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Syntheses of Tetrahydronaphthalenes. Part II

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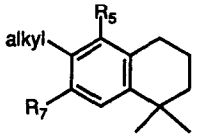
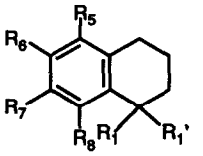
Abstract: *Syntheses utilizing the cyclodehydration method to prepare novel tetrahydronaphthalenes substituted with functional groups at each position of the aromatic ring and various alkyl groups at the 1-position of the non-aromatic ring are described.*

Reported earlier[1] were the preparation of substituted 6-alkyl-1,1-dimethyl-1,2,3,4-tetrahydronaphthalene's or 6-alkyl-1,1-dimethyltetralin's (tetralin is preferred over "1,2,3,4-tetrahydronaphthalene" according to the Ring Index) which demonstrated modest activity against important narrowleaf weeds in preemergent herbicidal assays. As part of a continued search for herbicidally active compounds of this type, a series of substituted tetralins were prepared. Several methods of synthesizing tetralins have been demonstrated in the literature: cyclization of ß-ionone by Bogert[2]: the cyclialkylation technique, discovered by Bruson and Kroeger[3]: the reaction of *p*-cymylcarbonium ion with 2,3-dimethyl-1-butene[4]: and finally the cyclodehydration method[5,6,7] of Bogert and co-workers. This report describes the expansion of the cyclodehydration method to prepare novel tetralins with substitution of functional groups at each position of the aromatic ring and substitution of various alkyl groups at the 1-position of the non-aromatic ring.

In our previous report[1], a variety of 6-alkyl-1,1-dimethyltetralin derivatives were prepared varying substituents at the 5- and 7-position (**I**). The first section of this report describes follow-up synthesis directed at substitution of functional groups at the various positions (R_5, R_6, R_7, R_8) of the aromatic ring and the second section describes variations at the 1-position (R_1, $R_{1'}$) of the non-aromatic ring.

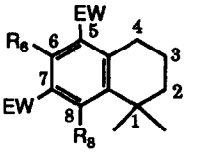


I



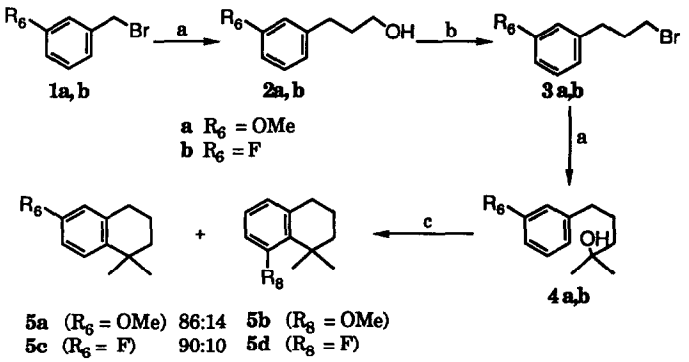
II

The first goal of the project was to diversify the substituents at the 6- and 8-position while electron withdrawing groups occupy the 5- and 7-position maintaining the 1,1-dimethyl substitution on the non-aromatic ring. Several targets were selected in which the 6- or (8)-position would be substituted with an alkoxy, amino, or thioalkyl.



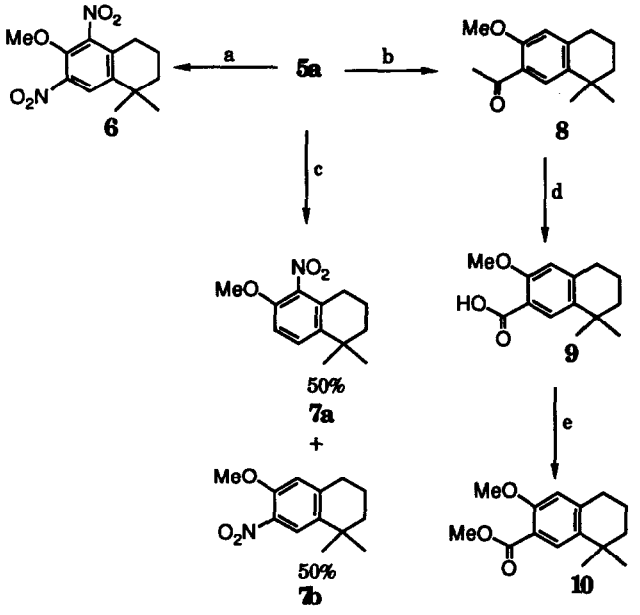
R_6 or R_8 = OR, NRR', SR

A synthesis utilizing the cylodehydration method was used to prepare the tetralin intermediates shown in Scheme 1. *m*-Substituted benzylbromides **1** were used as starting material in a Grignard condensation with ethylene oxide to yield the alcohols **2**. The alcohols **2** were reacted with PBr_3 to yield the bromo compounds **3**, followed by another Grignard condensation with acetone to afford the tertiary alcohols **4**. The tertiary alcohols **4** were cyclodehydrated using polyphosphoric acid (PPA) to afford the tetralin intermediates **5a-d**. The cyclodehydration of the tertiary alcohol **4a** using sulfuric acid led to ring sulphonation and as a result only PPA was used thereafter. Cyclodehydration of the alcohols led to ring closure both ortho and para to the R_6 substituent affording an 86:14 mixture of 6-methoxy (**5a**) and 8-methoxytetralin (**5b**) and a 90:10 mixture of 6-fluoro (**5c**) and 8-fluorotetralin (**5d**) respectively.



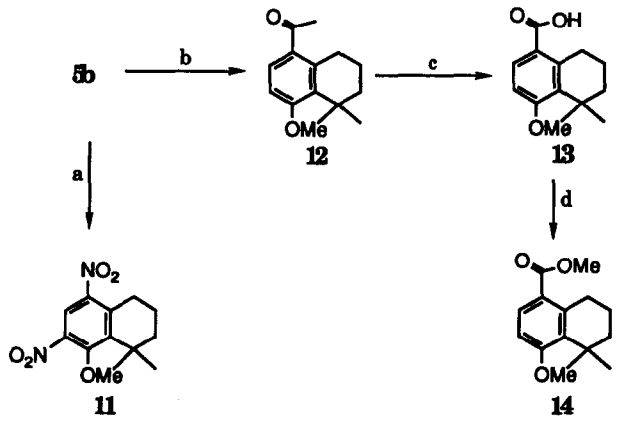
Scheme 1. a) Mg, ether, reflux 1 h then add epoxide or acetone at 0°C then r.t. 24 h (52-91% yield); b) PBr_3, pyridine, benzene, 0°C then r.t. 24 h (55-59%); c) PPA, r.t. 4 h (89-100%).

The 6-methoxytetralin (**5a**) was derivatized (Scheme 2) to incorporate electron withdrawing groups at the 5- and/or 7-position. Thus, 6-methoxytetralin (**5a**) can be nitrated using fuming nitric acid to afford the 6-methoxy-5,7-dinitrotetralin (**6**). Mono-nitration was achieved by using 70% nitric acid in a mixture of acetic acid/acetic anhydride (8:4) to yield a 50:50 mixture of the 6-methoxy-5-nitrotetralin (**7a**) and the 6-methoxy-7-nitrotetralin (**7b**). Friedel-Crafts acylation of the 6-methoxytetralin (**5a**) with acetyl chloride selectively afforded the 7-acyltetralin (**8**) which was oxidized using the haloform reaction to afford the carboxylic acid (**9**). The free acid, **9**, was converted to the acid chloride and from the latter, via reaction with methanol, the methyl ester (**10**) was prepared.



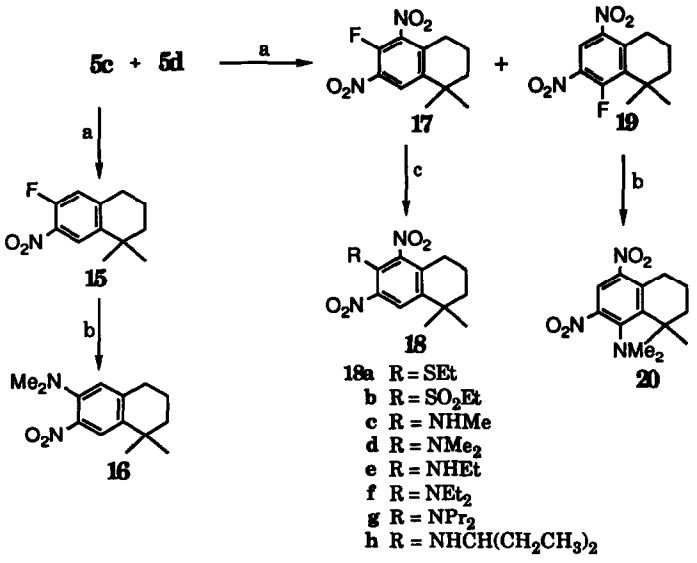
Scheme 2. a) fuming HNO_3, -5 °C then r.t. 7 h (64% yield); b) MeCOCl, $AlCl_3$, $ClCH_2CH_2Cl$, 0 °C then r.t. 24 h (89%); c) 70% HNO_3, acetic acid, 0 °C then r.t. 2 h (100%); d) NaOH, Br_2, H_2O, dioxane, 0 °C then r.t. 24 h (100%); e) $(COCl)_2$, CH_2Cl_2, MeOH, TEA (90%).

