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# ARYNIC CONDENSATION OF KETONE ENOLATES 18[1]
# EFFICIENT ACCESS TO BENZOCYCLENONES AND POLYCYCLIC INDANONE DERIVATIVES.

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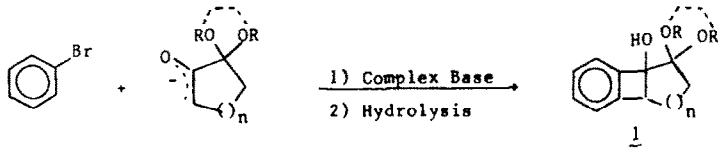
Abstract - It is shown that benzocyclobutenols 1 are excellent starting materials for the obtention of polycyclic aromatic ketones. Thus under basic conditions they lead to benzocyclenedione mono ketals which may be hydrolyzed into the corresponding benzocyclenediones. Under acidic conditions, a transposition takes place leading to indanone derivatives. The mechanism of this transposition is discussed.

In a previous publication[1] we reported that benzocyclobutenols 1 are easily obtained by arynic condensation of 1,2-diketone monoketal enolates (Scheme 1).

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Scheme 1

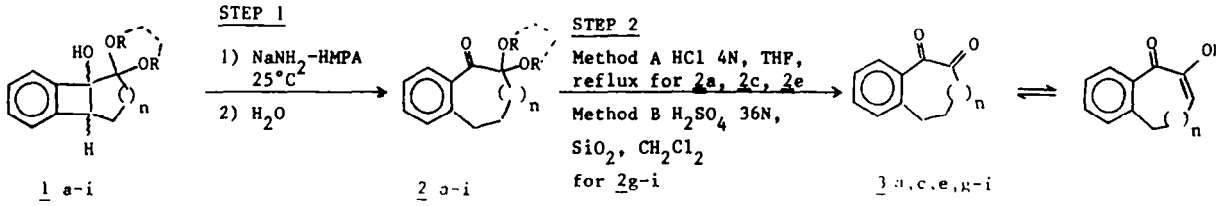
Besides their potential pharmacological interest[2a] alcohols 1 are excellent starting materials for synthesizing a number of polycyclic aromatic derivatives.[2b] We briefly evoked such syntheses in a short communication.[3] In the present publication we wish to give more details concerning such transformations and the chemical properties of 1.

## RESULTS AND DISCUSSION

### Synthesis of benzocyclene 1,2-diones

Though large as well as medium ring diketones 3 constitute interesting starting materials, they have rarely been synthesized. Indeed they can be obtained only by low overall yield, multistep reactions.[4]

On the orther hand, it is well established[5] that under appropriate conditions, benzocyclobutenols are easily transposed into the corresponding benzocyclenones. So synthesis of 3 according to Scheme 2 had to be considered.




1 a-i 2 a-i 3 a,c,e,g-i

Scheme 2

The results of the reactions performed are gathered in Table I.

| Starting alcohol 1 | | | Step 1 | | Step 2 | | | |
|---|---|---|---|---|---|---|---|---|
| | n | R | t, h | 2 yield % | Method | t, h | 3 % | Enol form % |
| a | 2 | $CH_3$ | 0.5 | 83 | A | 4 | 75 | - |
| b | 2 | $(CH_2)_2$ | 0.5 | 90 | | | | |
| c | 3 | $CH_3$ | 0.5 | 96 | A | 3 | 78 | - |
| d | 3 | $(CH_2)_2$ | 0.1 | 80 | | | | |
| e | 4 | $CH_3$ | 0.16 | 58 | A | 5.5 | 91 | - |
| f | 4 | $(CH_2)_2$ | 0.5 | 90 | | | | |
| g | 5 | $(CH_2)_2$ | 0.75 | 82 | B | 0.75 | 82 | - |
| h | 7 | $(CH_2)_2$ | 1.5 | 88 | B | 0.1 | 68 | 12[a] |
| i | 8 | $(CH_2)_2$ | 0.75 | 74 | B | 0.1 | 59 | 25[a] |

[a] Ratio determination by $^1H$ NMR

Table I

While base opening of the four membered ring presented no difficulties, the same did not hold true for the ketal hydrolysis.

