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Selective Syntheses of Substituted 6-Alkyl-1,1-dimethyl-1,2,3,4-tetrahydronaphthalenes

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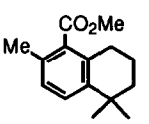
Abstract: *β-ionone is cyclized to 1,1,6-trimethyl-1,2,3,4-tetrahydronaphthalene in 80-95% yield. Selective derivatization at the 5- and/or 7-positions of 6-alkyl-1,1-dimethyl-1,2,3,4-tetrahydronaphthalenes was achieved by nitration, acylation, and reduction.*

As part of a systematic search for herbicidal compounds, a series of substituted 6-alkyl-1,1-dimethyl-1,2,3,4-tetrahydronaphthalenes were prepared. This project started when compound (**1**)[1] demonstrated significant preemergent activity on economically important narrowleaf weeds. Compound (**1**) was prepared by Tanis *et al.*[2] using a Diels-Alder reaction with methyl propiolate and 6,6-dimethyl-1-vinylcyclohexene to afford the hexahydronaphthalene followed by aromatization using DDQ to yield compound (**1**). In our synthetic follow up, we chose the method used by Bogert[3] *et al.* to prepare the tetrahydronaphthalene intermediate (**3**). This paper describes the synthesis of compounds (**3**) and the regioselectivity of electrophilic substitution at the 5- and 7-positions of the tetralin ring.



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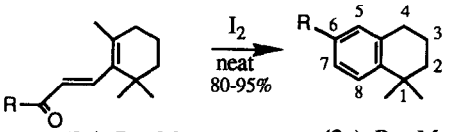
6-Methyltetrahydronaphthalene (6-methyltetralin) (**3a**) was prepared in one step from commercially available ß-ionone (**2a**). Optimization of this previously reported reaction[3,4] involved heating ß-ionone (**2a**) neat with a catalytic amount of iodine at 110°C for thirty minutes and upon cooling was extracted with hexane to afford (**3a**) in 80-95% yield, an increase from the reported 60% yield.

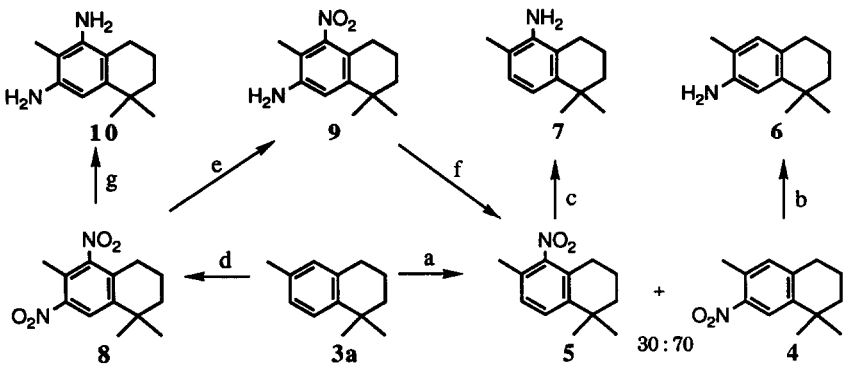


(**2a**) R = Me (**3a**) R = Me
(**2b**) R = Et (**3b**) R = Et

Scheme 1

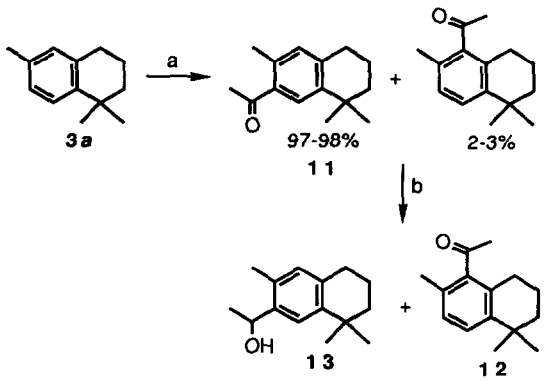
Reactivity of 6-alkyltetrahydronaphthalenes is not well known. Bogert found that (**3a**) readily sulfonated to afford the mono-sulfonated tetralin or nitrated to afford the dinitrotetralin. However, the position of substitution was not determined. The three unsubstituted aromatic carbons of (**3a**) are each activated towards electrophilic substitution, though only products resulting from substitution at the 5- and 7-positions were isolated. Presumably, substitution at the 8-position is hindered by the steric affects of the 1,1-dimethyl groups.

Nitration of (**3a**) with a mixture of sulfuric and nitric acid afforded 80% of the dinitrotetralin (**8**). Milder conditions were examined to see if the less crowded 7-position would selectively nitrate. Optimized conditions using acetic acid as solvent and 2.5 equivalents of nitric acid yielded a 70:30 mixture of mono-nitrotetralins (**4**) and (**5**), respectively; other nitrating conditions were tried but none afforded the 7-nitrotetralin (**4**) exclusively. The mono-nitrotetralins (**4**) and (**5**) were reduced using 10%Pd/C in very good yield to the corresponding amino derivatives (**6**) and (**7**). Reduction of 7-nitrotetralin (**4**) proceeded significantly faster than the 5-nitro isomer (**5**). Other hydrogenating catalyst were examined to see if the greater reactivity of the 7-nitro group could be used to a synthetic advantage. Reduction of the dinitrotetralin (**8**) using Adam's catalyst, while keeping the hydrogen pressure below 40psi, selectively reduced the 7-nitro group affording 7-amino-5-nitrotetralin (**9**) in 90% yield. Deamination of (**9**) via the diazonium salt provided a convenient route for the large scale preparation of the minor mono-nitrated tetralin (**5**).