The 8-methoxytetralin (**5b**) was nitrated using fuming nitric acid to afford the 8-methoxy-5,7-dinitrotetralin (**11**). Friedel-Crafts acylation of **5b** with acetyl chloride afforded exclusively the 5-acyltetralin (**12**) which was oxidized using the haloform reaction to afford the free acid (**13**), and from the latter the methyl ester (**14**) was prepared. It is interesting to note that acylation occurred only at the 5-position and none of the 7-acyl regioisomer was detected. The structural assignment of the 5-methyl ester tetralin (**14**) was confirmed by a long range hetcor NMR experiment in which the carbon at the 5-position, identified through carbon hydrogen correlation, did not possess a proton.



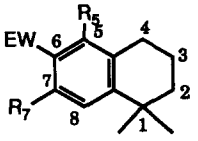
Scheme 3. a) fuming HNO_3, -5 °C then r.t. 7 h (66% yield); b) MeCOCl, $AlCl_3$, $ClCH_2CH_2Cl$, 0 °C then r.t. 24 h (82%); c) NaOH, Br_2, H_2O, dioxane, 0 °C then r.t. 24 h (99%); d) $(COCl)_2$, CH_2Cl_2, MeOH, TEA (72%).

It was feasible to consider the 6-fluorotetralin (**5c**) and the 8-fluorotetralin (**5d**) as potential intermediates for the synthesis of the targeted tetralins where R_6 or R_8 = NRR', SR. The planned course of action was to place the electron withdrawing groups at the 5- and/or 7-position thus activating the fluorine for displacement by a nucleophile. Small compact electron withdrawing groups (CN, NO_2, CO_2Me) at the 5- and 7-position tended to promote the most favorable herbicidal activity and so the substitution pattern of 5,7-dinitro was selected due to the related herbicidal activity and relative ease of preparation. The nitration of the mixture, 6-fluoro and 8-fluorotetralins (**5c,d**), using fuming nitric acid afforded the more easily separable dinitro derivatives (**17**) and (**19**) respectively. The 8-fluoro-5,7-dinitrotetralin (**19**) was reacted with dimethylamine to afford the 8-amino-5,7-dinitrotetralin (**20**). The 6-fluoro-5,7-dinitrotetralin (**17**) was subjected to nucleophilic attack by the sodium salt of ethanethiol to afford 6-ethylthio-5,7-dinitrotetralin (**18a**) followed by oxidation using MCPBA to the 6-ethanesulfone-5,7-dinitrotetralin (**18b**). Due to the relatively high herbicidal activity of the 6-amino-5,7-dinitrotetralins, several homologs were prepared by reacting various amines with the 6-fluoro-5,7-dinitrotetralin (**17**) to yield the 6-amino-5,7-dinitrotetralins (**18c-h**) as shown in Scheme 4. Also isolated was the 6-fluoro-7-nitrotetralin (**15**) from an incomplete nitration of the 6-fluorotetralin (**5c**) which was treated with dimethylamine to afford 6-amino-7-nitrotetralin (**16**).



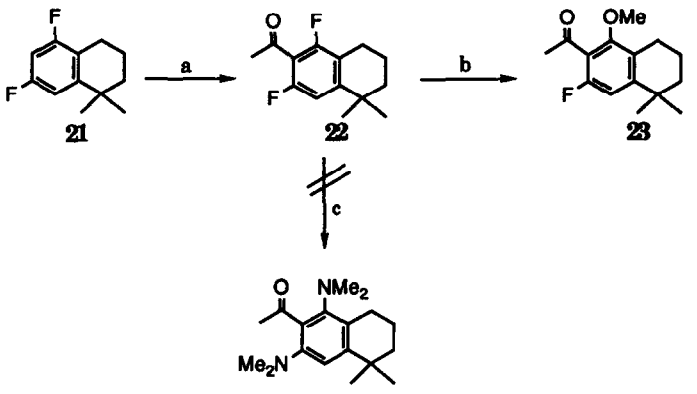
Scheme 4. a) fuming HNO_3, -5 °C then r.t. 7 h (5-37% yield); b) $HNMe_2$, CH_2Cl_2, reflux, 24 h (75-83%); c) thiolate or amine, CH_2Cl_2, reflux, 24 h (61-91%).

The next step of the project was to alter the substitution pattern of the aromatic ring in which R_6 = (an electron withdrawing group) and $R_5 = R_8$ = alkyl, OR, and NRR'.



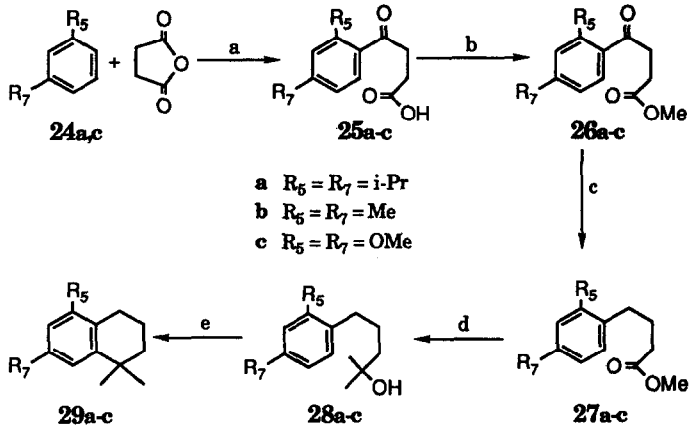
R_5 and/or R_7 = OR, NRR', alkyl

The synthetic sequence in Scheme 1 was repeated using 2,4-difluorobenzyl bromide as the starting material to afford the 5,7-difluorotetralin (**21**), a potential precursor to 5,7-disubstituted tetralin derivatives employing the same process of placing an electron withdrawing group at the 6-position to activate the fluorines for nucleophilic substitution. Friedel-Crafts acylation of the 5,7-difluorotetralin (**21**) using acetyl chloride afforded the 6-acyl tetralin (**22**) (Scheme 5). Initially, **22** was treated with dimethylamine resulting in no reaction. The second attempt involved the reaction of **22** and sodium methoxide in methanol at reflux with no evidence of product detected. Upon refluxing overnight, the methanol had evaporated and the slurry was heated neat to afford a mixture of products from which **23** was isolated in 46% yield. At this point it appeared that the electron withdrawing ability of the ketone was not sufficient to activate the fluorines toward displacement.



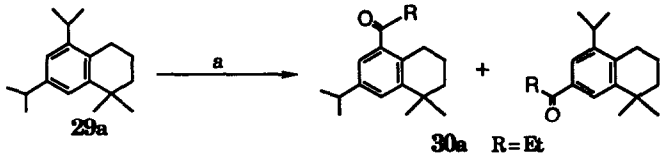
Scheme 5. a) MeCOCl, $AlCl_3$, $ClCH_2CH_2Cl$, 0 °C then r.t. 24 h (58% yield); b) NaOMe, MeOH, reflux 24 h (46%); c) $HNMe_2$, CH_2Cl_2, reflux, 24 h.

Based on the limited success in displacing the fluorines of **22** with methoxide, it was decided to synthesize the tetralin nucleus with the 5,7-substituents already intact. Another synthesis utilizing the cyclodehydration method is depicted in Scheme 6 to yield tetralins which possess the 5,7-disubstitution on the aromatic ring. The synthesis starts with a Friedel-Crafts reaction using a 1,3-disubstituted benzene (**24**) and succinic anhydride to afford the γ-keto-acid (**25**). The γ-keto-acid (**25**) was converted to the γ-keto-methyl ester (**26**) via the reaction of the acid chloride and methanol. The γ-keto-ester (**26**) was reduced using 10% Pd/C and HCl (6 eq) in aqueous ethanol at 55 psi of hydrogen to afford the methyl ester (**27**). The methyl ester (**27**) was reacted with 2 equivalents of methyl magnesium bromide to yield the tertiary alcohol (**28**). Cyclodehydration of the tertiary alcohol (**28**) afforded the tetralins **29a-c**.



Scheme 6. a) $AlCl_3$, $ClCH_2CH_2Cl$, 0 °C then r.t. 24 h (63-68% yield); b) $(COCl)_2$, CH_2Cl_2, MeOH, TEA (43-45%); c) 50 psi H_2, 10% Pd/C, HCl, H_2O, EtOH (24-71%); d) MeMgBr, ether, 0°C then r.t. 24 h (91-93%); e) PPA, r.t. 4 h (80-95%).

The first tetralin intermediate to be derivatized from Scheme 6 was 5,7-diisopropyltetralin (**29a**) as shown in Scheme 7. In an effort to prepare a 6-keto-5,7-diisopropyltetralin, two Friedel-Crafts reactions were tried with **29a** using acid chlorides resulting only in displacement of an alkyl group at either the 5- or 7-position. The first reaction using propionyl chloride afforded a mixture of 7-diisopropyl-5-propanonetetralin and 5-diisopropyl-7-propanonetetralin (**30a**) with none of the desired product seen by GC/MS. The reaction of **29a** and acetyl chloride gave the same results to afford a mixture of 5-acetyl-7-diisopropyltetralin and 7-acetyl-5-diisopropyltetralin (**30b**). It appears that the 5,7-diisopropyl groups are too bulky for acylation to occur at the 6-position which results in net displacement of propene for the ketone at either the 5- or 7-position. A similar example of this was observed by Wood *et al.*[4] in which acetylation of 6-*t*-butyl-1,1,4,4-tetramethyltetralin produces 6-acetyl-1,1,4,4-tetramethyltetralin.

