Access to Trifluoromethylindanes; Cycloalkylation of β-Phenyl Trifluoromethyl Ketones, β-Keto Esters, and Alcohols

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Cycloalkylation of β-phenyl trifluoromethyl ketones, β-keto esters, and alcohols provides indanic compounds bearing a CF_3 group.

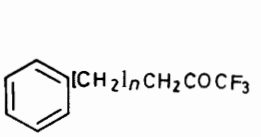
New methods are needed for the synthesis of alicyclic compounds containing the trifluoromethyl group, in view of the increased interest in this unit which affords special electronic effects and enhanced lipophilicity. We have recently reported a route to 1-trifluoromethyltetralins by Friedel–Crafts cyclization of ω-aryl trifluoromethyl alcohols [1] and ketones.[2] In spite of the well known difficulty of five-membered-ring formation,[3,4] we have attempted to prepare 1-trifluoromethylindane derivatives by intramolecular Friedel–Crafts alkylation of β-aryl trifluoromethyl ketones, alcohols, and non-enolizable β-keto esters. Some attempts at cyclization of δ-aryl trifluoromethyl ketones and alcohols to seven-membered rings have been performed.

Results

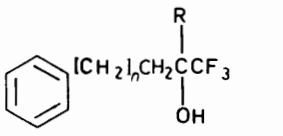
Ketone (**1b**) reacts with $AlCl_3$ or $TiCl_4$ (1 mol equiv.) to give, at low temperature, the tetralol (**2b**); at 0 °C this leads to the chloride (**3b**) or the tetralin (**4b**) when the reaction is performed in benzene.[2] On the other hand, ketone (**1a**) did not react with $TiCl_4$ (run 1), and reacted very slowly with $AlCl_3$ to afford polymeric materials (run 2) (Table 1). So, we have attempted cyclization of ketones (**1a**) and (**1b**) in the presence of ethyl- or methylaluminium dichloride. At −78 °C, ketone (**1a**) could not cyclize with $EtAlCl_2$, but led to the reduced product (**12a**) (run 3); on the other hand, ketone (**1b**) afforded mainly the cyclized alcohol (**2b**) (60%) (run 6). Ketone (**1a**) did not react, at −78 °C, with 1 equiv. of $MeAlCl_2$; with 2 equiv. of $MeAlCl_2$, the reaction was complete when the temperature was allowed to rise to 0 °C, and led to a mixture of the indanol (**2a**) (30%) and the indane (**5a**) (20%) (run 5). In the same conditions, ketone (**1b**) afforded the tetralol (**2b**) in high yield (78%) (run 8). When reactions were performed with $AlCl_3$ in the presence of benzene (Table 2), the 1-phenylindane (**4a**) was obtained from ketone (**1a**) in excellent yield (77%), whereas ketone (**1b**) led, in the same conditions, to chloride (**3b**), a longer time of reaction being necessary for the introduction of benzene (runs 11 and 12). In solvolytic conditions (CF_3CO_2H, H_2SO_4), the 1-phenylindane (**4a**) was obtained from tertiary alcohol (**14a**), as well as in the tetralin series,[1] but with a lower yield (Table 3, run 14).

The attempted cyclizations of δ-phenyl ketone (**1c**) and alcohol (**14c**) to seven-membered-ring compounds failed; only polymeric and nucleophilic addition products or starting materials were recovered (runs 9 and 13).

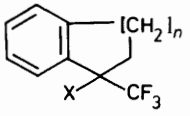
The reactions of β-keto esters (**6**), (**7**), and (**8**), with $EtAlCl_2$ (3 mol equiv.) led respectively to the 1-trifluoromethyl indan-1-ols (**9**), (**10**), and (**11**) in 90% yield,† without any formation of reduced products (Table 4). Reactions with $TiCl_4$ were faster, and needed only 1 mol equiv. of Lewis acid. The reactions are stereoselective: only one diastereoisomer was obtained. The *cis* relationship between hydroxy and carboxylate stereocentres was established on the basis of i.r. absorption frequencies of the O–H and C=O stretches which indicate strong intramolecular H-bonding.[6,7],‡ In the same solvolytic conditions as for compounds (**14**), the indanol (**11**) was partly cyclized into tetracyclic compound (**17**), bearing an angular trifluoromethyl group, and also gave the fragmented ester (**18**).