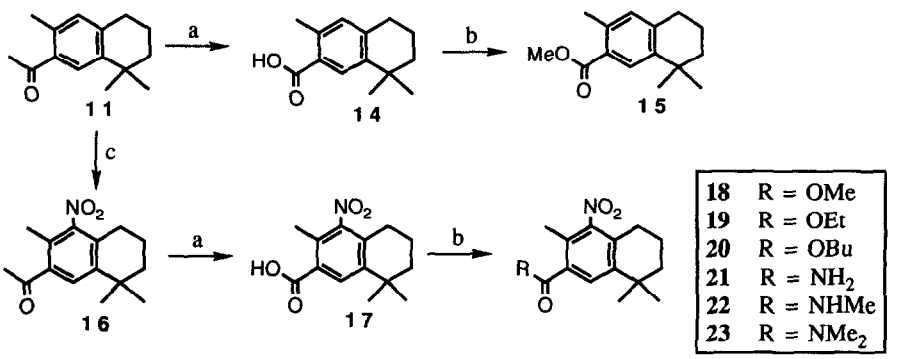
Scheme 2. a) 70% HNO_3, H_3CCO_2H, $(MeCO)_2O$, 0 °C then r.t. 1 h (86% yield); b) 50 psi H_2, 10% Pd/C, EtOH (75%); c) 50 psi H_2, 10% Pd/C, EtOH, 40 °C (99%); d) 70% HNO_3, 96% H_2SO_4, 0 °C then r.t 1 h (80% yield); e) below 40 psi H_2, PtO_2, EtOH, r.t. (90%); f) 35% H_2SO_4, $NaNO_2$, EtOH/Cu, reflux 1 h (87%); g) 50 psi H_2, PtO_2, EtOH, r.t. (77%).

Preference for the 7-position of the tetralin ring to undergo electrophilic substitution during nitration was also observed for Friedel-Craft acylation. Reacting (**3a**) with acetyl chloride and aluminum chloride afforded a 97% yield of the 7-acyl regioisomer (**11**) and only 3% of the 5-acyl regioisomer (**12**) (Scheme 3). The difference in regioselectivity of acylation vs. nitration can be explained by the relatively large size of the acyl-aluminum chloride complex compared to the nitro group. The 7-acyltetralin (**11**) crystalized from the reaction mixture in pure form. Compound (**12**) was obtained in pure form from a large scale reduction of a mixture of (**11**) and (**12**) with sodium borohydride. The 7-acyltetralin (**11**) reduced to the corresponding alcohol (**13**), while the 5-acyltetralin (**12**) was unreactive under these conditions allowing its isolation from the reaction mixture in pure form. The acyl group at the 5-position failed to react most likely due to steric hindrance. It is known[5,6,7] that conjugative groups on aromatic rings with two ortho substituents can experience steric crowding great enough to force the group out of plane with the benzene ring. It is believed that the same phenomena is occurring at the 5-position of tetralin (**12**). With the carbonyl group orthogonal to the plane with the benzene ring, borohydride is prevented from reducing it since the o-methyl and o-methylene groups effectively prevent the hydride approach.



Scheme 3. a) *MeCOCl, $AlCl_3$, $ClCH_2CH_2Cl$, 0 °C then r.t. 2 h (96% yield);* b) *$NaBH_4$, MeOH, 0 °C then r.t. 3 h (80%).*

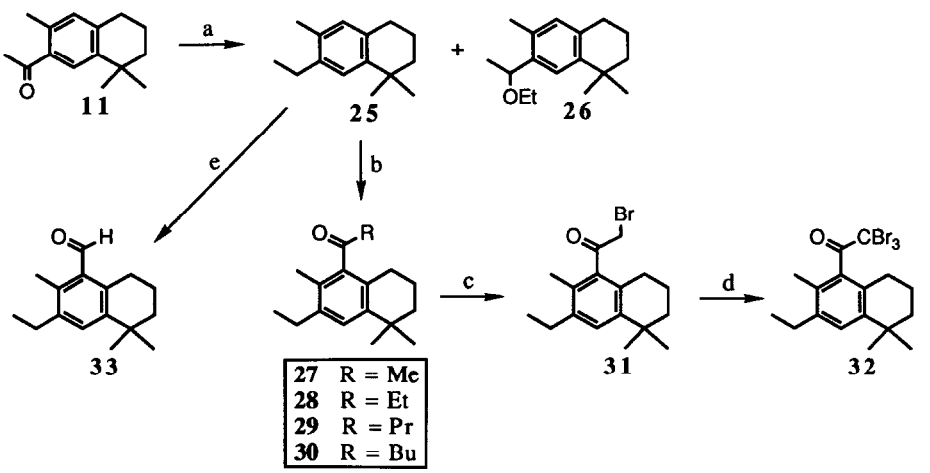
Scheme 4 shows several derivatives of the readily available 7-acyltetralin (**11**). The regioisomer of the lead compound (**1**) was prepared by the oxidation of the 7-acyltetralin (**11**) using the haloform reaction to afford the carboxylic acid (**14**), and from the latter the methyl ester (**15**) was prepared. The 7-acyltetralin (**11**) was nitrated at the 5-position to afford (**16**), which was also oxidized to the carboxylic acid (**17**) from which a series of esters and amides were prepared (**18-23**).



Scheme 4. a) NaOH, Br_2, H_2O, dioxane, 0 °C then r.t 24 h (95% yield); b) $(COCl)_2$, CH_2Cl_2, RH, TEA (66-100%); c) 70% HNO_3, 96% H_2SO_4, 0 °C then r t. 1 h (78% yield)

Since the Friedel-Craft acylation of (**3a**) afforded only 3% of the 5-acyl regioisomer (**12**) (Scheme 3), other routes were explored in an effort to obtain sufficient amounts of 5-ketotetralins to derivatize. Routes involving protecting the 7-position of compound (**3a**) followed by acylation at the 5-position and then deprotecting the 7-position were unsuccessful Preparing 5-acyl precursors via the diazonium salt of 5-aminotetralin (**7**) was successful but yields were very low. Finally, the 7-acyltetralin (**11**) was reduced to the 7-ethyltetralin (**25**), thus blocking the 7-position leaving only the 5-position available for substitution. The 7-

acyltetralin (**11**) was reduced using 10% Pd/C, and HCl (6 eq) in aqueous ethanol at 55 psi of hydrogen to afford the 7-ethyl derivative (**25**). If an insufficient amount of HCl (3.5 eq) was used, the ethyl ether (**26**) was isolated as an impurity in 30% yield. The 7-ethyl derivative (**25**) was acylated under Friedel-Craft conditions using various acid chlorides to afford 7-ethyl-5-ketotetralins (**27-30**). An attempt to oxidize 5-acyl-7-ethyltetralin (**27**) to the carboxylic acid via the haloform reaction initially gave (**31**) and upon heating afforded the 5-tribromomethyl ketone (**32**). As was observed previously, the carbonyl group of the 5-acyltetralin (**32**) was unreactive to nucleophilic attack probably due to the blocking affect of the two ortho substituents preventing attack of hydroxide ion. In fact, the steric crowding of the o-methyl and o-methylene groups of (**32**) completely restrict the rotation of the carbonyl group which is supported by the proton nmr showing the *gem*-dimethyl groups to be non-equivalent each exhibiting a different chemical shift. A second attempt to prepare the acid at the 5-position was tried using 7-ethyltetralin (**25**) and oxalyl chloride under Friedel-Craft conditions only to afford the 5-formyltetralin (**33**) with no desired product seen by GC/MS. Further attempts to prepare the 5-carboxylic acid of (**25**) were unsuccessful.