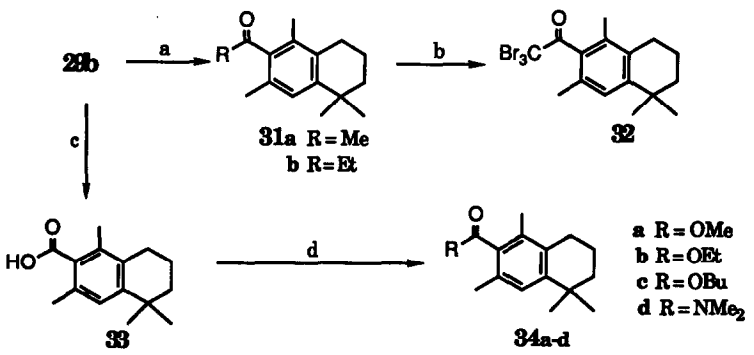


29a

30a R=Et
b R=Me

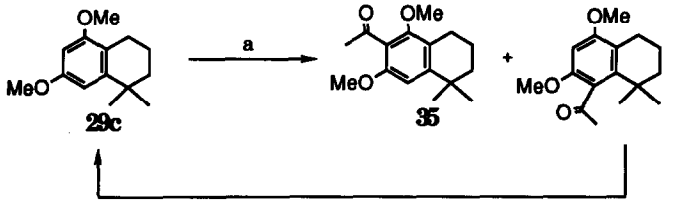
Scheme 7. a) RCOCl, $AlCl_3$, $ClCH_2CH_2Cl$, 0 °C then r.t. 24 h (23-43% yield).

A second effort at preparing a 6-keto-5,7-dialkyltetralin led to the synthesis of 5,7-dimethyltetralin (**29b**) (Scheme 6). Friedel-Crafts acylation with 5,7-dimethyltetralin (**29b**) using acetyl chloride and propionyl chloride afforded the 6-ketotetralins (**31a,b**) respectively as shown in Scheme 8. An attempt to oxidize the 6-acyltetralin (**31a**) via the haloform reaction to the carboxylic acid only afforded **32**. It seems reasonable that the acyl group at the 6-position failed to react due to steric hindrance as was seen in similar systems[1,8,9,10]. The carbonyl group is forced out of the plane of the benzene ring due to steric crowding preventing the hydroxide anion from attacking the keto-carbon. In fact the steric crowding of the *o*-methyl groups of **32** completely restrict the rotation of the carbonyl group. This is supported by the proton NMR showing the *gem*-dimethyl groups to be non-equivalent each exhibiting a different chemical shift. The failure to oxidize the 6-acyltetralin (**31a**) led to a Friedel-Crafts reaction with the 5,6-dimethyltetralin (**29b**) using oxalyl chloride to afford the carboxylic acid (**33**) in 56% yield. From the carboxylic acid (**33**), several esters and an amide (**34a-d**) were prepared.



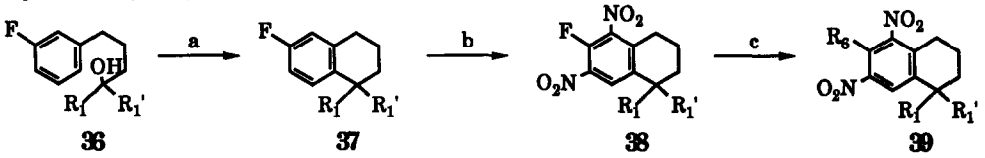
Scheme 8. a) RCOCl, $AlCl_3$, $ClCH_2CH_2Cl$, 0 °C then r.t. 24 h (79-87% yield); b) NaOH, Br_2, H_2O, dioxane, 0 °C then r.t. 24 h (89%); c) $(COCl)_2$, $AlCl_3$, $ClCH_2CH_2Cl$, 0 °C then r.t. 24 h (56%); e) $(COCl)_2$, CH_2Cl_2, RH, TEA (71-93%).

The 5,7-dimethoxytetralin (**29c**) was also prepared (Scheme 6) and used in a Friedel-Crafts reaction with acetyl chloride to afford **35** as shown in Scheme 9. The Friedel-Crafts acylation with **29c** proceeded in an unusual manner to form what was believed to be a mixture of the 6- and 8-acetyl-5,7-dimethoxytetralins, but only the 6-acetyl-5,7-dimethoxytetralin (**35**) was isolated following work-up. Based on GC and GC/MS data it appeared that the 8-acetyl-5,7-dimethoxytetralin isomer formed extremely rapid (52% immediately after complete addition of **29c**), but then reversed back to **29c** over the course of the next 15 minutes. Several different conditions were examined for this reaction, but each resulted in only a 5% isolated yield of the 6-acetyl-5,7-dimethoxytetralin (**35**). The position of attachment of the acyl group in (**35**) was confirmed by a NOSEY experiment in which the hydrogen at the 8-position showed a NOE with the 1,1-dimethyl groups. The only evidence that could be obtained supporting the structure of the 8-acetyl-5,7-dimethoxytetralin was that its MS fragmentation was identical to **35**.



Scheme 9. a) $AlCl_3$, $ClCH_2CH_2Cl$, 0 °C then r.t. 24 h (5% yield).

Thus far the emphasis has been placed on variations of the aromatic ring substituents, this section describes variations at the 1-position of the non-aromatic ring. In an effort to increase the herbicidal activity of these tetralins, substitution of various alkyl groups at the 1-position was performed. The 6-amino-5,7-dinitro substitution pattern on the aromatic ring was selected based on the fact that the analogs with this substitution pattern demonstrated the more favorable herbicidal activity. The synthesis was carried out as shown in Scheme 10. The Grignard of *m*-fluorophenylpropyl bromide was prepared and reacted with several ketones and aldehydes to afford the alcohols (**36a-e**) as shown in Scheme 10. The alcohols (**36a-e**) were cyclodehydrated using PPA to yield the corresponding fluorotetralins (**37a-d**). Most of the cyclodehydration reactions afforded the desired products except in a few cases. A methyl migration occurred during the cylodehydration of **36c** to afford the 1-methyl-1-isopropyltetralin (**37b**). The cyclodehydration of **36b** afforded a mixture of products with none of the desired product seen by GC/MS. It is interesting to note that only alcohol **36a** gave both the 6-fluoro and 8-fluoro tetralin regioisomers (**37a**) as was seen with the alcohols in Scheme 1 with a dimethyl substitution at the carbon bearing the alcohol. It is believed that the steric bulk at the carbon bearing the alcohol inhibits ring closure ortho to the fluorine as was seen with alcohols **36c-e** to afford exclusively the 6-fluorotetralin regioisomers (**37b-d**). Nitration of the fluorotetralins (**37a-d**) afforded the 5,7-dinitrotetralins (**38a-d**) which were treated with amines resulting in fluorine displacement to afford the 6-amino-1,1-dialkyltetralins (**39a-i**) as shown in Scheme 10.



36

	R_1	R_1'
36a	Me	H
b	Me	CH_2OMe
c	t-Bu	H
d	Pr	Pr
e	Cyclohex	

37

	R_1	R_1'
37, 38a	Me	H
	--	--
b	i-Pr	Me
c	Pr	Pr
d	Cyclohex	

38

39

	R_1	R_1'	R_6
39a	Pr	Pr	$NCH(Et)_2$
b	Pr	Pr	NMe_2
c	Pr	Pr	NMe_2
d	i-Pr	Me	$NCH(Et)_2$
e	i-Pr	Me	NMe_2
f	i-Pr	Me	OMe
g	H	Me	$NCH(Et)_2$
h	Cyclohex		$NCH(Et)_2$
i	Cyclohex		NMe_2

Scheme 10. a) PPA, r.t. 4 h (82-100% yield); b) fuming HNO_3, -5 °C then r.t. 7 h (20-67%); c) $HNMe_2$, CH_2Cl_2, reflux, 24 h (61-100%). **37a*** 88:12 mixture of 6- and 8-fluorotetralins.

In summary, the synthesis of substituted tetrahydronaphthalene analogs utilizing the cyclodehydration method were described detailing their regiochemistry and reactivity. It has been demonstrated that an array of substituents and substitution patterns on the aromatic ring can be achieved. Of the tetrahydronaphthalenes

prepared, compounds **18h** and **34a** were the most active, exhibiting activity in the 0.5 lb/acre region on preemergent narrowleaf weeds. However, none of the analogs had commercial levels of activity.

EXPERIMENTAL

Melting points were determined with a Mettler PF62 capillary melting point apparatus and are uncorrected. ^{1}H, ^{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. Compounds **1b, 3a, 24a,c, 25b** were obtained from commercial sources.

