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# One-pot synthesis of functionalized indenols from 2-bromoalkenyl trifluoromethyl ketones

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ABSTRACT

An elegant one-pot synthesis of indenols was successfully realized starting from 3-aryl-2-bromopropenyl trifluoromethyl ketones and secondary amines. The synthesis proceeds through domino reactions including captodative aminoenones as a key intermediate. When bromoenones having a donor substituent in *meta*-position of the aromatic ring were subjected to this reaction, the mixture of two isomeric indenols was formed.



## 1. Introduction

Small bicyclic molecules are frequently found in nature and are attracting increased attention from organic and pharmaceutical chemists.[1] Among these compounds, indenols have a particular value due to both their broad spectrum of biological activity and their wide-ranging utility as synthetic tools in the design of various bioactive molecules.[2] In light of this interest in the indene skeleton, much attention has been done in the development of their efficient synthesis. The most typical reported methods toward the synthesis of indenol derivatives include different transition metal catalyzed carbocyclizations,[2a,b] a modified Vilsmeier reaction,[2a] and oxidation of preformed indan structures.[3] Recently, the first example of the preparation of 1-indenols through acid mediated intramolecular electrophilic aromatic substitution process has been reported.[4]

At the same time the intensive development of organofluorine chemistry over the last decades is well documented.[5] Reasons for the popularity of such compounds is the dramatic effects on the chemical, physical, and biological properties of the parent compound caused by the introduction of a fluorine-containing group into the molecule. In this respect, the fluorinated functionalized indenols are of great interest from both synthetic and biological points of view. Very recently we have developed a synthesis of 1-trifluoromethyl-2-aminoindenols (**3**) from 2-bromoalkenyl trifluoromethyl ketones (**1**) and secondary amines.[6] As a continuation of these studies we have now examined the dependence of the above reaction on the structure of the initial bromoenones. In this paper, the reaction features and the extension of this methodology to enones containing a substituent in the *meta*-position of the aromatic ring are discussed.

## 2. Results and discussion

Trifluoromethyl(alkenyl)ketones **1** are now readily available building blocks and widely used for the construction of different carbo- and heterocycles.[7] The synthesis of their halogen-bearing derivatives **3a–d** was carried out in high yield by a bromination–dehydrobromination sequence without isolation of the intermediate dibromoderivatives **2a–d** as described previously (Scheme 1).[6]

According to NMR spectroscopic data, the bromoenones **3a–d** exist as a single geometric isomer. Since these compounds have only one olefinic proton, the determination of their configuration is a non-trivial task. The (*Z*)-configuration of *para*-substituted enones **3c**,**d** was assigned on the basis of the concerted application of $^{1}$H–$^{1}$H 2D homonuclear experiment NOESY and $^{1}$H–$^{13}$C 2D heteronuclear experiment HMBC, as well as $^{13}$C NMR spectra without proton decoupling (Fig. 1). For example, in the spectrum of enone **3c** there is one NOE peak between the resonance of the olefinic proton and the *ortho*-protons of the aromatic ring. The value of the vicinal coupling constant $^{3}J_{C-H}$ between the proton of the H–C= group and the carbonyl carbon atom in enone **3c** is 5.2 Hz. It is known, that this constant lies between 0 and 6 Hz for the

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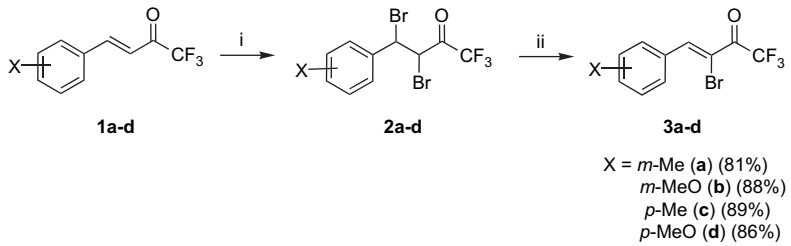