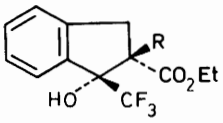
(**1**) a; n = 1
b; n = 2
c; n = 3



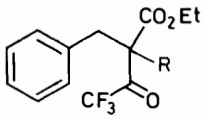
(**12**) R = H
(**13**) R = Me
(**14**) R = Ph
a; n = 1, b; n = 2, c; n = 3



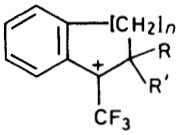
(**2**) X = OH
(**3**) X = Cl
(**4**) X = Ph
(**5**) X = H



(**9**) R = CH_2CH_2Me
(**10**) R = $CH_2CH{=}CH_2$
(**11**) R = CH_2Ph



(**6**) R = CH_2CH_2Me
(**7**) R = $CH_2CH{=}CH_2$
(**8**) R = CH_2Ph



(**15**) R = R' = H
(**16**) R = CO_2Et, R' = CH_2Ph

Discussion

These results show clearly the great difference of reactivity between β-, γ-, and δ-aryl trifluoromethyl ketones. As expected,

† The enolizable ethyl α-benzyltrifluoroacetoacetate did not cyclize with Lewis acid, but gave a metallic chelate.

‡ The procedure of conversion of β-hydroxy ester (**11**) into β-lactone as evidence of this *cis* relationship as in ref. 6 led to 2-benzyl-1-trifluoromethylindane. Nevertheless, the formation of this olefin confirms indirectly the *cis* relationship between the hydroxy and ethoxycarbonyl groups, since it is very probable that this olefin would be formed from the benzylic and very strained β-lactone.[7]

Table 1. Cycloalkylation of ketones (**1**) by Lewis acid

Run	Ketone[a] 10^{-4}M	Lewis acid (mol equiv.)	Conditions Temp./°C (*t*/h)	Solvent	Yield[b] Cyclized products (**2**)	(**3**)	(**5**)	Other products (**1**)[f]	(**12**)	(**13**)
1	(**1a**)	$TiCl_4$ (2)	0(2.5)	CH_2Cl_2				98		
2	(**1a**)	$AlCl_3$ (1)[c]	0(0.5)	CH_2Cl_2		9		65		
3	(**1a**)	$EtAlCl_2$ (2)	−78(0.5)	Hexane				18(15)	80(75)	
4	(**1a**)	$MeAlCl_2$ (1)	−78(0.5)	Hexane				96		
5	(**1a**)[d]	$MeAlCl_2$ (2)	−78 to 0(1.5)	Hexane	30(25)	2	20(17)	7(5)		10(7)
6	(**1b**)	$EtAlCl_2$ (1)	−78(0.5)	Hexane	60			3	30	
7	(**1b**)	$MeAlCl_2$ (1)	−78(0.5)	Hexane	19			64		
8	(**1b**)[e]	$MeAlCl_2$ (2)	−78 to 0(1.5)	Hexane	78(75)	2	6			
9	(**1c**)	$MeAlCl_2$ (2)	−78 to 0(1.5)	Hexane						18

[a] Ketones (**1a**) and (**1c**) were prepared by alkylation of ethyl 4,4,4-trifluoroacetoacetate;[5a] for ketone (**1b**), see ref. 13. [b] Yields estimated by g.l.c. with an internal standard. The parenthetic values are yields of isolated pure products. [c] Remaining products were polymeric materials. Using $AlCl_3$ (2 mol equiv.) or with a longer reaction time, no starting material was recovered, but only polymeric materials. [d] With a longer reaction time, the chloride (**3a**) was formed from the indanol (**2a**), and was then converted into polymeric materials. [e] On using $AlCl_3$ or $TiCl_4$ at 0 °C for 3 h, ketone (**1b**) gave the chloride (**3b**) in high yield.[2] [f] Recovered starting material.