General Procedure for Reacting a Grignard with Aldehydes, Epoxides and Ketones (2, 4, 28, 36)

To magnesium turnings (0.011 mol) stirring in anhydrous ether (50 mL) was added a couple of drops of 1,2-dibromoethane. The solution was brought to reflux (with heat gun), followed by the dropwise addition of the bromo compound (0.010 mol) in anhydrous ether (10 mL). The addition was at a rate so the solution would self reflux. Upon complete addition, the solution stirred an additional 15 minutes at room temperature. The solution was then cooled to 0°C and the aldehyde, epoxide or ketone (excess) was added dropwise. The addition was monitored keeping the temperature below 10°C and after complete addition the solution was stirred for one hour at room temperature. The solution was cooled to 0°C and 2N hydrochloric acid 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 the product. The product was purified by column chromatography (ethyl acetate-hexane).

3-Fluorobenzenepropanol (2b). A yellow oil (91%); ^{1}H NMR ($CDCl_3$) ppm: 1.87(m,2H), 2.70(t,2H), 3.66(t,2H), 6.90(m,3H), 7.23(m,1H); Anal. Calcd for $C_9H_{11}FO$: C, 70.11; H, 7.19. Found: C, 69.47; H, 7.12.

3-Methoxy-α,α-dimethylbenzenebutanol (4a). A clear oil (69%); ^{1}H NMR ($CDCl_3$) ppm: 1.16(s,6H), 1.46(m,2H), 1.57(m,2H), 1.61(s,3H), 2.52(t,2H), 3.74(s,3H), 6.67(m,3H), 7.12(m,1H); Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.19; H, 9.57.

3-Fluoro-α,α-dimethylbenzenebutanol (4b). A clear oil (77%); ^{1}H NMR ($CDCl_3$) ppm: 1.22(s,6H), 1.48(m,2H), 1.68(m,2H), 2.60(t,2H), 6.90(m,3H), 7.23(m,1H); Anal. Calcd for $C_{12}H_{17}FO$: C, 73.44; H, 8.73. Found: C, 73.52; H, 8.84.

α,α-Dimethyl-2,4-bis(1-methylethyl)benzenebutanol (28a). A clear oil (93%); ^{1}H NMR ($CDCl_3$) ppm: 1.14(s,6H), 1.23(d,6H), 1.25(d,6H), 1.61(m,4H), 2.61(t,2H), 2.86(septet,1H), 3.15(septet,1H), 3.67(s,3H), 6.98(dd,1H, J = 1.8,7.8Hz), 7.05(d,1H, J = 1.8Hz), 7.11(d,1H, J = 7.8Hz); Anal. Calcd for $C_{18}H_{30}O$: C, 82.38; H, 11.55. Found: C, 82.41; H, 11.48.

α,α,2,4-Tetramethylbenzenebutanol (28b). A clear oil (91%); ^{1}H NMR ($CDCl_3$) ppm: 1.21(s,6H), 1.58(m,4H), 2.28(s,3H), 2.29(s,3H), 2.57(t,2H), 6.96(m,3H); Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.58; H, 10.77.

2,4-Dimethoxy-α,α-dimethylbenzenebutanol (28c). A clear oil (91%); ^{1}H NMR ($CDCl_3$) ppm: 0.18(s,6H), 1.52(m,2H), 1.60(m,2H), 2.53(t,2H), 3.78(s,6H), 6.38(d,1H,J = 2.4Hz), 6.42(dd,1H,J = 2.4,8.0Hz), 7.01(d,1H,J = 8.0Hz); Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.33; H, 9.12.

3-Fluoro-α-methylbenzenebutanol (36a). A clear oil (71%); ^{1}H NMR ($CDCl_3$) ppm: 1.18(d,3H), 1.47(m,2H), 1.65(m,2H), 2.61(t,2H), 3.79(sextet,2H), 6.88(m,3H), 7.22(m,1H); Anal. Calcd for $C_{11}H_{15}FO$: C, 72.50; H, 8.30. Found: C, 72.05; H, 8.41.

3-Fluoro-α-(methoxymethyl)-α-methylbenzenebutanol (36b). A clear oil (50%); ^{1}H NMR ($CDCl_3$) ppm: 1.13(d,3H), 1.51(m,2H), 1.65(m,2H), 2.08(bs,1H), 2.60(t,2H), 3.21(q,2H), 3.36(s,2H), 6.88(m,3H), 7.22(m,1H); Anal. Calcd for $C_{13}H_{19}FO_2$: C, 69.00; H, 8.46. Found: C, 68.60; H, 8.41.

α-(1,1-Dimethylethyl)-3-fluorobenzenebutanol (36c). A yellow oil (57%); ^{1}H NMR ($CDCl_3$) ppm: 0.88(s,9H), 1.30(m,1H), 1.54(m,2H), 1.65(m,1H), 2.63(m,2H), 3.21(m,1H), 6.88(m,3H), 7.22(m,1H); Anal. Calcd for $C_{14}H_{21}FO$: C, 74.96; H, 9.44. Found: C, 74.67; H, 9.47.

3-Fluoro-α,α-dipropylbenzenebutanol (36d). A clear oil (60%); ^{1}H NMR ($CDCl_3$) ppm: 0.89(t,6H), 1.22-1.46(m,10H), 1.58(m,2H), 2.58(t,2H), 6.89(m,3H), 7.20(m,1H); Anal. Calcd for $C_{16}H_{25}FO$: C, 76.15; H, 9.99. Found: C, 76.11; H, 10.13.

1-[3-(3-Fluorophenyl)-propyl]-cyclohexanol (36e). A clear oil (69%); ^{1}H NMR ($CDCl_3$) ppm: 1.27-1.74(m,10H), 2.30(t,2H), 2.58(t,2H), 6.89(m,3H), 7.22(m,1H); Anal. Calcd for $C_{15}H_{21}FO$: C, 76.23; H, 8.96. Found: C, 76.59; H, 8.96.

1-(3-Bromopropyl)-3-fluorobenzene (3b). Pyridine (0.71 mL, 0.0087 mol) was added dropwise to a solution of phosphorous tribromide (1.6 mL, 0.016 mol) in benzene (30 mL). After stirring at room temperature for 15 minutes the solution was cooled to 0°C and a solution of 3-fluorobenzenepropanol (7.3 g, 0.047 mol) and pyridine (0.24 mL, 0.0030 mol) in benzene (15 mL) was added dropwise. The addition was monitored keeping the temperature below 5°C and after complete addition the solution stirred at room temperature overnight. The solution was poured over ice/water and 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 give the product. The product was purified by column chromatography (30% ethyl acetate-hexane) to give 18.4 g (55%) of a yellow oil of **3b**; ^{1}H NMR ($CDCl_3$) ppm: 2.16(m,2H), 2.77(t,2H), 3.38(t,2H), 6.90(m,3H), 7.25(m,1H). ^{19}F NMR ($CDCl_3$) ppm: -115.19(s). Anal. Calcd for $C_9H_{10}BrF$: C, 49.80; H, 4.64. Found: C, 49.67; H, 4.36.

General Procedure for Cyclodehydration of Benzenebutanols to Prepare Tetrahydronaphthalenes (5, 21, 29, 37)

The alcohol (0.010 mol) was added dropwise to a slightly cooled solution of polyphosphoric acid (PPA) (10.0 g) using a mechanical stirrer. The addition was monitored to maintain a temperature between 15-25°C. Upon complete addition, the solution was allowed to stir at room temperature for four hours. The solution was poured over ice/water (200 g) which was then 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 give the product. The product was purified by column chromatography (ethyl acetate-hexane).

1,2,3,4-Tetrahydro-6-methoxy-1,1-dimethylnaphthalene (5a). A clear oil (86%); ^{1}H NMR ($CDCl_3$) ppm: 1.18(s,6H), 1.56(m,2H), 1.70(m,2H), 2.66(t,2H), 3.69(s,3H), 6.49(d,1H,J = 2.3Hz), 6.64(dd,1H,J = 2.3Hz, 7.2Hz), 7.16(d,1H,J = 7.2Hz); Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 81.99; H, 9.52.

1,2,3,4-Tetrahydro-8-methoxy-1,1-dimethylnaphthalene (5b). A clear oil (14%); ^{1}H NMR ($CDCl_3$) ppm: 1.29(s,6H), 1.56(m,2H), 1.70(m,2H), 2.66(t,2H), 3.69(s,3H), 6.61(dd,2H,J = 6.3Hz, 6.7Hz), 6.97(t,1H,J = 6.3Hz, 6.7Hz); Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 82.06; H, 9.54.

1,2,3,4-Tetrahydro-6-fluoro-1,1-dimethylnaphthalene (5c). A clear oil (100%); ^{1}H NMR ($CDCl_3$) ppm: 1.22(s,6H), 1.66(m,2H), 1.80(m,2H), 2.75(t,2H), 6.72(dd,1H,J_{HH} = 2.8Hz,J_{HF} = 9.7Hz), 6.83(dt,1H,J_{HH} = 2.8Hz,8.6Hz,J_{HF} = 8.6Hz), 7.27(dd,1H,J_{HH} = 8.6Hz,J_{HF} = 5.8Hz); Anal. Calcd for $C_{12}H_{15}F$: C, 80.86; H, 8.48. Found: C, 80.87; H, 8.52.

1,2,3,4-Tetrahydro-8-fluoro-1,1-dimethylnaphthalene (5d). A clear oil (6%); ^{1}H NMR ($CDCl_3$) ppm: 1.38(d,6H), 1.66(m,2H), 1.80(m,2H), 2.75(t,2H), 6.79(m,2H), 7.03(m,1H); Anal. Calcd for $C_{12}H_{15}F$: C, 80.86; H, 8.48. Found: C, 80.83; H, 8.54.