**Scheme 1.** Reagents and conditions: (i) $Br_2$, 10 °C, $CHCl_3$; (ii) $Et_3N$, 10 °C, $Et_2O$.

*s-cis*-isomer and 9–14 Hz for the *s-trans*-one.[8] The additional confirmation of this assignment has been obtained by the analysis of their IR spectra: the ratio of integrated intensities observed for the C=O and C=C stretching bands strongly suggests a *s-cis*-conformation of the C=C–C=O moiety.[9] Enones **3a**,**b** bearing a substituent in *meta*-position of the aromatic ring have cross-peaks with both H-2 and H-6 aromatic protons in the NOE spectra. Their configuration was determined by measuring the coupling constant between the olefinic proton and the carbonyl carbon atom: for both enones the values of $^3J_{C-H}$ (ca. 5.7 Hz) correspond to *W* disposed H–C= and C=O groups.

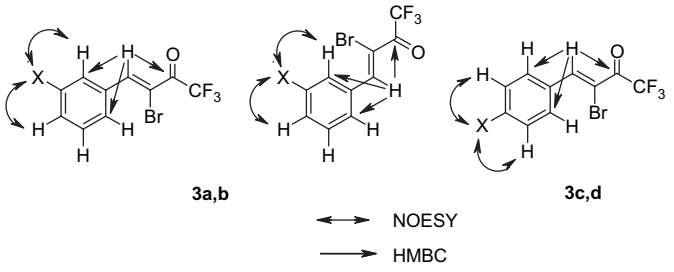


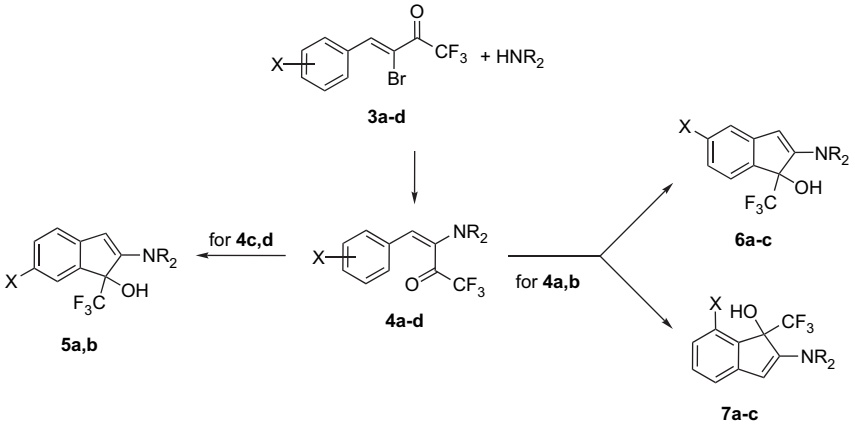

**Figure 1.** Main NOESY and HMBC correlations for bromoenones **3a**–**d**.

The IR spectra of bromoenones **3a**,**b** exhibit a carbonyl band at 1705–1707 $cm^{-1}$ and a more intensive band at 1585–1594 $cm^{-1}$ attributed to $\nu_{C=C}$. For this reason a *s-cis*-conformation of these molecules was deduced.

We found that the treatment of *p*-substituted 4-aryl-3-bromo-1,1,1-trifluorobut-3-en-2-ones **3c**,**d** with secondary amines (2 equiv) affords the target indenols in good yield under mild conditions (rt, ether as a solvent, without catalyst) (Scheme 2). In these cases, the intermediate aminoenones **4c**,**d** can be detected by NMR spectroscopy. Thus, when bromoenones **3c**,**d** were treated with dipropyl- or dibutylamine, a mixture of the corresponding aminoenones **4c**,**d** and indenols **5a**,**b** was formed in a certain period of time. In each case, the $^1$H NMR spectra exhibit two singlets of the olefinic proton of the aminoenones ($\delta_{CH=}$ 6.01 ppm for **4c**, $NR_2$=$NPr_2$ and 5.89 ppm for **4d**, $NR_2$=$NBu_2$) and the indenols ($\delta_{CH=}$ 5.38 and 5.25 ppm for **5a**,**b**, respectively). The molar ratio **4d**/**5b** was 10:1 after 15 h of reaction, the ratio **4c**:**5a** was 2.5:1 after a period of 20 h at rt.

