NALSAR PROXIMATE EDUCATION
NALSAR UNIVERSITY OF LAW, HYDERABAD
P.G.DIPLOMA IN PATENTS LAW

2006-07

Paper II – Practical

(Exploitation of Patents – Drafting, Specification & Patent Writing)

Time: 2 ½ hours. **Full marks: 60**

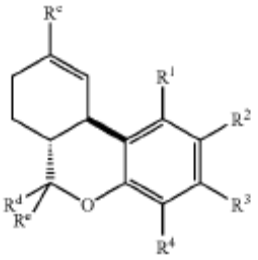
INSTRUCTIONS TO CANDIDATES

The questions to be interpreted as given and no clarification can be sought from the invigilator.

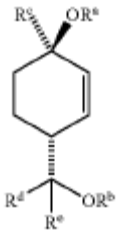
You are required to draft an US patent application with the following data and information. You are required to attempt either A or B (any one).

A)

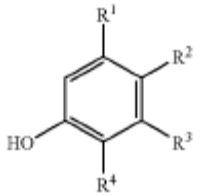
The proposed invention relates to a process for the production of compound (A) comprising reacting compound (B) with compound (C). A further ring closure reaction may be necessary. The invention further relates to certain novel compounds of formula (B).



A



B



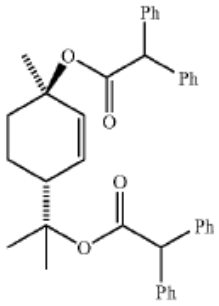
C

wherein R^c, R^d, R^e are independently H, alkyl, or substituted alkyl; and R^1 to R^4 are independently H, OH, OR' (R' is alkyl, aryl, substituted alkyl or aryl, silyl, acyl, or phosphonate), alkyl, substituted alkyl, aryl, acyl, halide, amine, nitrate, sulphonate or phosphonate

General Experimental Details - Anhydrous solvents were purchased from Aldrich Chemical Company (Milwaukee, Wis., USA). Samples of Δ^9-THC and Δ^8-THC were obtained from RBI/Sigma (Natick, Mass., USA). (+)-p-Menth-2-ene-1,8-diol was prepared as described in a co-pending patent application by the present inventors. TLC plates (silica gel GF, 250 micron, 10X20 cm) were purchased from Analtech (Newark, Del., USA). TLCs were visualized under short wave UV, and then by spraying with ceric ammonium nitrate/sulfuric acid and heating. Column chromatography was carried out using TLC grade silica gel purchased from Aldrich Chemical Company. NMR spectra were obtained on a Bruker 300 MHz instrument. HPLC area percentages reported here are not corrected. HPLCs were run on Shimadzu LC-10AD.

EXAMPLE 1a - One-Step Reaction of bis(diphenylacetate) Compound (4) with Olivetol (3) to Produce Δ^9-THC

Preparation of bis(diphenylacetate) Compound (4)



A 25 ml three-necked roundbottom flask with a stir bar was oven-dried, fitted with septa, and cooled under N_2 Pyridine (12 ml) was added and the pale yellow solution was stirred. Diphenylacetyl chloride (5.69 g, 4.2 eq.) was added. The solution turned brown. N,N-dimethylaminopyridine (0.1435 g, 0.2 eq.) was added. The mixture was stirred for 1 hour. (+)-p-Menth-2-ene-1,8-diol (1.00 g) was added. The mixture became a lighter colour and solids precipitated. The slurry was allowed to stir overnight at room temperature. The reaction was quenched with water. The mixture was extracted three times with ethyl acetate. The organics were combined and washed with 2M HCl, saturated $NaHCO_3$, and saturated NaCl (aq.), dried over Na_2SO_4, filtered and concentrated in vacuo to orange oil. The oil was dissolved in hot methanol and cooled to crystallize. The white solid was collected and washed twice with cold methanol. After drying under vacuum, the yield was 3.282 g (76.8% yield). ^{1}H NMR ($CDCl_3$): δ (ppm) 7.4 7.2 (m, 20H), 5.89 5.84 (dd, 1H), 5.51 5.47 (dd, 1H), 4.90 (s, 2H), 2.7 2.6 (m, 1H), 2.0 1.9 (m, 2H), 1.7 1.6 (m, 1H), 1.43 (s, 3H), 1.42 (s, 3H), 1.40 (s, 3H), 1.35 1.2 (m, 1H). ^{13}C NMR: δ(ppm) 171.47, 171.44, 139.06, 138.84, 132.38, 128.64, 128.56, 128.51, 128.46, 128.28, 127.11, 127.07, 127.02, 85.12, 80.91, 58.32, 57.86, 44.22, 33.81, 25.41, 23.32, 22.81, 21.41. M.p. 111.degree. C. Elemental Analysis: 81.66% C, 6.59% H. R_f (20% EtOAc/hexane): 0.54. $[\alpha]_D$25=+61.50 (c=1.00, CHCl.sub.3). IR (KBr, cm^{-1}): 3061, 3028, 1720.5 (carbonyl stretch).