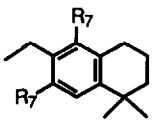


Scheme 5. a) 50 psi H_2, 10% Pd/C, HCl, H_2O, EtOH (86% yield); b) RCOCl, $AlCl_3$, $ClCH_2CH_2Cl$, 0 °C then r.t. 24 h (78-88%); c) NaOH, Br_2, H_2O, dioxane, 0 °C then r.t. 24 h (95% yield); d) NaOH, Br_2, H_2O, dioxane, reflux 24 h (83%); e) $(COCl)_2$, $AlCl_3$, CS_2, (27%).

6-Ethyl-1,1-dimethyltetrahydronaphthalene derivatives were prepared similarly to the 6-methyl derivatives. The cyclization of 1-methyl-ß-ionone (**2b**), heating neat with a catalytic amount of iodine at 140°C, afforded 6-ethyl-1,1-dimethyltetrahydronaphthalene (**3b**). Derivatives of (**3b**) were prepared by the

methodology previously described to yield the 5- and/or 7-substituted 6-ethyl-1,1-dimethyl-1,2,3,4-tetrahydronaphthalenes shown in Table 1. Compound (**3b**) exhibited the same regioselectivity and reactivity as compound (**3a**).

Table 1



cpd	R_5	R_7	method	yield
3b	H	H	a	83
34	NO_2	NO_2	b	32
35	NO_2	CN	c	90
36	NO_2	COMe	b	57
37	NO_2	CO_2H	d	77
38	NO_2	$CONH_2$	e	100
39	H	COMe	f	52
40	H	CO_2H	d	79
41	H	CO_2Me	g	70

Table 1. a) **2b**, I_2, 140 °C, 5 h; b) **3b**, **39**, 70% HNO_3, 96% H_2SO_4, 0 °C then r.t. 1 h; c) **38**, Cl_3COCl, TEA, CH_2Cl_2, 0 °C then r.t. 1 h; d) **36**, **39**, NaOH, Br_2, H_2O, dioxane, 0 °C then r.t. 24 h; e) **37**, $(COCl)_2$, CH_2Cl_2, RH, TEA; f) **3b**, MeCOCl, $AlCl_3$, $ClCH_2CH_2Cl$, 0 °C then r.t. 2 h; g) **40**, KOH, MeI, DMF, 45 °C, 4 h.

In summary, the synthesis of 5- and/or 7-(di)substituted-6-alkyl-1,1-dimethyltetrahydronaphthalene analogs has been described detailing the regioselectivity and reactivity of intermediates (**3a**) and (**3b**). The chemistry of intermediate (**3a**) has proven fruitful in providing an array of 5, 6, and 7-substituted tetrahydronaphthalene derivatives. More diverse substitution patterns of the aromatic ring and the 1-position of the non-aromatic ring are under investigation and will be described in future publications.

EXPERIMENTAL

Melting points were determined with a Mettler PF62 capillary melting point apparatus and are uncorrected. Refractive indices were determined with an Abbe refractometer apparatus at 25°C and are uncorrected. ^1H, ^{13}C, ^{19}F nuclear magnetic resonance spectra were recorded using a Bruker WM-360 and Varian XL-400 NMR spectrometers. Elemental analyses were performed by Atlantic Microlab Inc., Atlanta, GA. Sample purity was determined by GLC analysis on a Varian 3400 gas chromatograph utilizing a 1/8 inch diameter 6 foot length stainless steel column packed with 10% Supelco SP-2100 (methyl silicone) on 80/100 Supelcoport. Normally, a temperature program from 150°C to 300°C at 15°C/min was employed. Column chromatography was performed on a Waters preparative liquid chromatography Model 500 using silica gel columns and on a Rainin Gradient Autoprep HPLC system 3XP using a Dynamax-60A, 8um, C18 column (21.4mm ID x 25cm L). Most reported yields are unoptimized with emphasis on purity of products rather than quantity.

1,2,3,4-Tetrahydro-1,1,6-trimethylnaphthalene (3a). ß-ionone (**2a**) (18.9 g, 0.098 mol) and iodine (~1.0 g) were stirred neat and slowly heated to 110°C. When the temperature of the solution reached about 100°C, the evolution of steam began. At 110°C the reaction was vigorous at first, but gradually subsided and

G.C. showed the reaction to be complete after 30 minutes. The solution was diluted with hexane and the hexane was washed with water, and brine. The solution was dried over magnesium sulfate, filtered and the solvent was removed to afford the crude product. The product was purified by column chromatography (100% hexane) to afford 80-95% of a clear oil of **3a**, n_D^{25}= 1.6140; ^{1}H NMR ($CDCl_3$) ppm: 1.28(s,6H), 1.66(m,2H), 1.81(m,2H), 2.29(s,3H), 2.74(t,2H), 6.88(bs,1H), 6.98(d,1H,J = 6.6Hz), 7.24(d,1H,J = 6.6Hz). ^{13}C-NMR ($CDCl_3$) ppm: 19.93(s), 20.95(s), 30.84(s), 32.02(s), 33.62(s), 33.62(s), 39.57(s), 126.66(s), 126.83(s), 129.72(s), 134.71(s), 136.08(s), 142.93(s); Anal. Calcd for $C_{13}H_{18}$: C, 89.59; H, 10.41. Found: C, 89.56; H, 10.39.

6-Ethyl-1,2,3,4-tetrahydro-1,1,6-trimethylnaphthalene (3b). Following the procedure described for **3a**, 1-methyl-ß-ionone (**2b**) (7.68 g, 0.037 mol) and iodine (~0.1 g) were stirred neat at 140 °C to afford the crude product. The product was purified by column chromatography (100% hexane) to afford 5.7 g (83%) of a yellow oil of **3b**, n_D^{25}= 1.5299; ^{1}H NMR ($CDCl_3$) ppm: 1.23(t,3H), 1.28(s,6H), 1.66(m,2H), 1.79(m,2H), 2.58(q,2H), 2.76(t,2H), 6.89(bs,1H), 7.00(d,1H,J = 6.5Hz), 7.25(d,1H,J = 6.5Hz); Anal. Calcd for $C_{13}H_{18}$: C, 89.29; H, 10.71. Found: C, 89.34; H, 10.54.