It would be interesting to see whether aminoenone **4** is a precursor of the indenol **5**. To establish a sequence of transformations, we have monitored the reaction of bromoenone **3d** with dibutylamine. At first, in the $^1$H NMR spectrum there are two singlets in the field of the olefinic protons. As the reaction progresses, the intensity of the downfield peak decreases, while the intensity of highfield one increases. The analogous changes are observed in the $^{13}$C NMR spectra. For example, the quartet of the carbonyl carbon atom of enone **4d** ($NR_2$=$NBu_2$) (186.90 ppm) disappears and the signal of quaternary carbon atom C(OH)$CF_3$ of indenol **5b** (83.00 ppm) appears simultaneously. These facts indicate clearly that captodative aminoenones **4** are really direct precursor of the indenols **5**.

We next tested the hypothesis that the structure of the target indenol depends on the position of the substituent in the aromatic ring of the initial bromoenone. Indeed, as with enones **3c**,**d**, their analogs **3a**,**b**, having a *meta*-substituted aromatic ring containing an electron-donating group such as methyl- or methoxy, might lead at the first step to captodative aminoenones **4a**,**b**, which can undergo intramolecular electrophilic aromatic substitution on




**5**: X = Me, $NR_2$ = $NPr_2$ (**a**)
X = MeO, $NR_2$ = $NBu_2$ (**b**)

**3,4**: X = *m*-Me (**a**)
*m*-MeO (**b**)
*p*-Me (**c**)
*p*-MeO (**d**)

**6,7** : X = Me, $NR_2$ = $NEt_2$ (**a**)
X = Me, $NR_2$ = $NPr_2$ (**b**)
X = MeO, $NR_2$= $NEt_2$ (**c**)

**Scheme 2.** Conditions: $Et_2O$, rt.

both *ortho*-carbons. But in this case, the attack at positions 2 and 6 results in different indenol derivatives. In fact, when the reaction of secondary amines was performed with *meta*-substituted bromoenones **3a**,**b**, a mixture of two isomeric indenols **6** and **7** was always formed. The $^1$H NMR spectra of the reaction mixtures exhibit two singlets at 5.20–5.30 ppm arising from the olefinic proton of the indenols. No low-field signals of the proton of the CH═ group of their precursors were detected in these cases. Therefore, aminoenones **4a**,**b** become more active in the last step of the reaction then their *para*-substituted isomers **4c**,**d**. These results are not surprising and can be interpreted in terms of aromatic electrophilic substitution, since methyl- and methoxy groups are *ortho*, *para* directors and show activating effects in positions 2 and 6 of the aromatic ring. The reaction is quite regioselective: the ratio of isomeric indenols **6a**,**b**:**7a**,**b** is ~10:1, and in the cases of **6c**:**7c** achieves ~20:1. The preferable formation of indenol **6** is likely to be due to the steric hindrance by the *meta*-substituent.

The enamine moiety in indenols is easily hydrolyzed to give the corresponding carbonyl derivatives. The accompanying hydrolysis reaction begins during silica gel column chromatography. That is why some of the sample of the indenols **5**–**7** could not be chromatographed quantitatively. For this reason, the yield of the purified target compounds decreased, and some of the indenol and the respective indanone were isolated simultaneously. For instance, when the crude mixture obtained after the treatment of enone **3c** with dipropylamine was purified, the mixture of isomeric indenols (**6b** and **7b**) and indanone **8** was isolated in 46 and 23% yields, respectively. The same final product **8** was isolated in the yield of 35% when the indenol **6a** was treated with water in $CH_2Cl_2$ in the presence of HCl for a day at rt (Scheme 3).