Table 2. Cycloalkylation of ketones (**1**) by $AlCl_3$ in the presence of benzene[a]

Run	Ketone	Cyclized product yield[b] (**2**)	(**3**)	(**4**)	Starting material recovery (**1**)
10	(**1a**)			77(72)	
11	(**1b**)		90(82)	4	
12[c]	(**1b**)		7	55(52)	
13	(**1c**)				95

[a] Reactions were conducted at −78 °C by adding $AlCl_3$ (2 mol equiv.) to a 1 × 10^{-4}M solution of a ketone (**1**) in a mixture CH_2Cl_2–C_6H_6 (1:1), then warming to 0 °C for 1 h. [b] Yields estimated by g.l.c. with an internal standard. The parenthetic values are yields of isolated pure products. [c] In addition the reaction mixture was kept 3 h at 0 °C, or warmed to 5 °C for 4 h.[2]

Table 3. Cycloalkylation of alcohols (**14**) and (**11**)

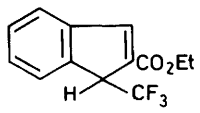
Run	Alcohol[a]	Time/h	Product	Yield[b]
14	(**14a**)	1	(**4a**)	53[c](100)
15[d]	(**14b**)	0.5	(**4b**)	83
16	(**14c**)	1		
17	(**11**)	0.3	(**17**)	20(39)
			(**18**)	25(43)

[a] Solution of 7 × 10^{-2}M of (**14**) or (**11**) in CF_3CO_2H (2 × 10^{-2}M) in H_2SO_4. [b] Yields of pure isolated products; the parenthetic values were determined by g.l.c. analysis. [c] No starting material was recovered, compound (**4**) was the only product detected; remaining products were polymeric materials. [d] Ref. 1.

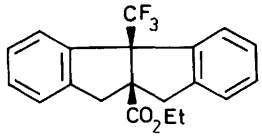
Table 4. Cycloalkylation of β-keto esters (**6**), (**7**), and (**8**)[a]

Run	Keto ester[b]	Lewis acid	Time/h	Indanol	Yield[c]
18	(**6**)	$TiCl_4$ (1.1)	7	(**9**)	85(75)
19	(**6**)	$EtAlCl_2$ (1.1)	16	(**9**)	23[d]
20	(**6**)	$EtAlCl_2$ (3)	3.5	(**9**)	83(78)
21	(**7**)	$TiCl_4$ (1.1)	4.5	(**10**)	93(77)
22	(**7**)	$EtAlCl_2$ (3)	3	(**10**)	95(80)
23	(**8**)	$TiCl_4$ (1.1)	3.5	(**11**)	83(77)
24	(**8**)	$EtAlCl_2$ (3)	6	(**11**)	85(80)

[a] Reactions were conducted, at 0 °C, by adding $TiCl_4$ to a 0.1M solution of β-keto ester in CH_2Cl_2, or by adding $EtAlCl_2$ (1M in hexane) to a 4 × 10^{-2}M solution of β-keto ester in CH_2Cl_2. [b] Prepared by dialkylation of ethyl 4,4,4-trifluoroacetoacetate.[5a] [c] Yields determined by g.l.c.; the parenthetic values are isolated yields of pure material. [d] 77% of starting material (**6**) was recovered too.



(**18**)



(**17**)

the six-membered-ring cyclization rate is greater than the five-membered-ring cyclization one, and much greater than the seven-membered-ring cyclization rate. Another interesting aspect is the difference in behaviour of benzylic derivatives (**2**) and (**3**) in the tetralin and in the indane series. In the tetralin series, products (**2b**) and (**3b**) are stable in the reaction medium; this remarkable stability of the tertiary benzylic alcohol (**2b**) and chloride (**3b**) under Lewis acid conditions is due to the destabilization of the incipient carbenium ion (**15b**) by the electron-withdrawing CF_3 group. In the indane series, this destabilization is partially compensated for by the great stability due to the indanyl structure of ion (**15a**).[8,9] Consequently, in the reaction medium, as soon as the indanol (**2a**) is formed, it gives, more or less quickly depending on the Lewis acid, *via* the chloride (**3a**), polymeric materials (runs 2 and 5) and also some of the unexpected reduced indane (**5a**) with $MeAlCl_2$* (run 5). On the other hand, if the reaction is performed in the presence of a good cation trap, *e.g.* benzene, a high yield of arylated indane is obtained. From chloride (**3b**), the Friedel–Crafts arylation is slower, as expected for the more destabilized incipient carbenium ion (**15b**).

In the solvolytic process, the moderate yield of cyclization from the alcohol (**14a**), in comparison with (**14b**), could be explained by the slower five-membered cyclization that allows intermolecular processes (*i.e.*, elimination, and therefore

* The reduction of a carbenium ion, or the nucleophilic displacement of a tertiary chloride, is well known with $EtAlCl_2$, but is not usual with $MeAlCl_2$.[10,11] Nevertheless, we showed that the chloride (**3b**) when treated with $MeAlCl_2$ (2 equiv.) gave, as a single product, the reduced tetralin (**5b**) (62%).

formation of polymeric materials) to occur. The failure of cyclization with compound (**14c**) to give a seven-membered ring confirms this point of view.