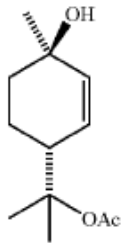
One-Step Reaction - A 25 ml roundbottom flask with a stir bar was oven-dried, fitted with septa, and cooled under N_2. The bis(diphenylacetate) (4) (279 mg, 0.499 mmol) and olivetol (90 mg) were added. Anhydrous CH_2Cl_2 (8 ml) was added and stirred. The solution was cooled to -5^{o}C internal temperature. $BF_3(OEt)_2$ (64 µl, 1.0 eq.) was added. The solution gradually darkened to orange. After 30 minutes, the reaction was quenched with 10% Na_2CO_3 (10 ml). The layers were separated and the organic layer was washed with 2X5 ml 10% Na_2CO_3. The aqueous washes were combined and extracted twice with CH_2Cl_2. The organics were combined and washed with water and saturated NaCl solution, then dried over Na_2SO_4, filtered, and concentrated in vacuo to light yellow oil. The oil was chromatographed on 5 g TLC mesh silica to yield 135.2 mg (86.1%) of Δ^9-THC. NMR did show a small amount of solvent present. HPLC showed 96.6 area percent Δ^9-THC. ^{1}H NMR agreed with published reports and commercial samples. ^{13}C NMR ($CDCl_3$): δ (ppm) 154.81, 154.16, 142.82, 134.41, 123.74, 110.11, 107.54, 77.18, 45.83, 35.47, 33.58, 31.52, 31.17, 30.63, 27.58, 25.03, 23.34, 22.53, 19.28, 13.99. HPLC R.T.: 28.34 min. R_f (10% MTBE/hexane): 0.30. $[\alpha]_D$25=-174.2.degree. (c=1.16, EtOH).

EXAMPLE 1b - Reaction of bis(diphenylacetate) (4) Compound with Olivetol to Produce Ring-Open Intermediate

Bis(diphenylacetate) (4) was prepared as for example 1a. A 25 ml 2-neck roundbottom flask with a stir bar was oven-dried, fitted with septa, and cooled under N_2. Bis(diphenylactetate) (4) (279 mg, 0.499 mmol) and olivetol (90 mg) were added. Anhydrous CH_2Cl_2 (8 ml) was added. The solution was stirred to dissolve the solids and then cooled to -20^{o}C. internal temperature. $BF_3(OEt)_2$ (16 .mu.l, 0.25 eq.) was added. The solution was stirred for 12 minutes and then quenched with 10% Na_2CO_3 (aq.) (6 ml). The mixture was extracted twice with CH_2Cl_2. The combined organics were washed with water and saturated NaCl, dried over Na_2SO_4, filtered, and concentrated in vacuo to oil. Chromatography on 10 g TLC mesh silica gel (2% MTBE/hexane--15%) yielded Δ^9-THC (fractions 16 22, 31.4 mg, 20.0% yield), but the predominant product was the diphenylacetate triol (the ring open product corresponding to compound D) (fr. 24 37, 160 mg, 60.7% yield). ^{1}H NMR ($CDCl_3$): δ (ppm) 7.26 71.8 (m, 10H), 6.26 (br s, 1H), 6.04 (br s, 1H), 5.35 (s, 1H),

4.51 (s, 1H), 3.92 (br d, 1H), 2.43 2.36 (m, 3H), 2.1 1.9 (m, 2H), 1.79 (m, 1H), 1.71 (s, 3H), 1.6 1.4 (m, 2H), 1.44 (s, 3H), 1.42 (s, 3H), 1.3 1.2 (m, 4H), 0.85 (t, 3H). ^{13}C NMR ($CDCl_3$): δ (ppm) 8 ppm 171.56, 142.87, 139.24, 139.08, 128.64, 128.36, 128.31, 126.92, 126.89, 124.93, 115.43, 87.27, 57.53, 45.94, 35.43, 33.46, 31.51, 30.60, 29.96, 24.04, 23.34, 23.20, 23.17, 22.48, 13.97. R_f (20% EtOAc/hexane): 0.48. $[\alpha]_D25$=-45.9.degree. (c=1.298, $CHCl_3$). Elemental Analysis: 78.69% C, 8.93% H.

EXAMPLE 2a - One-Step Reaction of Monoacetate Compound (8) with Olivetol to Produce Δ^9-THC



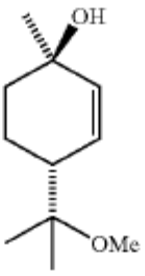
A 25 ml roundbottom flask with a stir bar was oven-dried, fitted with septa, and cooled under N_2. The monoacetate (8) (109 mg) and olivetol (92.5 mg) were added. Anhydrous CH_2Cl_2 (8 ml) was added and stirred. The solution was cooled to -5°C internal temperature. $BF_3(OEt)_2$ (65 µl, 1.0 eq.) was added. The solution gradually darkened to orange. After 24 minutes, the reaction was quenched with 10% Na_2CO_3. The layers were separated and the aqueous layer was extracted twice with CH_2Cl_2. The organics were combined and washed with water and saturated NaCl solution, then dried over Na_2SO_4, filtered, and concentrated in vacuo to oil. HPLC showed 64.0 area percent Δ^9-THC. The oil was chromatographed on 20 g TLC mesh silica to yield 58.7 mg (36.3%) of Δ^9-THC. ^1H NMR agreed with published reports and commercial samples.