5,7-Difluoro-1,2,3,4-tetrahydro1,1-dimethylnaphthalene (21). A clear oil (91%); ^{1}H NMR ($CDCl_3$) ppm: 1.24(s,6H), 1.62(m,2H), 1.79(m,2H), 3.46(t,2H), 6.55(dt,1H,J_{HH} = 2.5Hz,J_{HF} = 9.5Hz), 6.82(dd,1H,J_{HH} = 2.5Hz,J_{HF} = 10.3Hz); Anal. Calcd for $C_{12}H_{14}F_2$: C, 73.45; H, 7.19. Found: C, 73.48; H, 7.14.

1,2,3,4-Tetrahydro-1,1-dimethyl-5,7-bis(1-methylethyl)-naphthalene (29a). A clear oil (95%); ^{1}H NMR ($CDCl_3$) ppm: 1.19(d,6H), 1.25(d,6H), 1.31(s,6H), 1.63(m,2H), 1.82(m,2H), 2.74(t,2H), 2.86(septet,1H), 3.15(septet,1H), 6.97(d,1H, J = 1.8Hz), 7.08(d,1H, J = 1.8Hz); Anal. Calcd for $C_{18}H_{28}$: C, 88.45; H, 11.55. Found: C, 88.50; H, 11.49.

1,2,3,4-Tetrahydro-1,1,5,7-tetramethylnaphthalene (29b). A clear oil (94%); ^{1}H NMR ($CDCl_3$) ppm: 1.21(s,6H), 1.68(m,2H), 1.85(m,2H), 2.23(s,3H), 2.32(s,3H), 2.62(t,2H), 6.85(s,1H), 7.07(s,1H); Anal. Calcd for $C_{14}H_{20}$: C, 89.29; H, 10.71. Found: C, 89.14; H, 10.68.

1,2,3,4-Tetrahydro-5,7-dimethoxy-1,1-dimethylnaphthalene (29c). A clear oil (80%); ^{1}H NMR ($CDCl_3$) ppm: 1.19(s,6H), 1.52(m,2H), 1.68(m,2H), 2.48(t,2H), 3.70(s,3H), 3.72(s,3H), 6.19(d,1H,J = 2.4Hz), 6.42(d,1H,J = 2.4Hz); Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.35; H, 9.16.

6-Fluoro-1,2,3,4-tetrahydro-1-methylnaphthalene, mixt. with 8-fluoro-1,2,3,4-tetrahydro-1-methylnaphthalene (37a). A clear oil (82%); ^{1}H NMR ($CDCl_3$) ppm: 1.27(d,3H), 1.72(m,5H), 2.85(m,2H), 6.80(m,1H), 7.11(m,1H); 1.27(d,3H), 1.72(m,5H), 2.73(m,2H), 6.80(m,1H), 7.11(m,1H); Anal. Calcd for $C_{11}H_{13}F$: C, 80.45; H, 7.98. Found: C, 80.52; H, 7.99.

6-Fluoro-1,2,3,4-tetrahydro-1-methyl-1-(1-methylethyl)naphthalene (37b). A clear oil (100%); ^{1}H NMR ($CDCl_3$) ppm: 0.58(d,3H), 0.95(d,3H), 1.27(s,3H), 1.47(m,1H), 1.68(m,2H), 1.83(m,1H), 2.11(septet,1H), 2.66(t,2H), 6.69(dd,1H,J_{HH} = 2.8Hz,J_{HF} = 9.6Hz), 6.80(dt,1H,J_{HH} = 2.9,5.7Hz,J_{HF} = 8.4Hz), 7.19(dd,1H,J_{HH} = 8.7Hz,J_{HF} = 5.9Hz); Anal. Calcd for $C_{14}H_{19}F$: C, 81.51; H, 9.28. Found: C, 81.53; H, 8.73.

6-Fluoro-1,2,3,4-tetrahydro-1,1-dipropylnaphthalene (37c). A clear oil (96%); ^{1}H NMR ($CDCl_3$) ppm: 0.75(t,6H), 1.13-1.62(m,12H), 2.61(t,2H), 2.61(t,2H), 6.62(dd,1H,J_{HH} = 2.7Hz,J_{HF} = 9.7Hz), 6.72(dt,1H,J_{HH} = 2.7,8.7Hz,J_{HF} = 8.5Hz), 7.06(dd,1H,J_{HH} = 8.7Hz,J_{HF} = 5.9Hz); Anal. Calcd for $C_{16}H_{23}F$: C, 82.00; H, 9.89. Found: C, 81.89; H, 9.84.

6'-Fluoro-3',4'-dihydrospiro[cyclohexane-1,1'(2'H)-naphthalene] (37d). A clear oil (100%); ^{1}H NMR ($CDCl_3$) ppm: 1.19-1.72(m,16H), 2.64(t,2H), 6.64(dd,1H,J_{HH} = 2.8Hz,J_{HF} = 9.6Hz), 6.72(dt,1H,J_{HH} = 2.9,8.7Hz,J_{HF} = 8.7Hz), 7.06(dd,1H,J_{HH} = 8.8Hz,J_{HF} = 5.8Hz); Anal. Calcd for $C_{15}H_{19}F$: C, 82.53; H, 8.77. Found: C, 78.72; H, 9.00.

General Procedure for Nitration Using Fuming Nitric Acid (6, 11, 15, 17, 19, 38)

The tetralin (0.010 mol) was added in small portions over a period of 15-60 minutes to fuming nitric acid (20 mL) chilled to -5°C (methanol/ice). The addition was closely monitored to keep the temperature below 7°C. Upon complete addition the solution stirred at room temperature for 0-7 hours. The solution was poured over ice/water (500 g) which was then extracted with methylene chloride. The methylene chloride layer was washed with water, and brine. The solution was dried over magnesium sulfate, filtered and the solvent was removed to give the crude product. (If reaction would not go to completion, the same procedure was repeated on the mixture.) The product was purified by column chromatography (ethyl acetate-hexane) or crystallization.

1,2,3,4-Tetrahydro-6-methoxy-1,1-dimethyl-5,7-dinitronaphthalene (6). A white solid (64%), mp 109-110°C; ^{1}H NMR ($CDCl_3$) ppm: 1.32(s,6H), 1.70(m,2H), 1.84(m,2H), 2.66(t,2H), 3.95(s,3H), 8.03(s,1H); Anal. Calcd for $C_{13}H_{16}N_2O_5$: C, 55.71; H, 5.76. Found: C, 55.75; H, 5.75.

1,2,3,4-Tetrahydro-8-methoxy-1,1-dimethyl-5,7-dinitronaphthalene (11). A white solid (64%), mp 87-88°C; ^{1}H NMR ($CDCl_3$) ppm: 1.42(s,6H), 1.71(m,4H), 2.90(t,2H), 3.86(s,3H), 8.15(s,1H); Anal. Calcd for $C_{13}H_{16}N_2O_5$: C, 55.71; H, 5.76. Found: C, 55.64; H, 5.67.

6-Fluoro-1,2,3,4-tetrahydro-1,1-dimethyl-7-nitronaphthalene (15). A white solid (5%), mp 94-95°C; ^{1}H NMR ($CDCl_3$) ppm: 1.38(s,6H), 1.71(m,4H), 2.89(t,2H), 8.27(d,1H,J_{HF} = 6.6Hz); Anal. Calcd for $C_{12}H_{14}FNO_2$: C, 64.56; H, 6.32. Found: C, 63.61; H, 6.24.

6-Fluoro-1,2,3,4-tetrahydro-1,1-dimethyl-5,7-dinitronaphthalene (17). A white solid (30%), mp 92-93°C; ^{1}H NMR ($CDCl_3$) ppm: 1.38(s,6H), 1.71(m,4H), 1.86(m,2H), 2.75(t,2H), 8.17(d,1H,J_{HF} = 6.0Hz); Anal. Calcd for $C_{12}H_{13}FN_2O_4$: C, 53.73; H, 4.88. Found: C, 53.85; H, 4.78.

8-Fluoro-1,2,3,4-tetrahydro-1,1-dimethyl-5,7-dinitronaphthalene (19). A yellow oil (7%); ^{1}H NMR ($CDCl_3$) ppm: 1.38(s,6H), 1.71(m,4H), 2.89(t,2H), 8.28(d,1H,J_{HF} = 6.6Hz); Anal. Calcd for $C_{12}H_{13}FN_2O_4$: C, 53.73; H, 4.88. Found: C, 53.70; H, 4.87.

6-Fluoro-1,2,3,4-tetrahydro-5,7-dinitro-1,1-dipropylnaphthalene (38a). A yellow solid (67%), mp 144-145°C; ;^{1}H NMR ($CDCl_3$) ppm: 0.81(t,6H), 1.02(m,2H), 1.17(m,2H), 1.56(m,8H), 2.66(t,2H), 8.00(d,1H,J_{HF} = 6.1Hz); Anal. Calcd for $C_{16}H_{21}FN_2O_4$: C, 59.25; H, 6.53. Found: C, 59.52; H, 6.54.