Indeed the reactivity of the ketal group was lowered by the presence of the electron-withdrawing keto group. Thus whatever the nature of R was, HCl in acetone at room temperature[6] was inefficient. With R = Me, moderate yields of 3 were obtained with $Me_3SiCl$-NaI in MeCN.[7] On the other hand, ethylene ketals did not react with $PdCl_2(MeCN)_2$ in acetone.[8]

Finally we found that dimethyl ketals could be conveniently hydrolyzed by HCl 4N in refluxed THF. Ethylene ketals were successfully hydrolyzed by concentrated $H_2SO_4$ adsorbed on silica, a modification of the method used by Conia et al.[9]

In some cases (3h, 3i) diketones were obtained as an equilibrated mixture of the keto and enol forms. Both are very sensitive to oxidation and must be rapidly used or stored, preferentially at low temperature under strictly inert atmosphere.

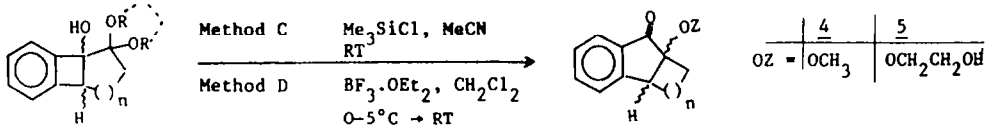
Note that the obtention of 3a (n = 2) in three steps with an overall average yield of 40 % compares very favorably with the five step synthesis of Ebine et al.[4] who obtained the same diketone with 14 % yield.

## Synthesis of indanone derivatives

Indanone derivatives are widespread compounds in organic chemistry.[10] Interestingly formation of such compounds must be expected from alcohols 1 under acidic conditions. Indeed it is well known that potential cyclobutyl methylene carbonium structures, very rapidly transpose into five membered rings.[11] Taking this potentiality into account, we studied this transformation by performing reactions in anhydrous and aqueous acidic conditions.

*Transposition of 1 under anhydrous conditions*

$Me_3SiCl$ in MeCN or $BF_3.OEt_2$ in $CH_2Cl_2$ converted alcohols 1 (R = Me, R,R = $(CH_2)_2$) into 4 or 5 (Scheme 3). These fast reactions are highly stereoselective as may be seen from the results reported in Table II.




Scheme 3

| | Starting alcohol 1 | | R | Method | Indanone derivative % | |
|---|---|---|---|---|---|---|
| | n | (H, OH) | | | 4 (H, $OCH_3$) or 5 (H, $OCH_2CH_2OH$) | |
| a | 2 | (cis) | $CH_3$ | C[a] | 81 (cis) | |
| c | 3 | (cis) | $CH_3$ | C[a] | 61 (cis)<br>5 (trans) | |
| e | 4 | (cis) | $CH_3$ | C[a] | 62 (trans) | |
| b | 2 | (cis) | $(CH_2)_2$ | D[b] | | 60 (cis) |
| d | 3 | (cis) | $(CH_2)_2$ | D[b] | | 78 (cis) |
| f | 4 | (cis) | $(CH_2)_2$ | D[b] | | 76 (trans) |
| g | 5 | (trans) | $(CH_2)_2$ | D[b] | | 79 (cis) |
| h | 7 | (trans) | $(CH_2)_2$ | D[b] | | 74 (cis) |
| i | 8 | (trans) | $(CH_2)_2$ | D[b] | | 54 (cis)<br>33 (trans) |

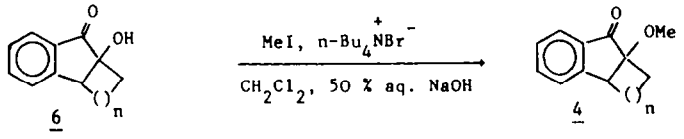
[a]Instantaneous reaction

[b]Complete reaction after warming to room temperature

Table II

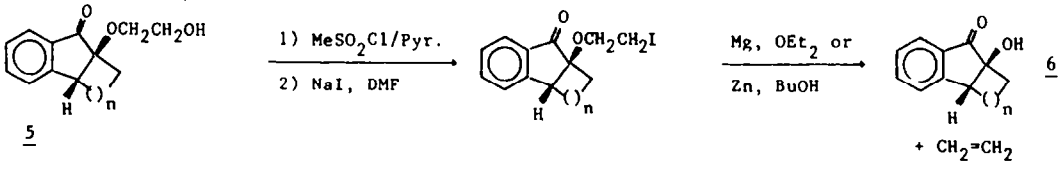
The stereochemistry of 4 and 5 was correlated to the stereochemistry of the corresponding alcohols 6 the structural determination of which will be described elsewhere.

Thus 4a,c cis and 4e trans were obtained from the corresponding alcohol by alkylation under phase transfer catalysis conditions (Scheme 4).




Scheme 4

On the other hand 5b,d,g,h,i cis were transformed into the corresponding alcohols 6 (Scheme 5) : the crude mesylates obtained from these alcohols 5 were converted into the corresponding iodo derivatives which afforded after olefine elimination the keto alcohols 6b,d,g,h,i cis.