The steric hindrance of the ketonic group of β-keto esters (**6**), (**7**), and (**8**) would be expected to slow down cyclization rates but also to suppress nucleophilic side-reactions. Effectively, cyclization rates from these β-keto esters did slow down with $EtAlCl_2$ and no reduction product was obtained, while it is the major product from ketone (**1a**). In contrast, compared with ketone (**1a**), the rates of cyclization of β-keto esters (**6**), (**7**), and (**8**) are very much increased with $TiCl_4$. This difference between $EtAlCl_2$ and $TiCl_4$ cannot be explained without assuming the occurrence of a peculiar stabilization of the intermediate complex between the β-keto ester and Lewis acid. This complexation of ketone and ester groups by a Lewis acid is undoubtedly the root cause of the stereospecificity of the reaction and the *cis* relationship between the hydroxy and ethoxy carbonyl groups.[6]

The surprising stability of tertiary benzylic indanols (**9**), (**10**), and (**11**), in Lewis acid medium contrasts with that of compounds (**2a**) and (**3a**). This is certainly due first to the impossibility of an elimination process (responsible for oligomer formation) and, second, to the steric hindrance which prevents any further nucleophilic substitution on the C-1 carbon. This stability explains the highly selective yield of indanols (**9**), (**10**), and (**11**). In solvolytic conditions, the indanol (**11**) gives the cation (**16**), and this latter cyclizes into the congested tetracyclic compound (**17**). However, because of the steric hindrance on the C-1 carbon, the cyclization is slowed down. Competitively, the cation (**16**) can undergo a fragmentation reaction[12] since there is no α-hydrogen, finding it easier to lose a relatively stable tropylium cation[12c] than to cyclize. Isomerization of the double bond then leads to the olefinic ester (**18**).

These results show the possibility of Friedel–Crafts cyclization as a route to 1-trifluoromethyl indanes as well as to 1-trifluoromethyltetralins. In particular, it is possible to obtain in this way highly functionalized trifluoromethyl indanols and 1-arylindanes in high yields.

Experimental

^1H and ^{19}F n.m.r. were recorded on a Varian EM360 apparatus (60 MHz for ^1H and 56 MHz for ^{19}F) and a Bruker AM300 (300 MHz) for $CDCl_3$ solutions with Me_4Si or $CFCl_3$ as internal standard where appropriate. ^{13}C N.m.r. spectra were determined on a Varian CFT20 (20 MHz) and a Bruker AM300 (75 MHz) for $CDCl_3$ solutions (Me_4Si as internal standard). Reported signal multiplicities are related to C–F coupling. Mass spectra were obtained on a Nermag R10-10 apparatus coupled to a gas-phase chromatograph (capillary column CPSIL-5, 25 m) and on a Kratos MS50 spectrometer. Gas chromatographic analysis was performed on a Carlo Erba 4130 chromatograph (capillary column SE30, 10 m or 25 m). FT i.r. spectra were recorded in CCl_4 and in $CHCl_3$ solutions on a Bruker 45 spectrometer. $TiCl_4$ was purchased from Aldrich, and $EtAlCl_2$ and $MeAlCl_2$ were purchased from Aldrich as 1M solutions in hexane.

Lewis Acid-facilitated Ketone Cyclization.—Unless otherwise specified, reactions were performed in dry solvents under argon, with reaction volume adjusted to produce a solution ~0.1M in ketones (**1a**) or (**1b**), or 0.04M in β-keto ester (**6**), (**7**), or (**8**). Solutions were cooled to the desired temperatures and the Lewis acid was added dropwise through a septum cap or in small portions. When starting material had disappeared, the mixture was hydrolysed with an equal volume of saturated aqueous NH_4Cl. The resulting mixture was allowed to come to room temperature and extracted with ether. The extracts were washed twice with brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The crude product was further purified by column chromatography (SiO_2 60, 70—230 mesh) using usually pentane, and then pentane–ether (95:5) as eluant.