6-Fluoro-1,2,3,4-tetrahydro-1-methyl-1-(1-methylethyl)-5,7-dinitronaphthalene (38b). A yellow solid (61%), mp 70-81°C; ^{1}H NMR ($CDCl_3$) ppm: 0.65(d,3H), 1.00(d,3H), 1.29(s,3H), 1.54(m,1H), 1.71(m,2H), 1.97(m,1H), 2.16(septet,1H), 2.67(t,2H), 8.00(d,1H,J_{HF} = 7.3Hz); Anal. Calcd for $C_{14}H_{17}FN_2O_4$: C, 56.75; H, 5.78. Found: C, 56.82; H, 5.78.

7-Fluoro-1,2,3,4-tetrahydro-1-methyl-5,7-dinitronaphthalene (38c). A yellow oil (20%); ^{1}H NMR ($CDCl_3$) ppm: 1.32(d,3H), 1.82(m,4H), 3.07(m,2H), 3.39(m,1H), 8.46(d,1H,J_{HF} = 6.9Hz);^{1}H NMR ($CDCl_3$) ppm: 1.32(d,3H), 1.82(m,4H), 3.07(m,2H), 3.39(m,1H), 8.46(d,1H,J_{HF} = 6.9Hz); Anal. Calcd for $C_{11}H_{11}FN_2O_4$: C, 51.97; H, 4.36. Found: C, 52.02; H, 4.36.

1,2,3,4-Tetrahydro-6-methoxy-1,1-dimethyl-5-nitronaphthalene (7a) and 1,2,3,4-tetrahydro-6-methoxy-1,1-dimethyl-7-nitronaphthalene (7b). At -0°C, **5a** (1,2,3,4-tetrahydro-6-methoxy-1,1-dimethylnaphthalene) (0.5 g, 0.0026 mol) dissolved in glacial acetic acid (10.0 mL) and acetic anhydride (1 mL), was treated with 70% nitric acid (0.50 g, 0.0055 mol) as a solution in glacial acetic acid (10.0 mL) and acetic anhydride (1.0 mL). The addition was closely monitored to maintain 0°C and after complete addition was stirred for two hours 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 give a mixture of two products. Fraction one of column chromatography (3% ethyl acetate-hexane) gave 0.31 g (50%) of a yellow oil of **7a**; ^{1}H NMR ($CDCl_3$) ppm: 1.18(s,6H), 1.56(m,2H), 1.70(m,2H), 2.56(t,2H), 3.77(s,3H), 6.77(d,1H,J = 8.8Hz), 7.30(d,1H,J = 8.8Hz); Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28. Found: C, 66.63; H, 7.31. Fraction two of column chromatography (3% ethyl acetate-hexane) gave 0.31 g (50%) of a white solid of **7b**, mp 130-131°C; ^{1}H NMR ($CDCl_3$) ppm: 1.20(s,6H), 1.60(m,2H), 1.73(m,2H), 2.72(t,2H), 3.84(s,3H), 6.64(s,1H), 7.79(s,1H); Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28. Found: C, 66.41; H, 7.32.

General Procedure for Friedel-Crafts Acylation (8, 12, 22, 25, 30, 31, 33, 35)

A solution of the tetrahydronaphthalene (0.010 mol) dissolved in 1,2-dichloroethane (10mL) was added dropwise to a cold (0°C) solution of anhydrous aluminium chloride (0.013 mol) and acid chloride (0.011 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 then 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 give the crude product. The product was purified by column chromatography (ethyl acetate-hexane) or crystallization.

1-(5,6,7,8-Tetrahydro-3-methoxy-8,8-dimethyl-2-naphthalenyl)ethanone (8). A white solid (89%), mp 79-80°C; ^{1}H NMR ($CDCl_3$) ppm: 1.25(s,6H), 1.65(m,2H), 1.79(m,2H), 2.57(s,3H), 2.76(t,2H), 3.85(s,3H), 6.59(s,1H), 7.73(s,1H); Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.64; H 8.69.

1-(5,6,7,8-Tetrahydro-4-methoxy-5,5-dimethyl-1-naphthalenyl)ethanone (12). A clear oil (82%); ^{1}H NMR ($CDCl_3$) ppm: 1.29(s,6H), 1.55(m,4H), 2.45(s,3H), 2.89(t,2H), 3.78(s,3H), 6.64(d,1H,J = 8.6Hz), 7.44(d,1H,J = 8.6Hz); Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.63; H 8.72.

1,3-Difluoro-5,6,7,8-tetrahydro-5,5-dimethyl-2-naphthalenecarboxaldehyde (22). A yellow oil (58%); ^{1}H NMR ($CDCl_3$) ppm: 1.24(s,6H), 1.62(m,2H), 1.79(m,2H), 2.55(t,3H, J_{HF} = 1.9Hz), 2.64(t,2H), 6.86(dt,1H,J_{HF} = 1.6,11.7Hz); Anal. Calcd for $C_{14}H_{16}F_2O$: C, 70.57; H, 6.77. Found: C, 70.56; H, 6.76.

1-[5,6,7,8-Tetrahydro-5,5-dimethyl-3-(1-methylethyl)-1-naphthalenyl]-1-propanone, mixt. with 1-[5,6,7,8-tetrahydro-8,8-dimethyl-4-(1-methylethyl)-2-naphthalenyl]-1-propanone (30a). A clear oil (82%); ^{1}H NMR ($CDCl_3$) ppm: 1.32(m,9H), 1.21(s,6H), 1.53(m,2H), 1.73(m,2H), 2.68(m,2H), 2.80(q,2H), 3.25(septet,1H), 7.18(m,2H); Anal. Calcd for $C_{18}H_{26}O$: C, 83.67; H, 10.14. Found: C, 83.70; H, 10.09.

5,6,7,8-Tetrahydro-5,5-dimethyl-3-(1-methylethyl)-1-naphthalenecarboxaldehyde, or 5,6,7,8-tetrahydro-8,8-dimethyl-4-(1-methylethyl)-2-naphthalenecarboxaldehyde (30b). A yellow oil (23%); ^{1}H NMR ($CDCl_3$) ppm: 1.16(d,6H), 1.25(s,6H), 1.57(m,2H), 1.75(m,2H), 2.51(s,3H), 2.71(t,2H), 3.10(septet,1H), 7.59(dd,1H,J = 1.8Hz), 7.74(dd,1H,J = 1.8Hz); Anal. Calcd for $C_{17}H_{24}O$: C, 83.55; H, 9.90. Found: C, 83.70; H, 9.86.

1-(5,6,7,8-Tetrahydro-1,3,5,5-tetramethyl-2-naphthalenyl)ethanone (31a). A white solid (79%), mp 102-103°C; ^{1}H NMR ($CDCl_3$) ppm: 1.25(s,6H), 1.60(m,2H), 1.80(m,2H), 2.06(s,3H), 2.18(s,3H), 2.44(s,3H), 2.54(t,2H), 7.01(s,1H); Anal. Calcd for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.52; H, 9.64.

1-(5,6,7,8-Tetrahydro-1,3,5,5-tetramethyl-2-naphthalenyl)-1-propanone (31b). A clear oil (87%); ^{1}H NMR ($CDCl_3$) ppm: 0.79(t,3H), 1.23(s,6H), 1.51(m,2H), 1.71(m,2H), 1.94(s,3H), 2.07(s,3H), 2.43(t,2H), 2.63(q,2H), 6.93(s,1H); Anal. Calcd for $C_{17}H_{24}O$: C, 83.55; H, 9.90. Found: C, 83.55; H, 9.95.

5,6,7,8-Tetrahydro-1,3,5,5-tetramethyl-2-naphthalenecarboxylic acid (33). A white solid (79%), mp 211-213°C; ^{1}H NMR ($CDCl_3$) ppm: 1.27(s,6H), 1.60(m,2H), 1.80(m,2H), 2.25(s,3H), 2.37(s,3H), 2.58(t,2H), 7.06(s,1H), 9.58(bs,1H); Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.01; H, 8.65.

1,3-Dimethoxy-5,6,7,8-tetrahydro-5,5-dimethyl-2-naphthalenecarboxaldehyde (35). A white solid (6%), mp 85°C; ^{1}H NMR ($CDCl_3$) ppm: 1.21(s,6H), 1.56(m,2H), 1.69(m,2H), 2.42(s,3H), 2.57(t,2H), 3.62(s,3H), 3.72(s,3H), 6.58(s,1H); Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.35; H, 8.49.

General Procedure for Haloform Reaction with Methyl Ketones (9, 13, 32)

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 1-14 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/hydrochloric acid (200 g) which was then 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 give the crude product. The product was purified by column chromatography (ethyl acetate-hexane) or crystallization.

5,6,7,8-Tetrahydro-3-methoxy-8,8-dimethyl-2-naphthalenecarboxylic acid (9). A white solid (100%), mp 132.5-133.5°C; ^{1}H NMR ($CDCl_3$) ppm: 1.25(s,6H), 1.58(m,2H), 1.74(m,2H), 2.73(t,2H), 3.94(s,3H), 6.62(s,1H), 8.06(s,1H); Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.14; H, 7.72.

5,6,7,8-Tetrahydro-4-methoxy-5,5-dimethyl-1-naphthalenecarboxylic acid (13). A white solid (99%), mp 192-193°C; ^{1}H NMR ($CDCl_3$) ppm: 1.36(s,6H), 1.65(m,4H), 3.09(t,2H), 3.85(s,3H), 6.74(d,1H,J = 8.8Hz), 7.90(d,1H,J = 8.8Hz); Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.23; H, 7.69.