**6a,b** **8**

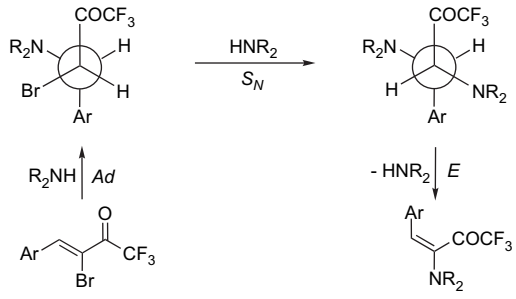
$NR_2$ = $NEt_2$, $NPr_2$

**Scheme 3.** Reagents and conditions: $H_2O/HCl/CH_2Cl_2$, rt.

The results obtained clearly indicate that the transformation of captodative bromoenones **3** to indenols under the treatment of secondary amines is a multi-step process. From a mechanistic point of view, the key steps of this reaction seem to be: (i) aza-Michael addition of the nucleophile to the conjugated system C═C–C═O; (ii) substitution of the bromine atom at the new tetrahedral carbon center by further amine; (iii) elimination of the β-amine to give a captodative system; and (iv) finally, intramolecular electrophilic aromatic substitution occurs leading directly to the target indenol.

Despite the absence of detecting or isolating any of the intermediates, the postulated scheme $Ad_N$–$S_N$–E–$S_E$ has been confirmed by the following studies. Firstly, in our previous paper, we have reported that the principal precursor of indenols was detected by NMR spectroscopy in some cases.[6] Secondly, we have shown that the geometry of aminoenones **4** is opposite to one of the initial bromoenones **3**. This fact can be easily explained in the terms of nucleophilic substitution of haloalkenes bearing electron-withdrawing group (EWG) at the *gem*-position, which, as well known, proceeds through a Michael addition–substitution–elimination domino sequence (Scheme 4).[10]

According to NMR spectroscopy, the intermediate β-aryl substituted aminoenones **4** have the (*E*)-configuration. It has been this configuration of aminoenones **4**, which, in all the cases, favors their intramolecular cyclization into indenols.




**3a-d** **4a-d**

**Scheme 4.** Ad–$S_N$–E sequence of nucleophilic vinylic substitution.

## 3. Conclusion

We have shown that bromoalkenyl trifluoromethyl ketones are suitable starting materials for one-pot conversion into functionally substituted 1-indenols. It is surprising that this reaction occurs in the very mild conditions without catalyst. This fact can be explained by the presence of a strong electron-withdrawing group $CF_3$. The presence of the enamine moiety in the indenols obtained reveals the possibility of their transformation into the corresponding indanones.

## 4. Experimental

### 4.1. General remarks

$^1$H, $^{13}$C, and $^{19}$F NMR spectra were recorded on a Bruker AVANCE 400 MHz spectrometer at 400.16, 100.61, and 376.5 MHz, respectively, for solution in $CDCl_3$. Chemical shifts ($\delta$) in parts per million are reported using residual chloroform (7.25 for $^1$H and 77.20 for $^{13}$C) as internal reference. The coupling constants ($J$) are given in hertz. The concerted application of $^1$H–$^1$H 2D homonuclear experiments COSY[11] and NOESY[12] as well as $^1$H–$^{13}$C 2D heteronuclear experiments HSQC[13] and HMBC[14] was used for the distinction of the carbon and proton resonances in all cases. The IR spectra were measured with a Specord IR-75 instrument. The GC/MS analyses were performed on a Hewlett–Packard HP 5971A instrument (EI, 70 eV). The silica gel used for flash chromatography was 230–400 mesh. All reagents were of reagent grade and were used as such or distilled prior to use. All the solvents were dried according to standard procedures and freshly distilled prior to use. Trifluoromethyl(alkenyl)ketones **1a**–**d** were prepared as reported previously.[15] The synthesis of bromoenone **3d** and the indenol **5b** was described in our previous paper.[6]

### 4.2. Bromination of ketones (1a–c). General procedure

Bromine (0.8 g, 5 mmol) in $CHCl_3$ (5 mL) was added dropwise over 30 min into a stirred solution of the ketones **1a**–**c** (5 mmol) in $CHCl_3$ (5 mL). During the addition the temperature was kept at +10 °C. The mixture was then stirred at rt until the orange color did not fade away. The solvent was evaporated and a light-yellow solid appeared. The crude products—dibromoderivatives **2a**–**c**—were found suitable for further transformation without any purification.