EXAMPLE 2b - Reaction of Monoacetate Compound (8) with Olivetol to Produce Ring-Open Intermediate

A 25 ml 2-neck roundbottom flask with a stir bar was oven-dried, fitted with septa, and cooled under N_2. The monoacetate (8) (109 mg, 0.514 mmol) and olivetol (92.5 mg) were added. Anhydrous CH_2Cl_2 (8 ml) was added. The solution was stirred to dissolve the solids and then cooled to -20 °C internal temperature. $BF_3(OEt)_2$ (16 .mu.l, 0.25 eq.) was added. The solution was stirred for 45 minutes and then quenched with 10% Na_2CO_3 (aq.) (4 ml). The mixture was extracted twice with CH_2Cl_2. The combined organics were washed with water, dried over Na_2SO_4, filtered, and concentrated in vacuo to colourless oil. Chromatography on silica gel yielded 90.5 mg (47.0% yield) of acetyl triol (the ring open product corresponding to compound D). ^1H NMR ($CDCl_3$): δ (ppm) 6.22 (br m, 2H,), 5.76 (br s, 2H), 5.36 (s, 1H), 4.00 (br d, 1H), 2.67 (dt, 1H), 2.40 (t, 2H), 2.26 2.16 (m, 1H), 2.07 1.90 (m, 2H), 1.73 (s, 3H), 1.51 (s, 3H), 1.49 (s, 3H), 1.42 (s, 3H), 1.32 1.24 (m, 41H), 0.85 (t, 3H). . ^{13}C NMR ($CDCl_3$): δ (ppm) 170.83, 142.69, 138.03, 124.99, 115.42, 85.90, 44.29, 35.38, 33.47, 31.49, 30.66, 30.09, 25.16, 24.65, 23.17, 22.57, 22.43, 21.84, 13.95. R_f (20% EtOAc/hexane): 0.37.

EXAMPLE 3a - One-Step Reaction of Monomethoxy Compound (9) with Olivetol to Produce Δ^9-THC.

A 25 ml roundbottom flask with a stir bar was oven-dried, fitted with septa, and



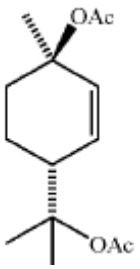
cooled under N_2. The monomethoxy compound (9) (91.9 mg) and olivetol (90 mg) were added. Anhydrous CH_2Cl_2 (8 ml) was added and stirred. The solution was cooled to -5°C. internal temperature. $BF_3(OEt)_2$ (16

µl, 0.25 eq.) was added. After 1 hour another 16 µl was added. Two hours later, another 32 µl was added. The solution gradually darkened to orange. TLC showed a mixture of Δ^9-THC and the ring open product, and major spots. The reaction was quenched with 10% Na_2CO_3. The layers were separated and the organic was washed with water and sat. NaCl, then dried over Na_2SO_4, filtered, and concentrated in vacuo to oil.

EXAMPLE 3b - Reaction of Monomethoxy Compound with Olivetol to Produce Ring-Open Intermediate

A 5 ml roundbottom flask with a stir bar was oven-dried, fitted with a septum, and cooled under N_2. The monomethoxy compound (9) (33.5 mg) in 1.5 ml of anhydrous methylene chloride was added. Olivetol (32.7 mg) and magnesium sulfate (134 mg) were added. p-Toluenesulfonic acid monohydrate (34.6 mg) was added. The slurry was stirred at room temperature for 30 minutes. Solid Na_2CO_3 (100 mg) was added and stirred. The solids were removed by filtration. The solution was washed once with 5% $NaHCO_3$ (aq.). The aqueous wash was extracted once with CH_2Cl_2. The organics were combined, washed with water, and dried over Na_2SO_4. The solution was concentrated in vacuo and chromatographed on silica gel. Colourless oil of the methoxy triol (the ring open product corresponding to compound D) (35.3 mg, 56.0% yield) was obtained. ^{1}H NMR ($CDCl_3$): δ (ppm) 7.90 (br s, 1H), 6.68 (br s, 1H), 6.33 6.21 (br d, 2H) 5.75 (s, 1H), 3.74 (s, 1H), 3.20 (s, 3H), 2.44 (t, 2H), 2.07 (br s, 2H), 2.00 1.77 (m, 3H), 1.80 (s, 3H), 1.54 (m, 2H), 1.31 (m, 3H), 1.14 (s, 3H, 1.13 (s, 3H), 0.87 (t, 3H). ^{13}C NMR ($CDCl_3$): δ (ppm) 186.50, 169.63, 166.85, 143, 41, 140.11, 123.58, 79.32, 48.63, 48.05, 35.51, 32.62, 31.52, 30.63, 27.76, 23.74, 23.01, 22.53, 21.95, 20.39, 13.99. Elemental Analysis: 73.3% C, 8.80% H. R_f (10% EtOAc/hexane): 0.25. $[\alpha]_D25$=-22.70 (c=0.088, $CHCl_3$).