2,2,2-Tribromo-1-(5,6,7,8-tetrahydro-1,3,5,5-tetramethyl-2-naphthalenyl)ethanone (32). A white solid (89%), mp 113-114°C; ^{1}H NMR ($CDCl_3$) ppm: 1.20(d,6H), 1.56(m,2H), 1.75(m,2H), 2.18(s,3H), 2.31(s,3H), 2.50(t,2H), 7.01(s,1H); Anal. Calcd for $C_{14}H_{18}O_3$: C, 41.15; H, 4.10. Found: C, 41.05; H, 4.08.

General Procedure for the Preparation of Carboxylate Esters and Amides (10, 14, 26, 34)

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 15 minutes-several hours the solvent was removed to give 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 15 minutes-several 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 give the product. The product was purified by column chromatography (ethyl acetate-hexane) or crystallization.

5,6,7,8-Tetrahydro-3-methoxy-8,8-dimethyl-2-naphthalenecarboxylic acid, methyl ester (10). A white solid (90%), mp 114.5-115°C; ^{1}H NMR ($CDCl_3$) ppm: 1.19(s,6H), 1.53(m,2H), 1.73(m,2H), 2.69(t,2H), 3.78(s,3H), 3.80(s,3H), 6.54(s,1H), 7.70(s,1H); Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.27; H, 8.07.

5,6,7,8-Tetrahydro-4-methoxy-5,5-dimethyl-1-naphthalenecarboxylic acid, methyl ester (14). A clear oil (72%); ^{1}H NMR ($CDCl_3$) ppm: 1.25(s,6H), 1.53(m,2H), 1.57(m,2H), 2.91(t,2H), 3.68(s,3H), 6.55(d,1H,J = 7.2Hz), 7.56(d,1H,J = 7.2Hz); Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.56; H, 8.09.

5,6,7,8-Tetrahydro-1,3,5,5-tetramethyl-2-naphthalenecarboxylic acid, methyl ester (34a). A clear oil (76%); ^{1}H NMR ($CDCl_3$) ppm: 1.17(s,6H), 1.53(m,2H), 1.72(m,2H), 2.06(s,3H), 2.18(s,3H), 2.48(t,2H), 3.80(s,3H), 6.96(s,1H); Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.89; H, 9.08.

5,6,7,8-Tetrahydro-1,3,5,5-tetramethyl-2-naphthalenecarboxylic acid, ethyl ester (34b). A clear oil (93%); ^{1}H NMR ($CDCl_3$) ppm: 1.18(s,6H), 1.30(t,3H), 1.54(m,2H), 1.73(m,2H), 2.07(s,3H), 2.18(s,3H), 2.49(t,2H), 4.29(q,2H), 6.96(s,1H); Anal. Calcd for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 77.94; H, 9.03.

5,6,7,8-Tetrahydro-1,3,5,5-tetramethyl-2-naphthalenecarboxylic acid, butyl ester (34c). A clear oil (75%); ^{1}H NMR ($CDCl_3$) ppm: 0.93(t,3H), 1.25(s,6H), 1.45(sextet,2H), 1.59(m,2H), 1.71(quintet,2H), 1.78(m,2H), 2.13(s,3H), 2.25(s,3H), 2.56(t,2H), 4.30(t,2H), 7.03(s,1H); Anal. Calcd for $C_{16}H_{22}O_2$: C, 79.12; H, 9.78. Found: C, 78.68; H, 9.54.

5,6,7,8-Tetrahydro-N,N,1,3,5,5-hexamethyl-2-naphthalenecarboxamide (34d). A white solid (71%), mp 97-98°C; ^{1}H NMR ($CDCl_3$) ppm: 1.15(s,3H), 1.20(s,3H), 1.54(m,2H), 1.71(m,2H), 1.99(s,3H),

2.10(s,3H), 2.47(t,2H), 2.74(s,3H), 3.08(s,3H), 6.94(s,1H); Anal. Calcd for $C_{17}H_{25}NO$: C, 78.72; H, 9.71. Found: C, 78.17; H, 9.76.

General Procedure for Reaction of Fluorotetralins with Nucleophiles (16, 18, 20, 23, 39)

To the fluorotetralin (0.010 mol) dissolved in dichloromethane (30 mL) or methanol was added the amine (excess) or alkoxide (excess). After stirring for 1-14 hours, the solution was washed with water, sodium bicarbonate, and brine. The solution was dried over magnesium sulfate, filtered and the solvent was removed to give the crude product. The product was purified by column chromatography (ethyl acetate-hexane) or crystallization.

5,6,7,8-Tetrahydro-N,N,5,5-tetramethyl-3-nitro-2-naphthalenamine (16). An orange oil (75%); ^1H NMR ($CDCl_3$) ppm: 1.25(s,6H), 1.63(m,2H), 1.79(m,2H), 2.74(t,3H), 2.82(s,6H), 6.69(s,1H), 7.74(s,1H); Anal. Calcd for $C_{14}H_{20}N_2O_2$: C, 67.72; H, 8.12. Found: C, 68.00; H, 7.96.

6-(Ethylthio)-1,2,3,4-tetrahydro-1,1-dimethyl-5,7-dinitronaphthalene (18a). A yellow solid (90%), mp 97-98°C; ^1H NMR ($CDCl_3$) ppm: 1.19(t,3H), 1.32(s,6H), 1.69(m,2H), 1.83(m,2H), 2.65(t,2H), 2.93(q,2H), 7.76(s,1H); Anal. Calcd for $C_{14}H_{18}SN_2O_4$: C, 54.18; H, 5.85. Found: C, 54.23; H, 5.84.

5,6,7,8-Tetrahydro-N,5,5-trimethyl-1,3-dinitro-2-naphthalenamine (18c). An orange solid (76%), mp 108-109°C; ^1H NMR ($CDCl_3$) ppm: 1.28(s,6H), 1.65(m,2H), 1.79(m,2H), 2.60(t,2H), 2.89(s,3H), 8.11(bs,1H), 8.27(s,1H); Anal. Calcd for $C_{13}H_{17}N_3O_4$: C, 55.91; H, 6.14. Found: C, 55.94; H, 6.20.

5,6,7,8-Tetrahydro-N,N,5,5-tetramethyl-1,3-dinitro-2-naphthalenamine (18d). A yellow solid (85%), mp 149-150°C; ^1H NMR ($CDCl_3$) ppm: 1.34(s,6H), 1.65(m,2H), 1.80(m,2H), 2.60(t,2H), 2.73(s,6H), 7.73(s,1H); Anal. Calcd for $C_{14}H_{19}N_3O_4$: C, 57.33; H, 6.53. Found: C, 57.08; H, 6.47.

N-Ethyl-5,6,7,8-tetrahydro-5,5-dimethyl-1,3-dinitro-2-naphthalenamine (18e). An orange solid (91%), mp 87-88°C; ^1H NMR ($CDCl_3$) ppm: 1.26(t,3H), 1.28(s,6H), 1.62(m,2H), 1.77(m,2H), 2.59(t,2H), 3.14(q,2H), 7.78(bs,1H), 8.26(s,1H); Anal. Calcd for $C_{14}H_{19}N_3O_4$: C, 57.33; H, 6.53. Found: C, 57.04; H, 6.48.

N,N-Diethyl-5,6,7,8-tetrahydro-5,5-dimethyl-1,3-dinitro-2-naphthalenamine (18f). A yellow solid (73%), mp 87-88°C; ^1H NMR ($CDCl_3$) ppm: 0.93(t,6H), 1.24(s,6H), 1.61(m,2H), 1.73(m,2H), 2.56(t,2H), 2.92(q,4H), 7.69(s,1H); Anal. Calcd for $C_{14}H_{19}N_3O_4$: C, 59.80; H, 7.21. Found: C, 59.52; H, 7.06.

5,6,7,8-Tetrahydro-5,5-dimethyl-1,3-dinitro-N,N-dipropyl-2-naphthalenamine (18g). An orange solid (76%), mp 105-106°C; ^1H NMR ($CDCl_3$) ppm: 0.74(t,6H), 1.24(s,6H), 1.36(sextet,4H), 1.61(m,2H), 1.73(m,2H), 2.56(t,2H), 2.80(m,4H), 7.67(s,1H); Anal. Calcd for $C_{18}H_{27}N_3O_4$: C, 61.87; H, 7.79. Found: C, 61.90; H, 7.80.

N-(1-Ethylpropyl)-5,6,7,8-tetrahydro-5,5-dimethyl-1,3-dinitro-2-naphthalenamine (18h). An orange oil (86%); ^1H NMR ($CDCl_3$) ppm: 0.80(t,6H), 1.22(s,6H), 1.38(m,4H), 1.59(m,2H), 1.73(m,2H), 2.52(t,2H), 3.08(m,1H), 7.45(bd,1H), 8.18(s,1H); Anal. Calcd for $C_{17}H_{25}N_3O_4$: C, 60.88; H, 7.51. Found: C, 60.93; H, 7.52.

5,6,7,8-Tetrahydro-N,N,8,8-tetramethyl-2,4-dinitro-1-naphthalenamine (20). A yellow solid (73%), mp 94-95°C; ^1H NMR ($CDCl_3$) ppm: 1.46(s,6H), 1.65(m,2H), 1.75(m,2H), 2.71(s,6H), 2.89(t,2H), 7.68(s,1H); Anal. Calcd for $C_{14}H_{19}N_3O_4$: C, 57.33; H, 6.53. Found: C, 57.60; H, 6.53.