Triethylamine (0.5 g, 5 mmol) in anhydrous ether (10 mL) was added dropwise over 5 min into a stirred solution of the dibromo ketones **2a**–**c** (5 mmol) in $Et_2O$ (10 mL) at +10 °C. The mixture was kept at rt overnight and filtered. After the solvent was evaporated, the α-bromoenones **3a**–**c** were obtained by column chromatography (**3a**) (silica gel, hexane/ether 1:1) or distillation at reduced pressure (**3b**,**c**).

*4.2.1. 3-Bromo-1,1,1-trifluoro-4-(3-methylphenyl)-3-buten-2-one (**3a**)*

Yield 81%; white solid, mp 29 °C; [Found: C, 44.97; H, 2.78; Br, 27.14; F, 19.16. $C_{11}H_8BrF_3O$ requires: C, 45.08; H, 2.75; Br, 27.26; F, 19.45%.] $\nu_{max}$ (KBr) 1585 (C=C), 1707 (C=O) $cm^{-1}$; $\delta_H$ (400 MHz, $CDCl_3$) 2.50 (s, 3H), 7.30–7.50 (m, 2H), 7.79 (s, 1H), 7.87 (d, $J$=7.5 Hz, 1H) 8.22 (s, 1H); $\delta_C$ (100.6 MHz, $CDCl_3$) 21.39 ($CH_3$), 116.04 (q, $J$=291.4 Hz, $CF_3$), 116.49 (=C–Br), 128.57 (C-6′), 128.76 (C-5′), 132.25 (C-2′), 132.95 (C-3′), 133.07 (C-4′), 138.63 (C-1′), 147.47 (q, $J$=3.8 Hz, CH=), 175.71 (q, $J$=35.3 Hz, C=O); $\delta_F$ (376.5 MHz, $CDCl_3$) −68.51; *m/z* (EI) 294 ($M^+$+1, 26), 292 ($M^+$−1, 26), 279, 277 (37), 225, 223 (20), 116 (100%).

*4.2.2. 3-Bromo-1,1,1-trifluoro-4-(3-methoxyphenyl)-3-buten-2-one (**3b**)*

Yield 88%; yellow liquid, bp 95–96 °C/1 mmHg; [Found: C, 42.62; H, 2.59; Br, 25.57; F, 18.78. $C_{11}H_8BrF_3O_2$ requires: C, 42.75; H, 2.61; Br, 25.85; F, 18.44%.] $\nu_{max}$ (liquid film) 1594 (C=C), 1707 (C=O) $cm^{-1}$; $\delta_H$ (400 MHz, $CDCl_3$) 3.87 (s, 3H), 7.09 (d, $J$=9.0 Hz, 1H), 7.41 (dd, $J$=9.0, 8.8 Hz, 1H), 7.49 (d, $J$=8.8 Hz, 1H), 7.58 (s, 1H), 8.18 (s, 1H); $\delta_C$ (100.6 MHz, $CDCl_3$) 55.55 ($OCH_3$), 115.93 (q, $J$=292.0 Hz, $CF_3$), 115.96 (C-2′), 116.92 (=C–Br), 118.32 (C-4′), 124.39 (C-6′), 129.91 (C-5′), 134.09 (C-1′), 147.43 (q, $J$=3.7 Hz, CH=), 159.72 (C-3′), 175.69 (q, $J$=35.5, 5.7 Hz, C=O); *m/z* (EI) 310 ($M^+$+1, 56), 308 ($M^+$−1, 56), 279 ($M^+$−MeO+1, 33), 277 ($M^+$−MeO−1, 33), 241, 239 (40), 132 (100%).