Attempted Cyclization of Ketone (**1a**).— *With* $EtAlCl_2$ (*run* 3). Reaction of compound (**1a**) (500 mg, 2.5 mmol) in hexane (20 ml) with $EtAlCl_2$ (5 ml of a 1M solution in hexane, 5 mmol) for 30 min at −78 °C gave, after work-up, a crude product (490 mg). Chromatography on SiO_2 yielded starting material (**1a**) (75 mg, 15% recovery) and the alcohol (**12a**) (375 mg, 75%); δ_H 1.3—3 (5 H, m), 3.8 (1 H, m, *H*COH), and 7.1—7.3 (5 H, m, Ph); δ_F −80.4 (d, *J* 6 Hz).

With $MeAlCl_2$ (*run* 5). A solution of (**1a**) (1 g, 5 mmol) in hexane (40 ml) with $MeAlCl_2$ (10 ml of a 1M solution in hexane, 10 mmol) was stirred for 30 min at −78 °C, then warmed slowly to 0 °C for 1 h. After work-up, crude product (950 mg) was chromatographed on SiO_2 to give successively the indane (**5a**) (80 mg, 17%), the chloride (**3a**) (traces), the starting material (**1a**) (25 mg, 5% recovery), the indanol (**2a**) (140 mg, 25%), and the alcohol (**13a**) (35 mg, 7%).

Compound (**5a**) showed M^+, 186.0660 ($C_{10}H_9F_3$ requires *M*, 186.0656); δ_H 2.2—3.2 (4 H, m), 3.6 (1 H, m), and 7.0—7.4 (4 H, m, ArH); δ_C 23.7, 39.8, 49.0 (q, *J* 28 Hz, *C*CF_3), 124.2, 125.1, 126.7, 127.6 (q, *J* 283 Hz, CF_3), 128.4, 141.9, and 145.0; δ_F −71 (d, *J* 6 Hz); *m/z* 186 (M^+, 29%), 117 ($M^+ - CF_3$, 100), 115 (31), and 91 (10).

Compound (**3a**) showed M^+, 220.0263 ($C_{10}H_8{}^{35}ClF_3$ requires *M*, 220.0266); δ_H 2.2—3.1 (4 H, m) and 7.2—7.8 (4 H, m, ArH); δ_C 29.9, 38.0, 74.2 (q, *J* 32 Hz, *C*CF_3), 125.0 (q, *J* 280 Hz, CF_3), 125.0, 127.6, 130.6, 138.1, and 144.0; δ_F −76.3 (s); *m/z* 220 (M^+, 58%), 222 (M^+, 14), 185 ($M^+ - Cl$, 100), 165 (66), 151 (27), 115 (100), and 63 (19).

Compound (**2a**) showed M^+, 202.0601 ($C_{10}H_9F_3O$ requires *M*, 202.0605); δ_H 2.1—3.1 (5 H, m) and 7.0—7.2 (4 H, m, ArH); δ_C 29.5, 35.4, 83.6 (q, *J* 30 Hz, *C*CF_3), 124.2, 125.2, 125.9 (q, *J* 283 Hz, CF_3), 127.2, 130.2, 139.2, and 144.0; δ_F −81.0 (s); *m/z* 202 (M^+, 24%), 133 ($M^+ - CF_3$, 3), and 91 (100).

Compound (**13a**) showed M^+, 218.0919 ($C_{11}H_{13}F_3O$ requires *M*, 218.0918); δ_H 1.3 (3 H, s, Me), 1.6—2.8 (5 H, m), and 7.0—7.2 (5 H, m, ArH); δ_C 20.2, 29.0, 37.0, 75.3 (q, *J* 30 Hz, *C*CF_3), 126.2, 126.5 (q, *J* 283 Hz, CF_3), 128.3, 128.6, and 141.2; δ_F −83.5 (s); *m/z* 218 (M^+, 25%), 200 ($M^+ - H_2O$, 7), 131 (52), 105 (36), and 91 (100).

With $AlCl_3$ *in benzene* (*run* 10). A solution of ketone (**1a**) (500 mg, 2.5 mmol) in CH_2Cl_2 (12.5 ml) and benzene (12.5 ml) containing $AlCl_3$ (680 mg, 5 mmol) was stirred for 30 min at −78 °C, then warmed to 0 °C for 1 h. The crude product obtained on work-up (510 mg) was purified by filtration through a short column of silica gel (pentane) to give the indane (**4a**) (470 mg, 72%) (Found: M^+, 262.0963. $C_{16}H_{13}F_3$ requires *M*, 262.0969); δ_H 2.4—3.0 (4 H, m) and 7.0—7.45 (9 H, m, ArH); δ_C 30.0, 36.8, 62.1 (q, *J* 28 Hz, *C*CF_3), 125.1, 126.2, 126.7, 127.6, 127.9 (q, *J* 282 Hz, CF_3), 128.2, 128.5, 129.1, 129.4, and 144.6; δ_F −70 (s).