1,2,3,4-Tetrahydro-1,1,6-trimethyl-5-nitronaphthalene (5).

Method A: At -5°C, compound **3a** (5.0 g, 0.029 mol) dissolved in glacial acetic acid (13.1 mL, 0.24 mol) and acetic anhydride (10.8 mL, 0.114 mol), was treated with 70% HNO_3 (6.5 g, 0.072 mol) as a solution in glacial acetic acid (13.1 mL, 0.24 mol) and acetic anhydride (10.8 mL, 0.114 mol). The addition was closely monitored to maintain 0°C and after complete addition, the solution was stirred for 15 minutes at room temperature. The solution was poured over ice/water (200 g) which was then extracted with methylene chloride. The methylene chloride layer was washed with water, sodium bicarbonate, and brine. The solution was dried over magnesium sulfate, filtered and the solvent was removed to afford a mixture of two products. Fraction two of column chromatography (100% hexane) afforded 1.6 g (25%) of a clear oil of **5**, n_D^{25}= 1.4479; ^{1}H NMR ($CDCl_3$) ppm: 1.19(s,6H), 1.63(m,2H), 1.78(m,2H), 2.22(s,3H), 2.63(t,2H), 7.05(d,1H,J = 6.7Hz), 7.33(d,1H,J = 6.7Hz); Anal. Calcd for $C_{13}H_{17}N_1O_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.40; H, 7.83; N, 6.45.

Method B: At 5°C, compound **9** (10.0 g, 0.043 mol) dissolved in 35% sulfuric acid (1000 mL) was treated dropwise with sodium nitrite (3.3 g, 0.047 mol) as a solution in water (25 mL). The addition was closely monitored to keep the temperature below 5°C. Upon complete addition, the solution stirred an addition 15 minutes at 5°C. This cold solution was then added dropwise to ethanol (150 mL) and Cu-bronze (1.0 g) at reflux. Upon complete addition, the solution stirred at reflux for one hour. The solution was cooled and extracted with dichloromethane. The dichloromethane layer was washed with water, and brine. The solution was dried over magnesium sulfate, filtered and the solvent was removed to afford the crude product. The product was purified by column chromatography (10% ethyl acetate-hexane) to afford 8.24 g (87%) of a clear oil of **5**.

1,2,3,4-Tetrahydro-1,1,6-trimethyl-7-nitronaphthalene (4). Following the same procedure described for **5** (method A), fraction one of column chromatography (100% hexane) afforded 3.8 g (60%) of a yellow oil of **4**, n_D^{25}= 1.4482; ^{1}H NMR ($CDCl_3$) ppm: 1.28(s,6H), 1.66(m,2H), 1.79(m,2H), 2.51(s,3H), 2.76(t,2H), 6.97(s,1H), 7.96(s,1H); Anal. Calcd for $C_{13}H_{17}N_1O_2$: C, 71.21; H, 7.81; N, 6.39 Found: C, 71.32; H, 7.80; N, 6.44.

5,6,7,8-Tetrahydro-3,8,8-trimethyl-2-naphthalenamine (6). Compound **4** (2.89 g, 0.013 mol) and 10% palladium on carbon were added to ethanol (100 mL) and the mixture was hydrogenated on a Parr Hydrogenator (~50 psi, room temperature) until hydrogen uptake stopped. The mixture was filtered through celite and the solvent was removed to afford the crude product. The product was purified by column chromatography (15% ethyl acetate-hexane) to afford 1.84 g (75%) of a clear oil of **6**, n_D^{25}= 1.4632; ^{1}H NMR ($CDCl_3$) ppm: 1.25(s,6H), 1.63(m,2H), 1.79(m,2H), 2.11(s,3H), 2.64(t,2H), 3.45(bs,2H), 6.65(s,1H), 7.24(s,1H); Anal. Calcd for $C_{13}H_{19}N_1$: C, 82.48; H, 10.12; N, 7.40. Found: C, 82.35; H, 10.09; N, 7.37.

5,6,7,8-Tetrahydro-2,5,5-trimethyl-1-naphthalenamine (7). Following the procedure described for **6**, compound **5** (14.0 g, 0.064 mol), 10% palladium on carbon and ethanol (350 mL) was hydrogenated on a Parr Hydrogenator (~50 psi, 40 °C) to afford the crude product. The product was purified by column chromatography (10% ethyl acetate-hexane) to afford 12.0 g (99%) of a light yellow oil of **7**, n_D^{25}= 1.4868; ^{1}H NMR ($CDCl_3$) ppm: 1.27(s,6H), 1.63(m,2H), 1.86(m,2H), 2.14(s,3H), 2.46(t,2H), 3.54(bs,2H), 6.77(d,1H,J = 6.6Hz), 6.91(d,1H,J = 6.6Hz); Anal. Calcd for $C_{13}H_{19}N_1$: C, 82.48; H, 10.12; N, 7.40. Found: C, 82.34; H, 10.12; N, 7.35.

5,6,7,8-Tetrahydro-2,5,5-trimethyl-1,3-naphthalenediamine (10). Compound **8** (2.0 g, 0.0076 mol) and Adam's Catalyst (PtO_2) (0.10 g) were added to ethanol (150 mL) and the mixture was hydrogenated on a Parr Hydrogenator (~50 psi, 40 °C) until hydrogen uptake stopped. The mixture was filtered through celite and the solvent was removed to afford the crude product. The product was purified by column chromatography (20% ethyl acetate-hexane) to afford 1.2 g (77%) of a brown oil of **10**, n_D^{25} could not be determined due to high viscosity; ^{1}H NMR ($CDCl_3$) ppm: 1.22(s,6H), 1.58(m,2H), 1.81(m,2H), 1.97(s,3H), 2.40(t,2H), 3.48(bs,4H), 6.27(s,1H); Anal. Calcd for $C_{13}H_{20}N_2$: C, 76.42; H, 9.87; N, 13.71. Found: C, 76.00; H, 9.81; N, 13.83.