*4.2.3. 3-Bromo-1,1,1-trifluoro-4-(4-methylphenyl)-3-buten-2-one (**3c**)*

Yield 89%; yellow liquid, bp 77 °C/1 mmHg; [Found: C, 44.82; H, 2.81; Br, 27.66; F, 19.48. $C_{11}H_8BrF_3O$ requires: C, 45.08; H, 2.75; Br, 27.26; F, 19.45%.] $\nu_{max}$ (liquid film) 1585 (C=C), 1705 (C=O) $cm^{-1}$; $\delta_H$ (400 MHz, $CDCl_3$) 2.41 (s, 3H), 7.26 (d, $J$=8.0 Hz, 2H), 7.87 (d, $J$=8.0 Hz, 2H), 8.13 (s, 1H); $\delta_C$ (100.6 MHz, $CDCl_3$) 21.85 ($CH_3$), 115.71 (=C–Br), 116.08 (q, $J$=290.1 Hz, $CF_3$), 129.70 (C-3′,5′), 130.28 (C-1′), 131.86 (C-2′,6′), 143.32 (C-4′), 147.24 (q, $J$=3.1 Hz, CH=), 175.67 (q, $J$=35.0, 5.3 Hz, C=O); $\delta_F$ (376.5 MHz, $CDCl_3$) −68.42; *m/z* (EI) 294 ($M^+$+1, 37), 292 ($M^+$−1, 37), 279, 277 (65), 225, 223 (44), 116 (100%).

### 4.3. The reaction of ketones (3a–d) with secondary amines. General procedure

A mixture of bromoenones **3a**–**d** and secondary amine (2 equiv) in ether was stirred at rt overnight. The solvent was removed and analytically pure samples of indenols **4a**,**d**–**f**, aminoenones **5a**,**b**, or indanone **8** were obtained by further column chromatography (silica gel, ether/hexane).

The following compounds were obtained by this procedure.

*4.3.1. 2-(Dipropylamino)-6-methyl-1-(trifluoromethyl)-1H-inden-1-ol (**5a**)*

Yield 43%; oil; [Found: C, 65.44; H, 6.65; N, 4.78. $C_{17}H_{22}F_3NO$ requires: C, 65.16; H, 7.08; N, 4.47%.] $\nu_{max}$ (liquid film) 1592 (C=C), 3373 (OH) $cm^{-1}$; $\delta_H$ (400 MHz, $CDCl_3$) 0.96 (t, $J$=7.3 Hz, 6H), 1.55–1.70 (m, 4H), 2.36 (s, 3H), 2.95–3.10 (m, 2H), 3.37 (br s, 1H), 3.45–3.60 (m, 2H), 5.35 (s, 1H), 6.81 (d, $J$=7.4 Hz, 1H), 6.78 (d, $J$=7.4 Hz, 1H), 7.16 (s, 1H); $\delta_C$ (100.6 MHz, $CDCl_3$) 11.65 ($CH_3$), 20.50 ($CH_2$), 21.32 ($CH_3$), 52.64 ($NCH_2$), 83.30 (q, $J$=30.2 Hz, C–OH), 104.24 (CH=), 117.89 (C-4), 123.84 (C-5), 124.88 (q, $J$=285 Hz, $CF_3$), 131.17 (C-7), 131.74 (C-6), 137.54 (C-8), 142.21 (C-9), 152.23 (=C–N).

*4.3.2. 2-(Diethylamino)-5-methyl- (**6a**) and 2-(diethylamino)-7-methyl-1-(trifluoromethyl)-1H-inden-1-ol (**7a**)*