Scheme 5

Finally for 5f trans the stereochemistry was determined by X ray diffraction of a derivative.[12]

The stereochemistry of these reactions may be explained by the intervention of two mechanisms which ratio depends on the structure of 1.

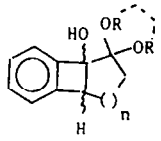
One of the mechanisms has a real carbocation as intermediate. Thus the ratio of the two isomers must be governed by the relative activations energies corresponding to the ring closure on one or the other of the cation faces.

The second mechanism is a concerted one with breaking of the carbon-oxygen bond of the alkoxide leaving group antiperiplanar to the migrating carbon-carbon bond.

Taking into accounts of the results given in the literature concerning this kind of transposition, it may be suggested that the formation of only one isomer could be due to a transposition with participation. On the contrary the formation of two compounds could be due to intervention, at least in part, of an actual cation.

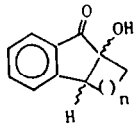
*Transposition of 1 under aqueous conditions*

Alcohols 1 with R = Me were easily hydrolyzed by dilute HCl leading to 6 (Table III). The ethylene ketals 1 (R,R = $(CH_2)_2$) were more difficult to hydrolyze and necessitated the use of HCl 12N in acetone. In all cases yields were good to excellent.




Method E dil. HCl/MeOH RT

Method F conc. HCl/acetone RT



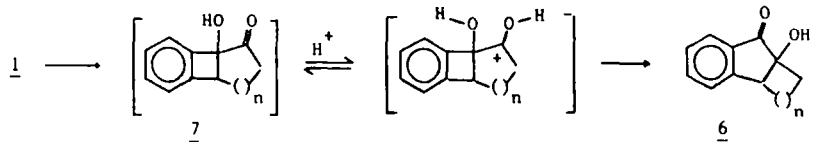

1 6

| | Starting alcohol 1 n | (H,OH) | R | Method | t, h | 6 % (H, OH) |
|---|---|---|---|---|---|---|
| a | 2 | (cis) | $CH_3$ | E | inst. | 87 (cis) |
| c | 3 | (cis) | $CH_3$ | E | inst. | 80 (cis) |
| e | 4 | (cis) | $CH_3$ | E | inst. | 76 (cis) |
| f | 4 | (cis) | $(CH_2)_2$ | F | 1 | 33 (cis) ; 20 (trans)[a] |
| f | 4 | (cis) | $(CH_2)_2$ | F + 1 ml $H_2O$ | 1 | 50 (cis) ; 27 (trans)[b] |
| f | 4 | (cis) | $(CH_2)_2$ | F + 5 ml $H_2O$ | 72 | 75 (cis)[b] |
| g | 5 | (trans) | $(CH_2)_2$ | F | 3 | 70 (cis)[c] |
| h | 7 | (trans) | $(CH_2)_2$ | F | 3 | 80 (cis) ; 18 (trans) |
| i | 8 | (trans) | $(CH_2)_2$ | F | 19 | 39 (cis) ; 52 (trans) |

[a]Formation of 5f (trans) in 30 % yield
[b]Formation of 5f (trans) in 10 % yield
[c]Formation of 5g (cis) in 13 % yield.

Table III

It is noteworthy that starting from alcohols 1f,h,i the isomer ratios were different from those observed under anhydrous conditions. These results are indicative of the intervention of the cationic mechanism due to the previous formation of butenol-one 7 (Scheme 6).



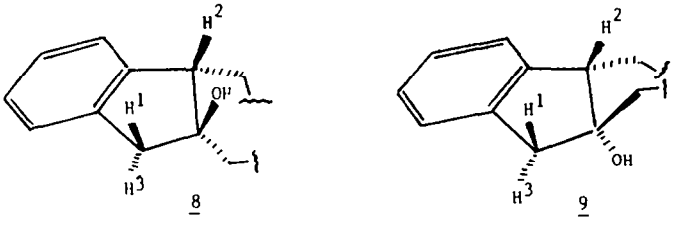
Scheme 6

So the ratio of the two isomers would be a reflexion of the accessibility of the two faces of the keto group during the ring closure.

In two cases from alcohols 1f and 1g we also observed the formation of a certain amount of the corresponding ethers 5f and 5g. Their stereochemistry were identical to those of the products obtained under anhydrous conditions. Furthermore we verified that these ethers were not transformed into 6 and that the alcohol 6f trans was not isomerized into 6f cis under the conditions used.