5,6,7,8-Tetrahydro-3,8,8-trimethyl-4-nitro-2-naphthalenamine (9). Compound **8** (24.2 g, 0.092 mol) and Adam's Catalyst (PtO_2) (0.50 g) were added to ethanol (350 mL) and the mixture was hydrogenated on a Parr Hydrogenator at room temperature keeping the pressure below 40 psi until hydrogen uptake stopped. The mixture was filtered through celite and the solvent was removed to afford the crude product. The product was purified by recrystallization from hexane to afford 19.44 g (90%) of a yellow solid of **9**, mp 172-172.5°C; ^{1}H NMR ($CDCl_3$) ppm: 1.23(s,6H), 1.58(m,2H), 1.71(m,2H), 1.99(s,3H), 2.50(t,2H), 3.63(bs,2H), 6.73(s,1H); Anal. Calcd for $C_{13}H_{18}N_2$: C, 66.64; H, 7.74; N, 11.96. Found: C, 66.72; H, 7.78; N, 11.95.

5,6,7,8-Tetrahydro-alpha-3,8,8-trimethyl-2-naphthalenemethanol (13). At 0°C, compound **11** (5.19 g, 0.024 mol) dissolved in methanol (30 mL) was treated in small portions with sodium borohydride (1.8 g, 0.047 mol). Upon complete addition, the solution stirred at room temperature for three hours. The solution was cooled to 0°C and 3% HCl was added until solution became acidic. The solution was extracted with ether and the ether layer was washed with water, and brine. The solution was dried over magnesium sulfate, filtered and the solvent was removed to give a mixture of two products. Fraction one of column chromatography (20% ethyl acetate-hexane) gave 4.19 g (80%) of a white solid of **13**, mp 92.5-93.5°C; ^{1}H NMR ($CDCl_3$) ppm: 1.21(s,6H), 1.39(d,6H), 1.57(m,2H), 1.61(m,2H), 2.20(s,3H), 2.63(t,2H), 5.00(q,2H), 6.75(s,1H), 7.39(s,1H); Anal. Calcd for $C_{15}H_{22}O_1$: C, 82.52; H, 10.16. Found: C, 82.45; H, 10.18.

1,2,3,4-Tetrahydro-7-ethyl-1,1,6-trimethylnaphthalene (25). Compound **11** (7.3 g, 0.034 mol), 37% hydrogen chloride (20 mL), water (40 mL), and 10% palladium on carbon (1.0 g) were added to ethanol (120 mL) and the mixture was hydrogenated on a Parr Hydrogenator (~50 psi, r.t.) until hydrogen uptake stopped. The mixture was filtered through celite and the solvent was removed to afford the crude product. The product was purified by column chromatography (100% hexane) to afford 5.9 g (86%) of a clear oil of **25**, n_D^{25}= 1.4629; ^{1}H NMR ($CDCl_3$) ppm: 1.19(t,3H), 1.54(s,6H), 1.66(m,2H), 1.79(m,2H), 2.25(s,3H), 2.59(q,2H), 2.71(t,2H), 6.84(s,1H), 7.11(s,1H); Anal. Calcd for $C_{15}H_{22}$: C, 89.04; H, 10.96. Found: C, 89.17; H, 10.85.

5,6,7,8-Tetrahydro-7-ethyl-1,1,6-trimethyl-2-naphthaleneacetic acid (26). Compound **17** (2.11 g, 0.0097 mol), 37% hydrogen chloride (5 mL), water (10 mL), and 10% palladium on carbon (0.1 g) were added to ethanol (100 mL) and the mixture was hydrogenated on a Parr Hydrogenator (~50 psi, r.t.) until hydrogen uptake stopped. The mixture was filtered through celite and the solvent was removed to afford the mixture of two products. Fraction two of column chromatography (100% hexane) afford 0.73 g (30%) of a clear oil of **26**, n_D^{25}= 1.5069; ^{1}H NMR ($CDCl_3$) ppm: 1.11(t,3H), 1.19(s,3H), 1.21(s,3H), 1.31(d,3H), 1.56(m,2H), 1.71(m,2H), 2.63(t,2H), 3.26(q,2H), 4.51(q,2H), 6.73(s,1H), 7.30(s,1H); Anal. Calcd for $C_{17}H_{26}O_1$: C, 82.87; H, 10.64. Found: C, 82.49; H, 10.53.

General Procedure for the Dehydration of Primary Amides

At 0°C, the primary amide (0.0010 mol) and triethylamine (0.0022 mol) dissolved in dichloromethane (50 mL) was treated with trichloroacetyl chloride (0.0012 mol). After complete addition, the solution stirred at room temperature for 15 minutes-several hours. The dichloromethane layer was washed with water, and brine. The solution was dried over magnesium sulfate, filtered and the solvent was removed to afford the crude product. The product was purified by column chromatography (ethyl acetate-hexane) or crystallization.

5,6,7,8-Tetrahydro-3,8,8-trimethyl-4-nitro-2-naphthalenecarbonitrile (24). A white solid (88%), mp 131.2-132°C; ^{1}H NMR ($CDCl_3$) ppm: 1.28(s,6H), 1.67(m,2H), 1.74(m,2H), 2.39(s,3H), 2.65(t,2H), 7.67(s,1H); Anal. Calcd for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.99; H, 6.62; N, 11.44.

3-Ethyl-5,6,7,8-tetrahydro-8,8-dimethyl-4-nitro-2-naphthalenecarbonitrile (35). A white solid (90%), mp 133-134°C; ^{1}H NMR ($CDCl_3$) ppm: 1.18(t,3H), 1.23(s,2H), 1.70(m,6H), 1.60(m,2H), 1.74(m,2H), 2.58(t,2H), 2.66(q,2H), 7.63(s,1H); Anal. Calcd for $C_{15}H_{18}N_2O_2$: C, 69.74; H, 7.02. Found: C, 69.71; H, 7.03.

General Procedure for the Friedel-Craft Acylation

A solution of the tetrahydronaphthalene (0.0010 mol) dissolved in 1,2-dichloroethane (10mL) was added dropwise to a cold (0°C) solution of anhydrous aluminium chloride (0.0013 mol) and acid chloride (0.0011 mol) in 1,2-dichloroethane (50 mL). The addition was closely monitored to maintain 0°C and was stirred for 15 minutes-several hours after complete addition. The solution was poured over ice/water (500 g) which was extracted with ether. The ether layer was washed with water, and brine. The solution was dried over magnesium sulfate, filtered and the solvent was removed to afford the crude product. The product was purified by column chromatography (ethyl acetate-hexane) or crystallization.