Oil; $\delta_H$ (400 MHz, $CDCl_3$) major isomer **6a**: 1.15 (t, $J$=7.5 Hz, 6H), 2.30 (s, 3H), 3.20–3.30 (m, 2H), 3.45–3.55 (m, 2H), 5.30 (s, 1H), 6.69 (d, $J$=7.6 Hz, 1H), 6.70 (s, 1H), 7.17 (d, $J$=7.6 Hz, 1H); minor isomer **7a**: 1.07 (t, $J$=7.5 Hz, 6H), 2.47 (s, 3H), 3.20–3.30 (m, 2H), 3.45–3.55 (m, 2H), 5.31 (s, 1H), 6.67 (d, $J$=8.0 Hz, 1H), 6.70 (d, $J$=7.6 Hz, 1H), 7.06 (dd, $J$=7.6, 8.0 Hz, 1H); $\delta_C$ (100.6 MHz, $CDCl_3$) major isomer **6a**: 12.39 ($CH_3CH_2$), 21.86 ($CH_3$), 44.21 ($NCH_2$), 83.08 (q, $J$=30.3 Hz, C–OH), 103.71 (CH=), 118.96 (C-4), 122.70 (C-6), 122.79 (C-7), 124.94 (q, $J$=285.3 Hz, $CF_3$), 134.61 (C-8), 140.41 (C-5), 145.19 (C-9), 152.89 (=C–N); minor isomer **7a**: 12.52 ($CH_3CH_2$), 21.86 ($CH_3$), 44.32 ($NCH_2$), 85.30 (q, $J$=30 Hz, C–OH), 103.71 (CH=), 115.68 (C-4), 125.51 (q, $J$=286 Hz, $CF_3$), 125.75 (C-6), 130.31 (C-5), 134.85 (C-7), 135.44 (C-8), 145.65 (C-9), 152.54 (=C–N); $\delta_F$ (376.5 MHz, $CDCl_3$) major isomer **6a**: −78.27; minor isomer **7a**: −75.47; *m/z* (EI) 285 ($M^+$, 96), 270 (100%).

*4.3.3. 2-(Dipropylamino)-5-methyl- (**6b**) and 2-(dipropylamino)-7-methyl-1-(trifluoromethyl)-1H-inden-1-ol (**7b**)*

Yield 46%; oil; [Found: C, 65.11; H, 6.74; N, 4.21. $C_{17}H_{22}F_3NO$ requires: C, 65.16; H, 7.08; N, 4.47%.] $\delta_H$ (400 MHz, $CDCl_3$) major isomer **6b**: 0.95 (t, $J$=7.3 Hz, 6H), 1.55–1.70 (m, 4H), 2.32 (s, 3H), 2.95–3.10 (m, 2H), 3.40–3.55 (m, 2H), 5.28 (s, 1H), 6.70 (d, $J$=7.6 Hz, 1H), 6.71 (s, 1H), 7.16 (d, $J$=7.6 Hz, 1H); minor isomer **7b**: 0.95 (t, $J$=7.5 Hz, 6H), 1.55–1.70 (m, 4H), 2.47 (s, 3H), 2.95–3.10 (m, 2H), 3.40–3.55 (m, 2H), 5.30 (s, 1H), 6.67 (d, $J$=8.0 Hz, 1H), 6.70 (d, $J$=7.6 Hz, 1H), 7.06 (dd, $J$=7.6, 8.0 Hz, 1H); $\delta_C$ (100.6 MHz, $CDCl_3$) major isomer **6b**: 11.62 ($CH_3CH_2$), 20.55 ($CH_2$), 21.92 ($CH_3$), 52.63 ($NCH_2$), 83.13 (q, $J$=30.3 Hz, C–OH), 103.78 (CH=), 119.10 (C-4), 122.58 (C-6), 122.79 (C-7), 124.98 (q, $J$=285.3 Hz, $CF_3$), 134.40 (C-8), 140.67 (C-5), 145.24 (C-9), 153.15 (=C–N); minor isomer **7b**: 11.55 ($CH_3CH_2$), 18.28 ($CH_3$), 52.54 ($NCH_2$), 85.30 (q, $J$=30 Hz, C–OH), 103.24 (CH=), 115.46 (C-4), 125.49 (C-6), 125.54 (q, $J$=286 Hz, $CF_3$), 130.11 (C-5), 133.43 (C-8), 134.67 (C-7), 145.50 (C-9), 152.75 (=C–N); $\delta_F$ (376.5 MHz, $CDCl_3$) major isomer **6b**: −78.29; minor isomer **7b**: −75.50; *m/z* (EI) 313 ($M^+$, 64), 284 (100), 224 (44%).

