl)-α-(*p*-trifluoromethylphenyl)nitrone (12c)**.- mp 112°. R_f = 0.67 (Hexane/EtOAc: 2/1). ^{1}H NMR ($CDCl_3$, 300 MHz): d 1.97 (s, 6H), 7.35-7.42 (m, 4H), 7.45-7.50 (m, 2H), 7.62 (d, *J* = 8.2 Hz, 2H), 8.30 (d, *J* = 8.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): d 28.0, 77.0, 125.2 (*q*, *J* = 15.0 Hz), 128.2, 128.5, 128.8, 131.2, 134.0, 143.1.

Anal. Calcd. for $C_{17}H_{16}NOF_3$: C, 66.44; H, 5.25; N, 4.56. Found: C, 66.53; H, 5.47; N, 4.61

***N*-(1-Phenyl-2-methylpropan-2-yl)-α-phenylnitrone (15a)**.- mp 80-82°. Rf = 0.37 (Hexane/EtOAc: 2/1). ^{1}H NMR ($CDCl_3$, 300 MHz): d 1.54 (s, 6H), 3.17 (s, 2H), 7.05-7.12 (m, 3H), 7.15-7.20 (m, 3H), 7.35-7.40 (m, 3H), 8.20-8.25 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): d 26.1, 45.6, 73.4, 126.6, 127.2, 128.0, 128.2, 128.8, 130.0, 130.7, 131.3, 136.5.

Anal. Calcd. for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.85; H, 7.78; N, 5.54

***N*-(1-Phenyl-2-methylpropan-2-yl)-α-(*p*-methoxyphenyl)nitrone (15b)**.- mp 68-70°. R_f = 0.48 (Hexane/EtOAc: 1/2). ^{1}H NMR ($CDCl_3$, 300 MHz): d 1.53 (s, 6H), 3.17 (s, 2H), 3.81 (s, 3H), 6.92 (d, *J* = 8.8 Hz, 2H), 7.03 (s, 1H), 7.09-7.14 (m, 5H), 8.24 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): d 26.0, 45.5, 55.1, 72.6, 113.5, 121.9, 126.5, 127.9, 130.0, 130.6, 130.8, 136.6, 160.7.

Anal. Calcd. for $C_{18}H_{21}NO_2$: C, 76.30; H, 7.47; N, 4.94. Found: C, 76.31; H, 7.62; N, 4.91

***N*-(1-Phenyl-2-methylpropan-2-yl)-α-(*p*-trifluoromethylphenyl)nitrone (15c)**.- mp 98-100°. R_f = 0.48 (Hexane/EtOAc: 2/1). ^{1}H NMR ($CDCl_3$, 300 MHz): d 1.58 (s, 6H), 3.17 (s, 2H), 7.05-7.10 (m, 2H), 7.12-7.20 (m, 4H), 7.64 (d, *J* = 8.2 Hz, 2H), 8.34 (d, *J* = 8.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): d 26.1, 45.8, 74.3, 125.2 (q, *J* = 15.0 Hz), 126.9, 128.1, 128.7, 130.0, 130.9, 133.9, 136.3.

Anal. Calcd. for $C_{18}H_{18}NOF_3$: C,67.28; H, 5.65; N, 4.36. Found: C, 67.32; H, 5.69; N, 4.36

***N*-(1-Phenyl-2-methylpropan-2-yl)-α-(*p*-acetamindophenyl)nitrone (15d)**.- mp 186-188°. R_f = 0.53 (EtOAc/Acetone: 3/2). ^{1}H NMR ($CDCl_3$, 300 MHz): d 1.48 (s, 6H), 2.08 (s, 3H), 3.11 (s, 2H), 3.42 (s, 1H), 7.07-7.14 (m, 5H), 7.27 (s, 1H), 7.65 (d, *J* = 8.5 Hz, 2H), 8.26 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): d 22.3, 24.0, 43.1, 70.7, 116.5, 124.1, 124.6, 126.0, 127.5, 128.0, 128.4, 135.0, 138.7, 166.7.

Anal. Calcd. for $C_{19}H_{22}N_2O_2$: C, 73.52; H, 7.14; N, 9.03. Found: C, 73.36; H, 7.34; N, 8.93

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