1-(5,6,7,8-Tetrahydro-3,8,8-trimethyl-2-naphthalenyl)ethanone (11). A white solid (99%), mp 59.5-61°C; ^{1}H NMR ($CDCl_3$) ppm: 1.28(s,6H), 1.66(m,2H), 1.81(m,2H), 2.45(s,3H), 2.59(s,3H), 2.74(t,2H), 6.91(s,1H), 7.67(s,1H); Anal. Calcd for $C_{15}H_{20}O_1$: C, 83.29; H, 9.32. Found: C, 83.60; H, 9.51.

1-(5,6,7,8-Tetrahydro-2,5,5-trimethyl-1-naphthalenyl)ethanone (12). A clear oil (8%), n_D^{25} could not be determined due to insufficient amount of material; ^{1}H NMR ($CDCl_3$) ppm: 1.25(s,6H), 1.62(m,2H), 1.77(m,2H), 2.17(s,3H), 2.44(s,3H), 2.59(t,2H), 6.97(d,1H,J = 6.7Hz), 7.23(d,1H,J = 6.7Hz); Anal. Calcd for $C_{15}H_{20}O_1$: C, 83.29; H, 9.32. Found: C, 83.66; H, 9.39.

1-(3-Ethyl-5,6,7,8-tetrahydro-2,5,5-trimethyl-1-naphthalenyl)ethanone (27). A clear oil (79%), n_D^{25}= 1.4950; ^{1}H NMR ($CDCl_3$) ppm: 1.16(t,3H), 1.26(s,6H), 1.66(m,2H), 1.79(m,2H), 2.11(s,3H), 2.45(s,3H), 2.54(t,2H), 2.58(q,2H), 7.13(s,1H); Anal. Calcd for $C_{17}H_{24}O_1$: C, 83.55; H, 9.90. Found: C, 83.55; H, 9.91.

1-(3-Ethyl-5,6,7,8-tetrahydro-2,5,5-trimethyl-1-naphthalenyl)-1-propanone (28). A clear oil (88%), n_D^{25}= 1.3883; ^{1}H NMR ($CDCl_3$) ppm: 1.16(t,3H), 1.17(s,3H), 1.26(s,6H), 1.61(m,2H), 1.75(m,2H), 2.07(s,3H), 2.49(t,2H), 2.58(q,2H), 2.71(q,2H), 7.12(s,1H); Anal. Calcd for $C_{18}H_{26}O_1$: C, 83.67; H, 10.14. Found: C, 83.35; H, 10.10.

1-(3-Ethyl-5,6,7,8-tetrahydro-2,5,5-trimethyl-1-naphthalenyl)-1-butanone (29). A light yellow oil (88%), n_D^{25}= 1.4676; ^{1}H NMR ($CDCl_3$) ppm: 1.00(t,3H), 1.17(s,3H), 1.26(s,6H), 1.61(m,2H), 1.75(m,2H), 1.77(sextet,2H), 2.07(s,3H), 2.49(t,2H), 2.58(q,2H), 2.66(q,2H), 7.12(s,1H); Anal. Calcd for $C_{19}H_{28}O_1$: C, 83.77; H, 10.36. Found: C, 83.50; H, 10.40.

1-(3-Ethyl-5,6,7,8-tetrahydro-2,5,5-trimethyl-1-naphthalenyl)-1-pentanone (30). An orange oil (78%), n_D^{25}= 1.4452; ^{1}H NMR ($CDCl_3$) ppm: 1.00(t,3H), 1.26(s,3H), 1.37(s,6H), 1.41(m,2H),

1.61(m,2H), 1.70(m,4H), 2.07(s,3H), 2.49(t,2H), 2.58(q,2H), 2.66(q,2H), 7.12(s,1H); Anal. Calcd for $C_{20}H_{30}O_1$: C, 83.86; H, 10.56. Found: C, 83.85; H, 10.57.

3-Ethyl-5,6,7,8-tetrahydro-2,5,5-trimethyl-1-naphthalenecarboxaldehyde (33). An orange oil (27%), n_D^{25}= 1.6266; ^{1}H NMR ($CDCl_3$) ppm: 1.17(t,3H), 1.28(s,6H), 1.63(m,2H), 1.79(m,2H), 2.41(s,3H), 2.64(q,2H), 2.96(t,2H), 7.32(s,1H); Anal. Calcd for $C_{16}H_{22}O_1$: C, 83.43; H, 9.63. Found: C, 83.61; H, 9.89.

1-(3-Ethyl-5,6,7,8-tetrahydro-8,8-dimethyl-2-naphthalenyl)ethanone (39). An orange oil (52%), n_D^{25}= 1.5037; ^{1}H NMR ($CDCl_3$) ppm: 1.19(t,3H), 1.28(s,6H), 1.66(m,2H), 1.79(m,2H), 2.56(s,3H), 2.77(t,2H), 2.83(q,2H), 6.93(s,1H), 7.60(s,1H); Anal. Calcd for $C_{16}H_{22}O_1$: C, 83.43; H, 9.63. Found: C, 83.19; H, 9.78.

General Procedure for the Haloform Reaction

At 0°C, 2.5 N sodium hydroxide (52 mL, 0.13 mol) was treated dropwise with bromine (5.3 g, 0.033 mol). The addition was closely monitored to keep the temperature below 5°C. Upon complete addition, the solution was diluted with cold 1,4-dioxane (30 mL). This pre-made solution of sodium hypobromide was then added dropwise to a solution of the methyl ketone (0.010 mol) and water (30 mL) in 1,4-dioxane (100 mL) at 0°C. Upon complete addition, the solution stirred at room temperature for 1-24 hours. Anhydrous sodium sulfite (3.0 g) in water (15 mL) was added to destroy the remaining sodium hypobromide. The solution was poured over ice/HCl (200 g) which was extracted with ether. The ether layer was washed with water, and brine. The solution was dried over magnesium sulfate, filtered and the solvent was removed to afford the crude product. The product was purified by column chromatography (ethyl acetate-hexane) or crystallization.