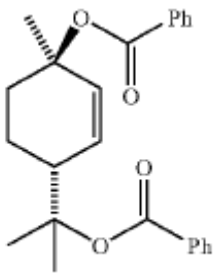
EXAMPLE 4 - One-Step Reaction of Diacetate (10) with Olivetol to Produce Δ^9-THC Preparation of Diacetate (10)



A 100 ml three-necked roundbottom flask with a stir bar was oven-dried, fitted with septa, and cooled under N_2 (+)-p-menth-2-ene-1,8-diol (10.00 g) was added. Triethylamine (68.7 ml, 8.4 eq.) was added and the slurry was stirred. N,N-dimethylaminopyridine (1.435 g, 0.2 eq.) was added. Acetic anhydride (23.3 ml) was placed in an addition funnel and added slowly over 15 minutes. The yellow solution became homogeneous. The solution was warmed to 35°C internal temperature and stirred for 2.5 hours, then raised to 40°C. for another three hours, then allowed to stir for 13 hours at room temperature. The reaction was quenched with water while cooling in ice. The mixture was extracted three times with hexane and once with ethyl acetate. The organics were combined and washed with saturated NaCl (aq.), dried over Na_2SO_4, filtered and concentrated in vacuo to an orange oil. Chromatography on 50 g TLC mesh silica yielded the diacetate (10) as colourless oil (12.3 g, 82.3%). The oil was cooled in dry ice to freeze the oil and then the solid was broken up with a spatula. It was allowed to warm to room temperature and it remained a white solid. ^{1}H NMR ($CDCl_3$): δ (ppm) 5.84 (dd, 1H), 5.54 (dd, 1H), 2.70 (m, 1H), 2.05 1.8 (m, 3H), 1.85 (s, 6H), 1.68 (m, 1H), 1.40 (s, 3H), 1.30 (s, 3H), 1.29 (s, 3H). ^{13}C NMR ($CDCl_3$): δ (ppm) 169.95, 169.89, 132.40, 127.88, 83.79, 79.73, 43.62, 33.85, 25.26, 23.10, 22.74, 22.05, 21.49. m.p. 28-31°C. Elemental Analysis: 65.26% C, 8.61% H. R_f (20% EtOAc/hexane): 0.52. $[\alpha]_D25$=+73.5.degree. (c=0.99, $CHCl_3$).

One-Step Reaction - A 25 ml roundbottom flask with a stir bar was oven-dried, fitted with septa, and cooled under N_2. The diacetate (10) (126.9 mg, 0.499 mmol) and olivetol (90 mg, 0.499 mmol) were added. Anhydrous CH_2Cl_2 (8 ml) was added and stirred. The solution was cooled to -5°C. internal temperature. $BF_3(OEt)_2$ (64 µl, 1.0 eq.) was added. The solution gradually darkened to red. After 15 minutes, the reaction was quenched with 10% Na_2CO_3. The layers were separated and the organic layer was washed with 10% Na_2CO_3. The combined aqueous were extracted once with CH_2Cl_2. The organics were combined and washed with water and saturated NaCl solution, then dried over Na_2SO_4, filtered, and concentrated in vacuo to a tannish oil (0.132 mg). HPLC showed 88.8 area percent Δ^9-THC. Chromatography on silica gel yielded 95.9 mg (61.0% yield) of Δ^9-THC. HPLC showed 94.9 area percent Δ^9-THC.

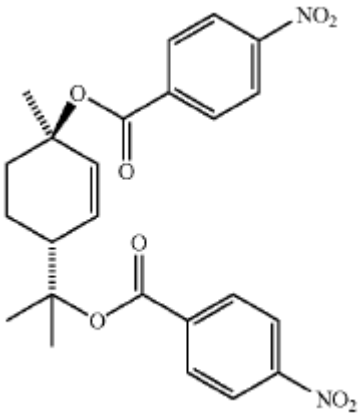
EXAMPLE 5 - One-Step Reaction of Dibenzoate (11) with Olivetol to Produce Δ^9-THC Preparation of Dibenzoate (11)



A 25 ml three-necked roundbottom flask with a stir bar was oven-dried, fitted with septa, and cooled under N_2. (+)-p-Menth-2-ene-1,8-diol (1.00 g) was added. Pyridine (6 ml, 12.6 eq.) was added and the pale yellow solution was stirred. N,N-dimethylaminopyridine (0.1435 g, 0.2 eq.) was added. Benzoyl chloride (2.73 ml, 4 eq.) was added. After 10 minutes, a solid precipitated. The slurry was allowed to stir overnight at room temperature. The reaction was quenched with water. The mixture was extracted three times with CH_2Cl_2. The organics were combined and washed with water and saturated NaCl (aq.), dried over Na_2SO_4, filtered and concentrated in vacuo. The oil was chromatographed on 25 g TLC mesh silica to yield colourless oil. The oil was cooled in dry ice and froze, but melted on warming to room temperature. ^{1}H NMR ($CDCl_3$): δ (ppm) 8.0 (dt, 4H), 7.51 (m, 2H), 7.40 (dt, 4H), 6.16 (dd, 1H), 5.88 (dd, 1H), 3.00 (m, 1H), 2.29 (m, 2H), 2.02 (m, 1H), 1.70 (s, 3H), 1.62 (s, 314), 1.60 (s, 3H), 1.25 (m, 1H). ^{13}C NMR ($CDCl_3$): δ (ppm) 165.53, 132.80, 132.53, 132.50, 131.77, 131.63, 129.40, 129.36, 128.39, 128.22, 128.16, 80.64, 44.55, 34.09, 25.81, 23.50, 23.10, 22.59, 21.99, 14.14, 14.05. Elemental Analysis: 76.21% C, 6.97% H. R_f (20% EtOAc/hexane): 0.57.