*4.3.4. 2-(Diethylamino)-5-methoxy- (**6c**) and 2-(diethylamino)-7-methoxy-1-(trifluoromethyl)-1H-inden-1-ol (**7c**)*

Yield 48%; oil; [Found: C, 59.77; H, 6.04; N, 4.73. $C_{15}H_{18}F_3NO_2$ requires: C, 59.79; H, 6.02; N, 4.65%.] $\nu_{max}$ (liquid film) 1168 (COC), 1592 (C=C), 3380 (OH) $cm^{-1}$; $\delta_H$ (400 MHz, $CDCl_3$) major isomer **6c**: 1.13 (t, $J$=7.5 Hz, 6H), 3.15–3.30 (m, 2H), 3.35–3.50 (m, 2H), 3.68 (s, 3H), 5.24 (s, 1H), 6.27 (dd, $J$=2.0, 8.1 Hz, 1H), 6.36 (d, $J$=2.0 Hz, 1H), 7.11 (d, $J$=8.1 Hz, 1H); minor isomer **7c**: 1.10 (t, $J$=7.5 Hz, 6H), 3.15–3.30 (m, 2H), 3.35–3.50 (m, 2H), 3.79 (s, 3H), 5.23 (s, 1H), 6.29 (m, 1H), 6.35 (m, 1H), 7.00 (m, 1H); $\delta_C$ (100.6 MHz, $CDCl_3$) major isomer **6c**: 12.37 ($CH_3CH_2$), 44.12 ($NCH_2$), 55.15 ($CH_3O$), 82.80 (q, $J$=29.9 Hz, C–OH), 102.70 (CH=), 104.70 (C-4), 106.06 (C-6), 123.92 (C-7), 125.04 (q, $J$=284.9 Hz, $CF_3$), 129.29 (C-8), 146.80 (C-9), 153.91 (=C–N), 161.97 (C-5); minor isomer **7c**: 12.37 ($CH_3CH_2$), 44.30 ($NCH_2$), 56.34 ($CH_3O$), 84.10 (q, C–OH), 101.30 (CH=), 110.6 (C-6), 115.30 (C-4), 122.4 (C-8), 125.2 (q, $CF_3$), 127.60 (C-5), 147.4 (C-9), 152.6 (=C–N), 155.35 (C-7); $\delta_F$ (376.5 MHz, $CDCl_3$) major isomer **6c**: −76.69; minor isomer **7c**: −74.10; *m/z* (EI) 285 ($M^+$, 96), 270 (100%).

*4.3.5. 1-Hydroxy-5-methyl-1-(trifluoromethyl)-1,3-dihydro-2H-indan-2-one (**8**)*

A mixture of bromoketone **3c** (293 mg, 1 mmol) and diethylamine (160 mg, 2.2 mmol) in ether (10 mL) was stirred at rt for 24 h. The solvent was removed giving a mixture (285 mg) containing mainly the target indenols **5a** and **6a**, which was used in the next step without any purification. Water (0.2 mL) and two drops of HCl (concd) were added to the residue in $CH_2Cl_2$ (10 mL) and the mixture was stirred for 24 h at rt. The solvent was removed, the residue was purified by column chromatography (silica gel, ether/hexane 1:2) to give **8** (80 mg, 35%) as a white solid, mp 79 °C; [Found: C, 57.69; H, 4.03. $C_{11}H_9F_3O_2$ requires: C, 57.40; H, 3.94%.] $\nu_{max}$ (KBr) 1760 (C=O), 3420 (O–H) $cm^{-1}$; $\delta_H$ (400 MHz, $CDCl_3$) 2.43 (s, 3H), 3.55 (A part of AB-system, $J$=21.6 Hz, 1H), 3.73 (s, 1H), 3.81 (B part of AB-system, $J$=21.6 Hz, 1H), 7.20 (s, 1H), 7.23 (d, $J$=8.0 Hz, 1H), 7.51 (d, $J$=8.0 Hz,

1H); $\delta_C$ (100.6 MHz, $CDCl_3$) 22.00 ($CH_3$), 41.39 ($CH_2$), 79.07 (q, $J$=30.6 Hz, C–OH), 123.40 (q, $J$=286.4 Hz, $CF_3$), 125.69 (C-4), 126.53 (C-7), 129.66 (C-6), 131.96 (C-9), 137.35 (C-8), 141.54 (C-5), 208.03 (C=O); $m/z$ (EI) 230 ($M^+$, 23), 161 (76), 133 (100), 105 (53%).

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## Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.06.069.

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