5,6,7,8-Tetrahydro-3,8,8-trimethyl-2-naphthalenecarboxylic acid (14). A white solid (95%), mp 187.5-188.5°C; ^{1}H NMR ($CDCl_3$) ppm: 1.29(s,6H), 1.66(m,2H), 1.80(m,2H), 2.56(s,3H), 2.75(t,2H), 6.93(s,1H), 8.06(s,1H); Anal. Calcd for $C_{14}H_{18}O_2$: C,77.03; H, 8.31. Found: C, 76.56; H, 8.25.

5,6,7,8-Tetrahydro-3,8,8-trimethyl-4-nitro-2-naphthalenecarboxylic acid (17). A white solid (94%), mp 230-231°C; ^{1}H NMR ($CDCl_3$) ppm: 1.34(s,6H), 1.72(m,2H), 1.86(m,2H), 2.40(s,3H), 2.61(t,2H), 8.12(s,1H), 11.58(bs,1H); Anal. Calcd for $C_{14}H_{17}N_1O_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.80; H, 6.59; N, 5.20.

2-Bromo-1-(3-ethyl-5,6,7,8-tetrahydro-2,5,5-trimethyl-1-naphthalenyl)ethanone (31). A white solid (93%), mp 67.5-68.5°C; ^{1}H NMR ($CDCl_3$) ppm: 1.19(t,3H), 1.26(s,6H), 1.62(m,2H), 1.75(m,2H), 2.10(s,3H), 2.49(t,2H), 2.59(q,2H), 4.29(s,2H), 7.17(s,1H); Anal. Calcd for $C_{17}H_{23}O_1Br_1$: C, 63.16; H, 7.17. Found: C, 63.22; H, 7.14.

2,2,2-Tribromo-1-(3-ethyl-5,6,7,8-tetrahydro-2,5,5-trimethyl-1-naphthalenyl)ethanone (32). A clear oil (83%), n_D^{25}= 1.5131; ^{1}H NMR ($CDCl_3$) ppm: 1.19(t,3H), 1.25(s,3H), 1.29(s,3H), 1.62(m,2H), 1.80(m,2H), 2.62(m,4H), 7.19(s,1H); Anal. Calcd for $C_{17}H_{21}O_1Br_3$: C, 42.45; H, 4.40. Found: C, 42.59; H, 4.32.

3-Ethyl-5,6,7,8-tetrahydro-8,8-dimethyl-4-nitro-2-naphthalenecarboxylic acid (37). A white solid (77%), mp 234-235°C; ^{1}H NMR ($CDCl_3$) ppm: 1.12(t,3H), 1.24(s,6H), 1.61(m,2H), 1.73(m,2H), 2.53(t,2H), 2.79(q,2H), 7 98(s,1H); Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.21; H, 8.66.

3-Ethyl-5,6,7,8-tetrahydro-8,8-dimethyl-2-naphthalenecarboxylic acid (40). A white solid (95%), mp 159-160°C; ^{1}H NMR ($CDCl_3$) ppm: 1.23(t,3H), 1.28(s,6H), 1.66(m,2H), 1.79(m,2H), 2.77(t,2H), 2.96(q,2H), 6.95(s,1H), 8.02(s,1H); Anal. Calcd for $C_{15}H_{19}N_1O_4$: C, 64.97; H, 6.91. Found: C, 64.98; H, 6.88.

General Procedure for Nitration

At -5°C, the tetrahydronaphthalene (0.010 mol) dissolved in 96% H_2SO_4 (25 mL), was treated with 70% HNO_3 (0.011 mol) as a solution in 96% H_2SO_4 (20 mL). The addition was closely monitored to maintain 0°C and was stirred for 15 minutes-several hours after complete addition. The solution was poured over ice/water (500 g) which was extracted with methylene chloride. The methylene chloride layer was washed with water, sodium bicarbonate, and brine. The solution was dried over magnesium sulfate, filtered and the solvent was removed to afford the crude product. The product was purified by column chromatography (ethyl acetate-hexane) or crystallization.

1,2,3,4-Tetrahydro-1,1,6-trimethyl-5,7-dinitronaphthalene (8). A tan solid (80%), mp 101.5-102°C; ^{1}H NMR ($CDCl_3$) ppm: 1.32(s,6H), 1.68(m,2H), 1.82(m,2H), 2.38(s,3H), 2.67(t,2H), 8.01(s,1H); Anal. Calcd for $C_{13}H_{16}N_2O_4$: C, 59.08; H, 6.10. Found: C, 58.72; H, 5.98; N, 10.71.

1-(5,6,7,8-Tetrahydro-3,8,8-trimethyl-4-nitro-2-naphthalenyl)ethanone (16). A white solid (78%), mp 84.5-85.5°C; ^{1}H NMR ($CDCl_3$) ppm: 1.30(s,6H), 1.66(m,2H), 1.81(m,2H), 2.30(s,3H), 2.57(s,3H), 2.61(t,2H), 7.68(s,1H); Anal. Calcd for $C_{15}H_{19}N_1O_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 69.02; H, 7.37; N, 5.32.

6-Ethyl-1,2,3,4-tetrahydro-1,1-dimethyl-5,7-dinitronaphthalene (34). A white solid (32%), mp 89.5-90.5°C; ^{1}H NMR ($CDCl_3$) ppm: 1.24(t,3H), 1.32(s,6H), 1.66(m,2H), 1.79(m,2H), 2.64(t,2H), 2.74(q,2H), 7.97(s,1H); Anal. Calcd for $C_{14}H_{18}N_2O_4$: C, 60.42; H, 6.52; N, 10.07. Found: C, 60.51; H, 6.55; N, 10.06.

1-(3-Ethyl-5,6,7,8-tetrahydro-8,8-dimethyl-4-nitro-2-naphthalenyl)ethanone (36). A white solid (57%), mp 112.5-113.5°C; ^{1}H NMR ($CDCl_3$) ppm: 1.15(t,3H), 1.28(s,6H), 1.66(m,2H), 1.79(m,2H), 2.56(s,3H), 2.60(t,2H), 2.68(q,2H), 7.68(s,1H); Anal. Calcd for $C_{16}H_{21}N_1O_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 69.81; H, 7.71; N, 5.08.

General Procedure for the Preparation of Carboxylate Esters and Amides.