One-Step Reaction - A 25 ml roundbottom flask with a stir bar was oven-dried, fitted with septa, and cooled under N_2. The dibenzoate (11) (189 mg, 0.499 mmol) and olivetol (90 mg) were added. Anhydrous CH_2Cl_2 (8 ml) was added and stirred. The solution was cooled to -5°C. internal temperature. $BF_3(OEt)_2$ (64 µl, 1.0 eq.) was added. The solution gradually darkened to red. After 15 minutes, the reaction was quenched with 10% Na_2CO_3. The layers were separated and the organic layer was washed with water and saturated NaCl solution, then dried over Na_2SO_4, filtered, and concentrated in vacuo to oil. HPLC showed 78.8 area percent Δ^9-THC.

EXAMPLE 6 - One-Step Reaction of di-p-nitrobenzoate (12) with Olivetol to Produce Δ^9-THC Preparation of di-p-nitrobenzoate (12)



A 25 ml three-necked roundbottom flask with a stir bar was oven-dried, fitted with septa, and cooled under N_2. (+)-p-Menth-2-ene-1,8-diol (1.00 g) was added. Pyridine (6 ml, 12.6 eq.) was added and the pale yellow solution was stirred. N,N-dimethylaminopyridine (0.1435 g, 0.2 eq.) was added. p-Nitrobenzoyl chloride (4.58 ml, 4.2 eq.) was added. After a few minutes, tan solid precipitated. More pyridine (12 ml) was added. The slurry was allowed to stir overnight at room temperature. The reaction was quenched with water. The mixture was extracted three times with ethyl acetate. The organics were combined and washed twice with saturated NaCl (aq.), dried over Na_2SO_4, filtered and concentrated in vacuo to light yellow solid. The solid

was recystallized from isopropyl alcohol and dried under vacuum. The yield was 3.303 g (120% yield), which clearly still contained pyridine and isopropyl alcohol by NMR. It was dried more and then recrystallized from ethyl acetate/hexane to give a lightly coloured solid (1.89 g, 68.7%). .sup.1H NMR (d.sub.6-acetone) still seemed to have too many aryl protons. ^{1}H NMR ($CDCl_3$): δ (ppm) 8.3 8.2 (m, 4H), 8.2 8.1 (m, 4H), 6.14 (dd, 1H), 5.88 (d, 1H), 3.04 (m, 1H), 2.29 (m, 2H), 2.00 (m, 1H), 1.70 (s, 3H), 1.62 (s, 3H), 1.60 (s, 3H0, 1.67 1.65 (m, 2H). ^{13}C NMR ($CDCl_3$): δ (ppm) 164.275, 164.244, 151.00, 133.00, 131.46, 131.09, 131.04, 129.29, 124.00, 123.96, 87.04, 82.75, 45.00, 34.55, 26.10, 23.83, 23.45, 22.64. m.p>200^{o}C. (decomposition). Elemental Analysis: 59.68% C, 4.71% H, 6.07% N. Rf (20% EtOAc/hexane): 0.41. $[\alpha]_D$25=+38.0.degree. (c=0.21, $CHCl_3$).

One-Step Reaction - A 10 ml roundbottom flask with a stir bar was oven-dried, fitted with septa, and cooled under N_2. The di-p-nitrobenzoate (12) (116.5 mg) and olivetol (45 mg) were added. Anhydrous CH_2Cl_2 (4 ml) was added and stirred. The solution was cooled to -5^{o}C. internal temperature. $BF_3(OEt)_2$ (32 µl, 1.0 eq.) was added. The cloudy solution gradually darkened to orange. After 2 hours, the reaction was quenched with 10% Na_2CO_3. The layers were separated and the organic layer was washed with water and sat. NaCl, then dried over Na_2SO_4, filtered, and concentrated in vacuo to yellow oil. HPLC showed 71.5 area percent Δ^9-THC.

The chemical synthesis and isolation of Δ^9-THC are both challenging. Δ^9-THC is a very high boiling, viscous liquid. It is very prone to acid-catalysed isomerization to the thermodynamically more stable Δ^8-THC isomer, it is easily oxidized by oxygen to inactive cannibinol, and it is sensitive to light and heat. All of these factors make purification difficult, especially on an industrial scale, and chromatography has generally been used.