Cyclization of Ketone (**1b**).—*With* $EtAlCl_2$ (*run* 6). Reaction of ketone (**1b**) (300 mg, 1.41 mmol) in hexane (13 ml) with $EtAlCl_2$ (1.5 ml of a 1M solution in hexane, 1.5 mmol) for 30 min at −78 °C gave a crude product (280 mg), a mixture of alcohols (**2b**)[2] and (**12b**)[1] (65:35).

With $MeAlCl_2$ (*run* 8). A solution of ketone (**1b**) (530 mg, 2.5 mmol) in hexane (20 ml) with $MeAlCl_2$ (5 ml of a 1M solution in hexane, 5 mmol) was stirred for 30 min at −78 °C, then was warmed slowly to 0 °C for 1 h. After work-up, the crude product

(450 mg) was chromatographed on SiO_2 to give the alcohol (**2b**)[2] (405 mg, 75%).

With $AlCl_3$ *in benzene* (*run* 11). A solution of ketone (**1b**) (530 mg, 2.5 mmol) in CH_2Cl_2 (12.5 ml) and benzene (12.5 ml) containing $AlCl_3$ (680 mg, 5 mmol) was stirred for 30 min at −78 °C, then warmed to 0 °C for 1 h. The crude product obtained on work-up (520 mg) was eluted on an SiO_2 column to give the chloride (**3b**)[2] (480 mg, 82%).

(*Run* 12). A solution of ketone (**1b**) (530 mg, 2.5 mmol) in CH_2Cl_2 (12.5 ml) and benzene (12.5 ml) containing $AlCl_3$ (680 mg, 5 mmol) was stirred for 15 min at −78 °C, then warmed to 0 °C during 1 h, and stirred for 3 h at 0 °C. The crude product obtained on work-up (450 mg) was purified by SiO_2 chromatography to give compound (**4b**)[2] (360 mg, 52%).

Reactions with Ketone (**1c**).—*With* $MeAlCl_2$ (*run* 9). A solution of ketone (**1c**) (230 mg, 1 mmol) in hexane (8 ml) containing $MeAlCl_2$ (2 ml of a 1M solution in hexane, 2 mmol) was stirred for 30 min at −78 °C, then warmed to 0 °C for 1 h. The crude product (200 mg) was eluted on an SiO_2 column to give the alcohol (**13c**) (45 mg, 18%); δ_H 1.3 (3 H, m, Me), 1.4—2.4 (7 H, m, $CH_2CH_2CH_2$ and OH), 2.5—2.9 (2 H, m, CH_2Ph), and 7.2 (5 H, s, ArH); δ_F −84 (s).

With $AlCl_3$ *in benzene* (*run* 13). A solution of ketone (**1c**) (230 mg, 1 mmol) in CH_2Cl_2 (5 ml) and benzene (5 ml) containing $AlCl_3$ (270 mg, 2 mmol) was stirred for 30 min at −78 °C, then warmed to 0 °C for 1 h. The crude product obtained on work-up (230 mg) was eluted on an SiO_2 column to give the starting material (**1c**) (215 mg, 94% recovery).

Solvolysis of the Alcohol (**14a**) (*Run* 14).—Alcohol (**14a**) (500 mg, 1.8 mmol) was dissolved in a 0.2M solution of H_2SO_4 in trifluoroacetic acid (TFA) (25 ml) and the solution was refluxed (72 °C) for 1 h. The TFA was evaporated off under reduced pressure. After being cooled, the mixture was diluted with CH_2Cl_2, washed successively with aqueous sodium hydrogen carbonate and water, dried, and evaporated to dryness. Chromatography on silica gel with pentane yielded the indane (**4a**) (200 mg, 53%).

Solvolysis of the Alcohol (**14c**) (*Run* 16).—Alcohol (**14c**) (200 mg, 0.7 mmol) was dissolved in a 0.2M solution of H_2SO_4 in TFA (10 ml) with an internal standard [1-bromo-3-(*m*-chlorophenyl)propane] and the solution was refluxed for 1 h. G.l.c. monitoring showed the progressive disappearance of starting material. Work-up and chromatography gave only polymeric materials besides the internal standard.