To the acid (0.010 mol) dissolved in dichloromethane (50 mL) was added oxalyl chloride (0.050 mol) followed by a drop of dimethyl formamide. After stirring at room temperature for 1-24 hours the solvent was removed to afford the acid chloride. The acid chloride (0.010 mol) dissolved in dichloromethane (20 mL) was added to a solution of the alcohol or amine (0.011 mol) and triethylamine (2 mL) in dichloromethane (20 mL). After stirring at room temperature 1-24 hours the solvent was removed and the residue was stirred with ether and water. The mixture was washed with water, 3% aqueous hydrochloric acid, water, saturated sodium bicarbonate, water and brine. The solution was dried over magnesium sulfate, filtered and the solvent was removed to afford the product. The product was purified by column chromatography (ethyl acetate-hexane) or crystallization.

Methyl 5,6,7,8-tetrahydro-3,8,8-trimethyl-2-naphthalenecarboxylate (15). A clear oil (100%), n_D^{25}= 1.6170; ^{1}H NMR ($CDCl_3$) ppm: 1.25(s,6H), 1.63(m,2H), 1.79(m,2H), 2.50(s,3H), 2.73(t,2H), 3.86(s,3H), 6.90(s,1H), 7.88(s,1H); Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.00; H, 8.60.

Methyl 5,6,7,8-tetrahydro-3,8,8-trimethyl-4-nitro-2-naphthalenecarboxylate (18). A white solid (82%), mp 69.5-71°C; ^{1}H NMR ($CDCl_3$) ppm: 1.28(s,6H), 1.67(m,2H), 1.74(m,2H), 2.34(s,3H), 2.56(t,2H), 3.84(s,3H), 7.85(s,1H); Anal. Calcd for $C_{15}H_{19}N_1O_4$: C, 64.97; H, 6.91; N, 5.05. Found: C, 64.97; H, 6.91; N, 4.99.

Ethyl 5,6,7,8-tetrahydro-3,8,8-trimethyl-4-nitro-2-naphthalenecarboxylate (19). A white solid (67%), mp 66.5-67°C; ^{1}H NMR ($CDCl_3$) ppm: 1.28(s,6H), 1.34(t,3H), 1.59(m,2H), 1.74(m,2H), 2.39(s,3H), 2.56(t,2H), 4.30(q,2H), 7.87(s,1H); Anal. Calcd for $C_{16}H_{21}N_1O_4$: C, 65.96; H, 7.27; N, 4.81. Found: C, 65.99; H, 7.27; N, 4.81.

Butyl 5,6,7,8-tetrahydro-3,8,8-trimethyl-4-nitro-2-naphthalenecarboxylate (20). A clear oil (66%), n_D^{25}= 1.4981; ^{1}H NMR ($CDCl_3$) ppm: 0.97(t,3H), 1.28(s,6H), 1.47(sextet,2H), 1.67(m,2H), 1.74(m,4H), 2.39(s,3H), 2.62(t,2H), 4.33(t,2H), 7.94(s,1H); Anal. Calcd for $C_{18}H_{25}N_1O_4$: C, 67.69; H, 7.89; N, 4.39. Found: C, 67.58; H, 7.88; N, 4.21.

5,6,7,8-Tetrahydro-3,8,8-trimethyl-4-nitro-2-naphthalenecarboxamide (21). A white solid (81%), mp 190-191°C; ^{1}H NMR ($CDCl_3$) ppm: 1.28(s,6H), 1.67(m,2H), 1.74(m,2H), 2.31(s,3H), 2.61(t,2H), 5.78(bs,1H), 6.18(bs,1H), 7.50(s,1H); Anal. Calcd for $C_{14}H_{18}N_2O_3$: C, 64.11; H, 6.92; N, 10.68. Found: C, 63.86; H, 6.87; N, 10.63.

5,6,7,8-Tetrahydro-N,3,8,8-tetramethyl-4-nitro-2-naphthalenecarboxamide (22). A white solid (79%), mp 118.5-119.5°C; ^{1}H NMR ($CDCl_3$) ppm: 1.28(s,6H), 1.67(m,2H), 1.74(m,2H), 2.25(s,3H), 2.56(t,2H), 2.98(d,3H), 5.78(bs,1H), 7.39(s,1H); Anal. Calcd for $C_{15}H_{20}N_2O_3$: C, 65.18; H, 7.30; N, 10.14. Found: C, 65.06; H, 7.35; N, 9.91.

5,6,7,8-Tetrahydro-N,N,3,8,8-pentamethyl-4-nitro-2-naphthalenecarboxamide (23). A white solid (66%), mp 109-110°C; ^{1}H NMR ($CDCl_3$) ppm: 1.20(s,6H), 1.58(m,2H), 1.74(m,2H), 2.07(s,3H), 2.56(t,2H), 2.78(s,3H), 3.06(s,3H), 7.19(s,1H); Anal. Calcd for $C_{16}H_{22}N_2O_3$: C, 66.19; H, 7.64; N, 9.65. Found: C, 66.14; H, 7.65; N, 9.80.

3-Ethyl-5,6,7,8-tetrahydro-8,8-dimethyl-4-nitro-2-naphthalenecarboxamide (38). A white solid (100%), mp 215.5-216.5°C; ^{1}H NMR ($CDCl_3$) ppm: 1.20(t,3H), 1.24(s,6H), 1.65(m,2H), 1.80(m,2H), 2.60(t,2H), 2.70(q,4H), 5.81(bd,2H), 7.48(s,1H); Anal. Calcd for $C_{15}H_{20}N_2O_3$: C, 65.20; H, 7.30. Found: C, 65.22; H, 7.31.

Methyl 3-ethyl-5,6,7,8-tetrahydro-8,8-dimethyl-2-naphthalenecarboxylate (41). To a solution of compound **40** (0.90 g, 0.0039 mol) in dimethylformamide (20 mL) was added potassium hydroxide (0.25 g, 0.0045 mol). After stirring for 1 hour at 45° C, methyl iodide (0.3 mL, 0.0048 mol) was added and the solution stirred at 45° C for 2 hours. The solution was poured into water (200 ml) and extracted with ether. The ether layer was washed with water, sodium bicarbonate, and brine. The solution was dried over magnesium sulfate, filtered and the solvent was removed to afford the crude product. The product was purified by column chromatography (5% ethyl acetate-hexane) to afford 0.67 g (70%) of a clear oil of **41**, n_D^{25}= 1.4837; ^{1}H NMR ($CDCl_3$) ppm: 1.19(t,3H), 1.28(s,6H), 1.66(m,2H), 1.79(m,2H), 2.74(t,2H), 2.90(q,2H), 3.86(s,3H), 6.93(s,1H), 7.83(s,1H); Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.73; H, 8.94.

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