Previous syntheses of Δ^9-THC have tended to be either lengthy or low-yielding. Most involve coupling of a chiral terpene to a resorcinol derivative. The primary difficulty has been lack of selectivity in the coupling. Acid catalysed couplings have generally led to mixtures of products (*Crombie et al, J Chem Soc. Perkin Trans. I 1988 1243*). Attempts to avoid the selectivity problem by using base-catalysed coupling reactions have involved lengthier syntheses overall (*Rickards et al, J. Org. Chem. 1984 49 572*). Syntheses not using chiral terpenes have yielded racemic product (*Childers et al, J. Org. Chem. 1984 49 5276*).

In seemingly the best known method (US 5,227,537), Stoss claims that acid-catalysed coupling of (+)-p-menth-2-ene-1,8-diol (1) with olivetol (2) can be stopped at the intermediate Friedel-Crafts product (3), and then the intermediate (3) can be isolated and converted in good yield to . Δ^9-THC using $ZnBr_2$ (24 hours, refluxing CH_2Cl_2). The present inventors have encountered several problems with this scheme. The initial p-toluenesulfonic acid catalysed Friedel-Crafts reaction was difficult to stop cleanly at the intermediate (3) under Stoss' conditions and gave mixtures of the intermediate (3) and Δ^9-THC, the ring-closed product. Any Δ^9-THC formed is likely to isomerize to Δ^8-THC under the disclosed conditions. The use of a heavy metal such as $ZnBr_2$ in the last step of an industrial process is highly undesirable as it may lead to traces of metal in the product, and this is especially undesirable for pharmaceuticals. Stoss' method therefore appears to offer no real advantage in yield or purity of Δ^9-THC over a one-pot coupling that goes directly to Δ^9-THC. Razdan has published a one-pot method for coupling of (+)-p-menth-2-ene-1,8-diol (1) with olivetol (2) to produce Δ^9-THC (*Razdan et al, Tet. Lett. 1983 24 3129*). This also suffers from several problems: it uses nearly 14 equivalents of ZnCl.sub.2 as the acid, and uses six equivalents of olivetol (2). Even under these conditions, the yield is still only 28% from (+)-p-menth-2-ene-1,8-diol (1).

B)

The proposed invention is for a safe method of stopping a stolen car without chasing at high speeds, utilizing a bar code implanted between the inner layer and outer layer of a rear safety glass is comprised of steps: 1) scan the barcode, 2) compare the read in barcode with those of the stolen cars stored in the police computer net, 3) trigger one of the three stopping means of this invention. Those three stopping means are: 1) turn off the engine, 2) puncture the rear tires with bullets, and 3) puncture the rear tires by mechanical means.

The invention is explained with the help of the following figures:-

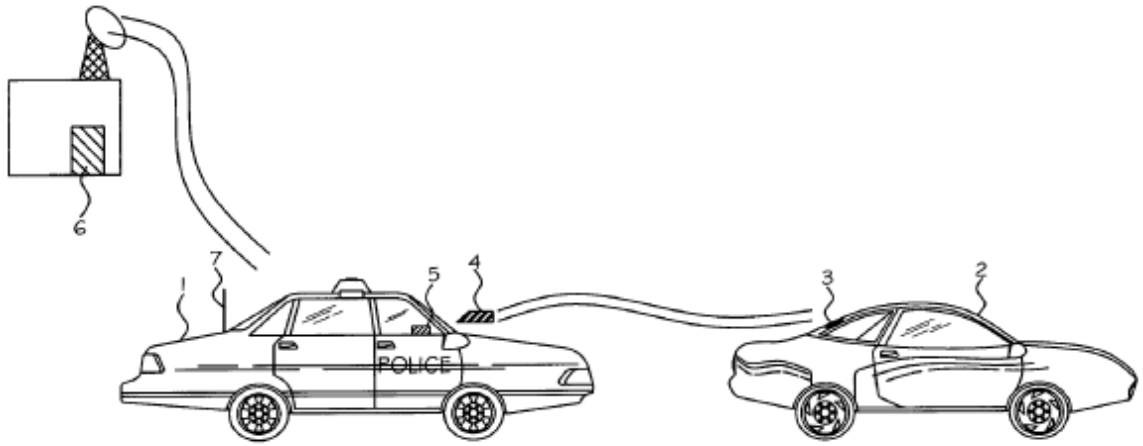


FIG. 1

FIG. 1 is a schematic diagram of stopping a stolen car. When a police car (1) on patrol finds a suspicious car (2), the police officer in the car (not shown in the figure) starts scanning the bar code (3) of the suspicious car (2) with portable bar code scanner (4) which is connected to a police mobile computer (5) installed in the police car (1). The mobile computer (5) is connected to the main police host computer (6) by wireless radio (7). The bar code (3) used for the above purpose is installed on the rear safety glass (8) as shown in FIG. 2.