Solvolysis of the Indanol (**11**) (*Run* 17).—Indanol (**11**) (540 mg, 1.5 mmol) was dissolved in a 0.2M solution of H_2SO_4 in a mixture of TFA (5 ml) and CH_2Cl_2 (5 ml) and the solution was refluxed for 20 min. Work-up and chromatography on SiO_2 (pentane–Et_2O, 99:1) gave the indane (**18**) (96 mg, 25%), *m/z* 256 (M^+, 91%), 228 (12), 211 (100), 197 (33), 183 (62), 164 (56), 133 (62), and 115 (37); δ_H(300 MHz) 1.35 (3 H, t, *J* 7 Hz, OCH_2Me), 4.33 (2 H, q, *J* 7 Hz, OCH_2Me), 4.54 (1 H, q, *J* 8.4 Hz, $CHCF_3$), and 7.21—7.82 (5 H, m, ArH); δ_F −67 (d, *J* 9 Hz, $CHCF_3$); δ_C 14.2, 53.0 (q, *J* 30 Hz, CCF_3), 61.0, 124, 125.2 (q, *J* 280 Hz, CF_3), 125.4, 128.8, 129.1, 145.6, and 163.6; and then tetracyclic compound (**17**) (104 mg, 20%); *m/z* 346 (M^+, 28%), 273 (43), 272 (99), 233 (32), 203 (100), 101 (21), and 91 (27); δ_H(300 MHz) 1.16 (3 H, t, *J* 7 Hz, OCH_2Me), 2.95 and 3.83 (4 H, q, J_{AX} 16 Hz, 2 × CH_2), 4.15 (2 H, q, *J* 7Hz, OCH_2Me), and 7.28 and 7.47 (8 H, m, 2 × C_6H_4); δ_F −69.4 (s); δ_C 13.7, 41.8, 61.4, 63.4, 72.7 (q, *J* 28 Hz, CCF_3), 124.6, 124.7, 126.4 (q, *J* 223 Hz, CF_3), 127.3, 128.6, 138.4, 142.7, and 172.8.

Cyclization of β-*Keto Ester* (**6**).—*With* $TiCl_4$ (*run* 18). A solution of β-keto ester (**6**) (400 mg, 1.3 mmol) in CH_2Cl_2 (13 ml) was stirred with $TiCl_4$ (271 mg, 1.43 mmol) for 7 h at 0 °C. After the usual work-up, the crude product (370 mg) was chromatographed on SiO_2 to give the *indanol* (**9**) (300 mg, 75%) (Found: M^+, 316.1285. $C_{16}H_{19}F_3O_3$ requires *M*, 316.1286); δ_H(300 MHz) 0.96 [3 H, m, $(CH_2)_2Me$], 1.04—1.9 (2 H, m, CH_2Me), 1.18 (3 H, t, *J* 7 Hz, OCH_2Me), 2.05 (2 H, m, CH_2CH_2Me), 3.26 (2 H, q, J_{AB} 15.8 Hz, 3-H_2), 4.12 (2 H, q, 7 Hz, OCH_2Me), 5.16 (1 H, s, OH), and 7.3 (4 H, m, ArH); δ_C 13.9, 14.5, 19.4, 35.2, 40.3, 61.8, 62.1, 85.5 (q, *J* 28 Hz, CCF_3), 124.1, 125.2 (q, *J* 287 Hz, CF_3), 125.3, 127.1, 129.8, 139.5, 140.9, and 175.3; δ_F −75.5 (s); *m/z* 298 (M^+ − 18, 39%), 278 (48), 241 (47), 225 (100), 205 (48), 197 (63), 177 (37), 145 (35), 115 (29), and 91 (18). $\nu_{max.}$(FT) ($CHCl_3$) 3 570, 3 370 (OH), and 1 695 cm^{-1} (CO_2Me).

With $EtAlCl_2$ (*run* 20). A solution of keto ester (**6**) (150 mg, 0.47 mmol) in CH_2Cl_2 (12 ml) was stirred with $EtAlCl_2$ (1.4 ml of a 1M solution in hexane, 1.4 mmol) for 3.5 h at 0 °C. After the usual work-up, the crude product was eluted on SiO_2 to give the indanol (**9**) (120 mg, 78%).