1-(3-Fluoro-5,6,7,8-tetrahydro-1-methoxy-5,5-dimethyl-2-naphthalenyl)ethanone (23). A yellow oil (46%); ^1H NMR ($CDCl_3$) ppm: 1.18(s,6H), 1.56(m,2H), 1.70(m,2H), 2.48(d,3H, J_{HF} = 1.6Hz), 2.60(t,2H), 3.66(s,3H), 6.78(dt,1H,J_{HF} = 11.4Hz); Anal. Calcd for $C_{15}H_{19}FO_2$: C, 71.98; H, 7.65. Found: C, 71.96; H, 7.60.

N-(1-Ethylpropyl)-5,6,7,8-tetrahydro-1,3-dinitro-5,5-dipropyl-2-naphthalenamine (39a). An orange solid (65%), mp 86.5-88°C; ^{1}H NMR ($CDCl_3$) ppm: 0.81(m,12H), 1.01(m,2H), 1.19(m,2H), 1.33-1.67(m,12H), 2.48(t,2H), 3.06(bs,1H), 7.43(bs,1H), 8.06(s,1H); Anal. Calcd for $C_{21}H_{33}N_3O_4$: C, 64.43; H, 8.50. Found: C, 64.44; H, 8.53.

5,6,7,8-Tetrahydro-N,N-dimethyl-1,3-dinitro-5,5-dipropyl-2-naphthalenamine (39b). An orange oil (61%); ^{1}H NMR ($CDCl_3$) ppm: 0.81(t,6H), 1.01(m,2H), 1.19(m,2H), 1.44-1.67(m,8H), 2.51(t,2H), 2.68(s,6H), 7.60(s,1H); Anal. Calcd for $C_{18}H_{27}N_3O_4$: C, 61.87; H, 7.79. Found: C, 61.92; H, 7.80.

5,6,7,8-Tetrahydro-N,N-dimethyl-3-nitro-5,5-dipropyl-2-naphthalenamine (39c). An orange oil (28%); ^{1}H NMR ($CDCl_3$) ppm: 0.81(t,6H), 1.01(m,2H), 1.19(m,2H), 1.44-1.67(m,8H), 2.63(t,2H), 2.75(s,6H), 6.61(s,1H), 7.58(s,1H); Anal. Calcd for $C_{18}H_{28}N_2O_2$: C, 71.02; H, 9.27. Found: C, 70.98; H, 9.27.

N-(1-Ethylpropyl)-5,6,7,8-tetrahydro-5-methyl-5-(1-methylethyl)-1,3-dinitro-2-naphthalenamine (39d). An orange oil (97%); ^{1}H NMR ($CDCl_3$) ppm: 0.63(d,3H), 0.80(t,3H), 0.91(t,3H), 0.96(d,3H), 1.24(s,3H), 1.45-1.63(m,8H), 2.06(septet,1H), 2.52(t,2H), 3.12(quintet,1H), 7.50(bs,1H), 8.18(s,1H); Anal. Calcd for $C_{19}H_{29}N_3O_4$: C, 62.79; H, 8.04. Found: C, 62.52; H, 8.01.

5,6,7,8-Tetrahydro-N,N,5-trimethyl-5-(1-methylethyl)-1,3-dinitro-2-naphthalenamine (39e). A yellow solid (100%), mp 111-112°C; ;^{1}H NMR ($CDCl_3$) ppm: 0.63(d,3H), 0.98(t,3H), 1.25(s,3H), 1.55(m,1H), 1.66(m,2H), 1.91(m,1H), 2.09(septet,1H), 2.56(t,2H), 2.74(s,6H), 7.72(s,1H); Anal. Calcd for $C_{16}H_{23}N_3O_4$: C, 59.80; H, 7.21. Found: C, 59.88; H, 7.24.

1,2,3,4-Tetrahydro-6-methoxy-1-methyl-1-(1-methylethyl)-5,7-dinitronaphthalene (39f). A yellow oil (46%); ;^{1}H NMR ($CDCl_3$) ppm: 0.60(d,3H), 0.93(d,3H), 1.22(s,3H), 1.50(m,1H), 1.65(m,2H), 1.88(m,1H), 2.06(septet,1H), 2.55(m,2H), 3.90(s,3H), 7.92(s,1H); Anal. Calcd for $C_{16}H_{20}N_2O_5$: C, 58.43; H, 6.54. Found: C, 58.57; H, 6.56.

N-(1-Ethylpropyl)-5,6,7,8-tetrahydro-5-methyl-1,3-dinitro-2-naphthalenamine (39g). An orange oil (92%); ^{1}H NMR ($CDCl_3$) ppm: 0.75(t,3H), 0.92(t,3H), 1.22(d,3H), 1.40-1.81(m,10H), 2.96(m,3H), 3.34(quintet,1H), 6.83(bs,1H), 8.49(s,1H); Anal. Calcd for $C_{16}H_{23}N_3O_4$: C, 59.80; H, 7.21. Found: C, 59.20; H, 7.10.

N-(1-Ethylpropyl)-3',4'-dihydro-5',7'-dinitrospiro[cyclohexane-1,1'(2'H)-naphthalene]-6'-amine (39h). A yellow solid (100%), mp 93.5-94.5°C; ^{1}H NMR ($CDCl_3$) ppm: 0.81(m,6H), 1.42-1.70(m,14H), 2.48(t,2H), 3.06(bs,1H), 7.45(bd,1H), 8.27(s,1H); Anal. Calcd for $C_{20}H_{29}N_3O_4$: C, 63.98; H, 7.79. Found: C, 63.90; H, 7.81.

3',4'-Dihydro-N,N-dimethyl-5',7'-dinitrospiro[cyclohexane-1,1'(2'H)-naphthalene]-6'-amine (39i). A yellow solid (87%), mp 95-96°C; ^{1}H NMR ($CDCl_3$) ppm: 1.56-1.73(m,14H), 2.53(t,2H), 2.67(s,6H), 7.82(s,1H); Anal. Calcd for $C_{17}H_{23}N_3O_4$: C, 61.25; H, 6.95. Found: C, 61.30; H, 6.96.

6-(Ethylsulfonyl)-1,2,3,4-tetrahydro-1,1-dimethyl-5,7-dinitronaphthalene (18b). To a solution of **18a** (6-(ethylthio)-1,2,3,4-tetrahydro-1,1-dimethyl-5,7-dinitronaphthalene) (0.50 g, 0.0016 mol) in dichloromethane (25 mL) was added slowly a solution of (50%) m-chloroperoxybenzoic acid (1.06 g, 0.0033 mol) in dichloromethane (30 mL) at 0°C. The solution was stirred at room temperature for two hours. The solution was washed with water, sodium bicarbonate, and brine. The solution was dried over magnesium sulfate, filtered and the solvent was removed to give the crude product. The product was purified by recrystallization from hexane to give 0.51 g (76%) of a yellow solid of **18b**, mp 152.5-153.5°C; ^{1}H NMR ($CDCl_3$) ppm: 1.35(s,6H), 1.50(t,3H), 1.55(m,2H), 1.73(m,2H), 2.68(t,2H), 3.65(q,2H), 7.24(s,1H), 8.26(s,1H); Anal. Calcd for $C_{14}H_{18}N_2O_6S$: C, 64.42; H, 8.50. Found: C, 64.44; H, 8.53.

General Procedure for the Reduction of γ-Keto-Esters (27)

The γ-keto-ester (0.01 mol), 37% hydrogen chloride (0.062 mol), water (0.025 mol), and 10% palladium (1.0 g) on carbon were added to methanol (250 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 give the crude product. The product was purified by column chromatography (ethyl acetate-hexane).

2,4-Bis(1-methylethyl)benzenebutanoic acid, methyl ester (27a). A clear oil (86%); ^{1}H NMR ($CDCl_3$) ppm: 1.24(d,6H), 1.25(d,6H), 1.90(quintet,2H), 2.39(t,2H), 2.65(t,2H), 2.87(septet,1H), 3.15(septet,1H), 3.67(s,3H), 6.98(dd,1H, J = 1.8,7.8Hz), 7.05(d,1H, J = 1.8Hz), 7.12(d,1H, J = 7.8Hz); Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 78.24; H, 10.00.

2,4-Dimethylbenzenebutanoic acid, methyl ester (27b). A clear oil (97%); ^{1}H NMR ($CDCl_3$) ppm: 1.88(quintet,2H), 2.27(s,3H), 2.28(s,3H), 2.37(t,2H), 2.59(t,2H), 3.67(s,3H), 6.96(m,3H); Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.92; H, 8.89.

2,4-Dimethoxybenzenebutanoic acid, methyl ester (27c). A clear oil (24%); ^{1}H NMR ($CDCl_3$) ppm: 1.81(quintet,2H), 2.23(t,2H), 2.06(t,2H), 3.58(s,3H), 3.71(s,3H), 3.71(s,3H), 6.32(d,1H,J = 2.0Hz), 6.35(dd,1H,J = 2.0,6.7Hz), 6.92(d,1H,J = 6.7Hz); Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.43; H, 7.58.

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