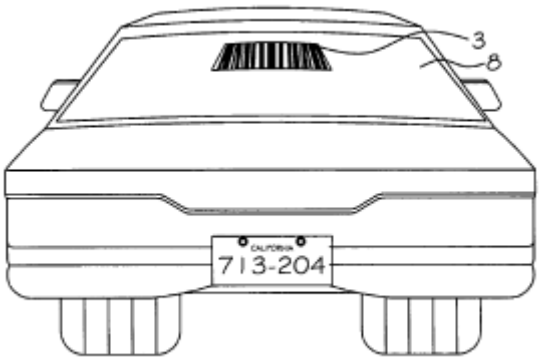


FIG. 2

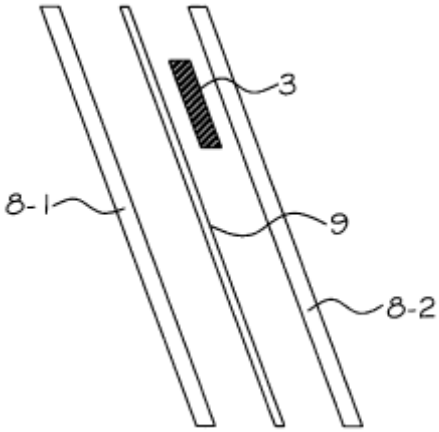


FIG. 3

FIG. 3 is a cross sectional view of the bar code (3) embedded between two glasses. To avoid damage and change, the bar code (3) is inserted between inner- and outer layer glasses (8-1 and 8-2) and outer side of the safety film (9), which is made of transparent adhesive elastic polymer.

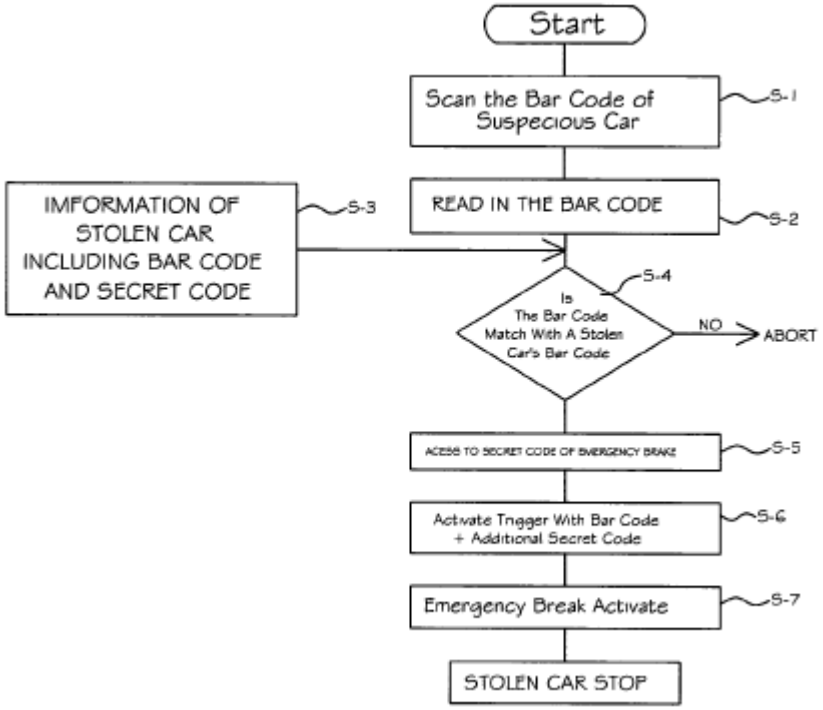


FIG. 4

FIG. 4 is a schematic logic diagram of stolen car stopping method. When a police officer scans the bar code (3) on a suspicious car (2) in step S-1, the code on the suspicious car (2) is read in by the same scanner (4) in step S-2. The read of the bar code information is transferred to the mobile computer (5) installed in the police car (1). At the same time, the police officer requests the updated list of stolen cars and their information, including the bar codes, to the host computer (6) of police department in step S-3.

In step S-4, the bar code (3) of the suspicious car (2) is compared with the bar codes of stolen cars. If there is no matched bar code, the procedure is aborted. If there is a bar code match with the bar code (3) of the suspicious car (2), go to step S-5.

In step S-5, a secret code for the emergency brake, which is provided from the original owner and manufacturer, is opened to the police officer when the bar code (3) of the suspicious car matches with one of the stolen cars.

In step S-6, the police officer sends a signal activating the emergency brake to the central process computer or electric trigger of the suspicious car with the bar code (3) information and an additional secret code for emergency brake.

In step S-7, the emergency brake system of the car is activated and the suspicious car (2) stops.