Cyclization of β-*Keto Ester* (**7**).—*With* $TiCl_4$ (*run* 21). A solution of keto ester (**7**) (400 mg, 1.3 mmol) in CH_2Cl_2 (13 ml) was stirred with $TiCl_4$ (265 mg, 1.4 mmol) for 4.5 h at 0 °C. After the usual work-up, the crude product (370 mg) was purified by elution on an SiO_2 column to give *compound* (**10**) (310 mg, 77%) (Found: M^+, 314.1129. $C_{16}H_{17}F_3O_3$ requires *M*, 314.1129); δ_H(300 MHz) 1.18 (3 H, t, *J* 7 Hz, OCH_2Me), 2.66—2.92 (2 H, m), 3.32 (2 H, q, J_{AB} 16 Hz, 3-H_2), 4.13 (2 H, q, 7 Hz, OCH_2Me), 5.1—5.22 (3 H, m, CH_2=C and OH), 5.88 (1 H, m), and 7.33 (4 H, m, ArH); δ_C 13.6, 37.4, 39.7, 61.5, 61.8, 85.5 (q, *J* 29 Hz, CCF_3), 118.7, 124.2, 125.2, 125.3 (q, *J* 287 Hz, CF_3), 127.3, 129.9, 139.0, 141.0, and 174.3 (CO_2Me); δ_F −75.5; $\nu_{max.}$ (FT) ($CHCl_3$) 3 570, 3 395 (OH), and 1 695 (CO_2Me); *m/z* 296 (M^+ − 18, 79%), 276 (16), 248 (27), 233 (100), 183 (51), 171 (38), 155 (25), 153 (28), 128 (28), 115 (31), 91 (20), 77 (21), and 57 (20).

With $EtAlCl_2$ (*run* 22). A solution of keto ester (**7**) (300 mg, 0.96 mmol) in CH_2Cl_2 (24 ml) was stirred with $EtAlCl_2$ (2.9 ml of a 1M solution in hexane, 2.9 mmol) for 3 h at 0 °C. The usual work-up gave a crude product (270 mg), which was purified by elution on an SiO_2 column to give the indanol (**10**) (240 mg, 80%).

Cyclization of β-*Keto Ester* (**8**).—*With* $TiCl_4$ (*run* 23). A solution of keto ester (**8**) (400 mg, 1.1 mmol) in CH_2Cl_2 (11 ml) was stirred with $TiCl_4$ (220 mg, 1.21 mmol) at 0 °C for 3.5 h. After the usual work-up, the crude product was purified on an SiO_2 column to give the indanol (**11**) (310 mg, 77%) (Found: M^+, 364.1283. $C_{20}H_{19}F_3O_3$ requires *M*, 364.1286); δ_H (300 MHz) 0.87 (3 H, t, *J* 7.2 Hz, OCH_2Me), 3.32 (2 H, q, J_{AB} 15.7 Hz, 3-H_2), 3.34 (2 H, q, J_{AB} 13.3 Hz, CH_2Ph) 3.85 (2 H, q, 7.2 Hz, OCH_2Me), 5.27 (1 H, m, OH), and 7.26 (9 H, m, ArH); δ_C 13.4, 38.5, 61.9, 63.1, 85.2 (q, *J* 28 Hz, CCF_3) 124.1, 125.3 (q, *J* 287 Hz, CF_3), 125.5, 127.0, 127.1, 128.3, 129.8, 130.0, 136.7, 138.7, 141.5, and 173.9; δ_F −75.2; $\nu_{max.}$(FT) ($CHCl_3$) 3 568, 3 396 (OH), and 1 697 cm^{-1} (CO_2Me); *m/z* 346 (M^+ − 18, 5%), 326 (6), 298 (13), 273 (26), and 91 (100).

With $EtAlCl_2$ (*run* 24). A solution of keto ester (**8**) (300 mg, 0.82 mmol) in CH_2Cl_2 (20 ml) was stirred with $EtAlCl_2$ (2.5 ml of a 1M solution in hexane, 2.46 mmol) at 0 °C for 6 h. After the usual work-up, the crude product (280 mg) was purified on an SiO_2 column to give the indanol (**11**) (240 mg, 80%).

Acknowledgements

We are pleased to acknowledge Mrs. H. Le Pesant (ENSCP) for the FT i.r. measurements and Mrs. M. Charpentier-Morize for stimulating discussions.

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Received 13*th May* 1988; *Paper* 8/01893F