Three emergency brake systems are illustrated as follows in Fig. 5,6 and 7:

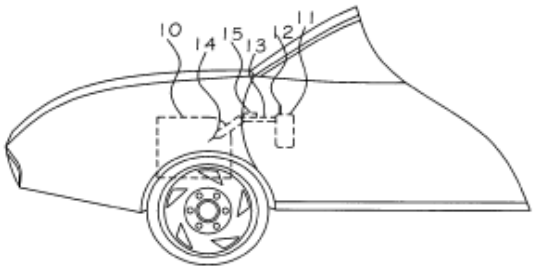


Fig 5

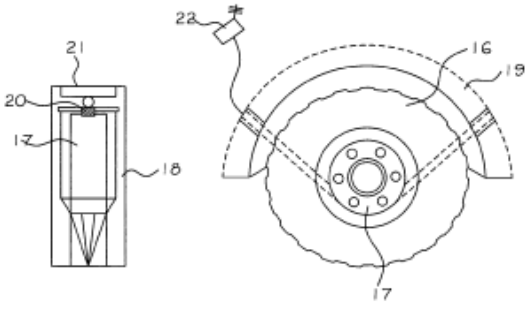


Fig 6

FIG. 5 is a schematic diagram of emergency brake system that turns off the car's engine (10). For this purpose, the main computer (11) of the car has a wireless data input means (12) for receiving the bar code (3) and the secret code, and has a program to disconnect the power supply (13) to the ignition plug (14)

activated by the bar code and the secret code. The other way is to install a power disconnector (15), which is activated by the bar code and secret code, in the middle of the power line to the ignition plug.

FIG. 6 is a schematic diagram of emergency brake system of puncturing rear tires (16) with bullets (17). Two sets of one bullet (17) in a short barrel (18) are installed at the inside of one rear wheel cover (19). Another two sets of bullet (17) in a short barrel (18) are installed at the inside of rear wheel cover of opposite site. The percussion (20) of the bullet (17) is connected to an electric trigger line (21). The electric trigger line is connected to the main computer (11) of FIG. 5. or another wireless trigger (22) responding to the bar code (3) information with another secret code.

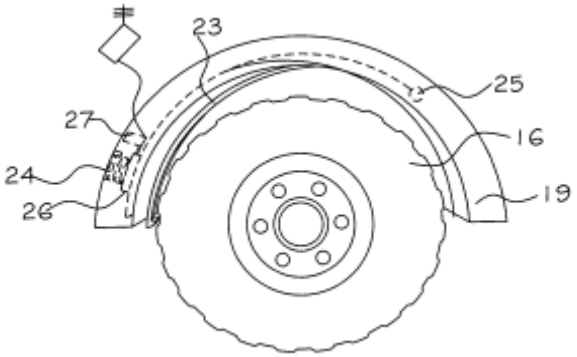


Fig 7

FIG. 7 is a schematic diagram of emergency brake system of puncturing rear tires (16) with hook blades (23). One hook blade (23) connected to a spring (24) is installed at the inside of rear wheel cover. Another set of hook blades (23) connected to a spring (24) is installed at the inside of another rear wheel cover of opposite side. One end of the hook blade (23) is pivotally fixed to the rear wheel cover (19) with bolt and nut (25). The other side of the hook blade (23) is captured by a trigger (26), which is connected to an electric trigger line (27). The electric trigger line is connected to the main computer (11) of FIG. 5 or another wireless trigger (21) responding to the bar code (3) information with another secret code.

US 5,415,553 to Szmidla illustrates a device for identifying an object that includes a graphic representation of an object and an omni directional bar code representing information relative to the object. Using a bar code reader connected to a transducer that converts the bar code into humanly detectable signals, the user can scan the bar code in any direction to learn the name of the object or other information about the object. US 6,283,375 to Wilz, Sr., *et al.* illustrates a hand-held, automatically activated barcode reading mechanism with a manually activated data transmission switch. US 6,283,370 to Watanabe, *et al.* illustrates a bar code reader, bar code reading method and computer readable medium. US 2001/0001131 to Miller illustrates a process and apparatus for the preparation of custom blended fuels. A bar code on a fuel tank or vehicle, such as an automobile, is scanned by a bar code reader operatively associated with a fuel dispensing means to convey information about a fuel required or desired to a computer controlled customized blender associated with the fuel dispensing means. US 2002/0020742 to Streicher, *et al.* illustrates a fuel dispensing system wherein the fuel is provided only to authorize vehicles through verification of identification information, such as scanning a bar code disposed on the vehicle or fuel storage container. None of the prior art illustrates a car stopping method utilizing a bar code as demonstrated in this invention.

Utilizing a bar code implanted between the inner layer and outer layer of a rear safety glass, this invention provides a safe method of stopping a stolen car without chasing at high speeds. The method is comprised of three steps 1) scanning the barcode, 2) comparing the read in bar code with the stolen car list in police computer net, 3) activating the trigger of one of three stopping means of this invention. The three stopping means are 1) turning off the engine by cutting the electricity supplied to the engine, 2) puncturing the rear tires with pistol bullets which are installed inside of rear wheel cover, and 3) puncturing the rear tires by mechanical means, which also are installed inside of the rear wheel cover. When a police identifies a stolen car, the police will activate the trigger of the stolen car by transferring the bar code of the stolen car to the trigger installed in the stolen car. Then the stolen car will stop immediately by one of the stopping means, i.e., the engine of the stolen car will stop if the stopping means is turning off the engine. If the stopping means are puncturing the rear tires, the stolen car will come to halt due to the punctured rear tires. These bar codes will allow police to identify stolen cars even if the license plate or the paint job on a car has been changed.