Studying the behaviour of 1f we also noticed a curious role played by water. Indeed, in experiments performed under the above conditions but with the addition of increasing amounts of water, an increase of the cis/trans ratio from 62/38 to 100/0 was observed. We have no clear explanation for this phenomenon.

The stereochemistry of 6 cannot be determined with certainty on the substrates themselves. However, derivatives 8 and 9 saturated at the benzylic position present a local symmetry on the five membered ring and might be expected to be characterized with $^1$H NMR lanthanide shift experiments.



A modified Wolff-Kishner reduction, where a mixture of the carbonyle derivative, diethyle glycol, 90 % hydrazine hydrate and potassium hydroxide pellets was heated up to 175°C, was efficient in reducing 6a,c.

The $^1$H NMR spectra of the hydrogenolyzed products 8 (n = 2, 3) thus obtained, performed in the presence of increasing amounts of Eu(fod)$_3$ led to the curves where the protons $H^1$ and $H^2$ shift at the same rate and more rapidly than $H^3$.

This result was confirmed by X ray diffraction study of a derivative of 6c.[12]

X ray diffraction study of 6g, of the minor isomer of 6h and of derivatives of the minors isomers of 6f and 6i indicated that the structures were cis, trans, trans and cis respectively.[12]

With these data in hand, we compared the $^{13}$C NMR data corresponding to the different isomers of 6a,c,f,g,h,i isolated. The results are reported in Table IV. It may be seen that with one exception 6c the chemical shift of the benzylic carbon bearing a hydrogen may be of help in determining the nature of the junction.

| | a | c | f | g | h | i |
|---|---|---|---|---|---|---|
| n | 2 | 3 | 4 | 5 | 7 | 8 |
| 6 cis | 51.90 | 44.60 | 51.74 | 51.37 | 49.68 | 50.94 |
| 6 trans | - | - | 46.59 | - | 43.40 | 45.13 |

Table IV

## CONCLUSION

Benzocyclobutenols, easily obtained by Complex Bases initiated arynic condensation of 1,2-diketone monoketal enolates, are interesting materials for the obtention of aromatic polycyclic derivatives

(i) very sensitive to bases, they open to give benzocyclenedione monoketals. The air sensitive benzocyclenedione themselves may be reached by hydrolysis, under appropriate conditions, of the ketal group,

(ii) very sensitive to acids, they transpose with enlargement of the four membered ring, into polycyclic indanone derivatives, the stereochemistry of which depends upon the stereochemistry of the starting material and the experimental conditions.

## EXPERIMENTAL SECTION

General methods. Melting points were determined on a Köfler melting point apparatus. $^{13}C$ NMR spectra were recorded on a Bruker WP 80 and on a Bruker AM 400 spectrometers and $^1H$ NMR spectra on a Perkin-Elmer R 12 B instrument at 60 MHz and on a Bruker AM 400 instrument at 400 MHz with $Me_4Si$ as internal standard. Ultraviolet spectra were obtained with methanol solutions on a Beckman Model DK 2A instrument. Infrared spectra with NaCl film or KBr pellets were recorded on a Perkin-Elmer 580 instrument. Low-resolution mass spectra were obtained by using electron-impact ionization (70 ev) unless otherwise specified. Samples run with chemical ionization (denoted by CI) were run with $NH_3$ as the ionizing gas, unless otherwise stated. Elemental analyses were performed by CNRS laboratory (Vernaison) and by Mrs François M. (Strasbourg). Thin-layer chromatography was performed by using Kieselgel G (Merck) with a hexane-EtOAc mixture as eluent. The silica gels used for liquid phase chromatography and flash chromatography were respectively Kieselgel 0.063 (0.2 mm) and Kieselgel 0.04 (0.063 mm). High-pressure liquid chromatography was carried out on a Waters PREP 500 chromatograph with a silica gel column. Analytical HPLC was performed in a Waters Model 6000 A instrument with a stainless steel column Merck Hibar RT 250-4 (Lichrosorb Si 60-5 μM).

Materials. Degussa sodamide was washed with appropriate solvents and finely ground with a mortar under solvent. Tetrahydrofuran (THF) freshly distilled from a benzophenone-sodium couple stored under sodium was used, hexamethylphosphoramide (HMPA) was distilled before use, dichloromethane ($CH_2Cl_2$) and acetonitrile (MeCN) were distilled from $P_2O_5$. The starting benzocyclobutenols 1 were prepared as previously described.[1]

General procedure for the basic ring opening of the benzocyclobutenols 1. Reactions were carried out with magnetic stirring under a nitrogen atmosphere and monitored by TLC analysis.

Typically, a solution of the alcohol 1 (1 mmol) in 10 ml of HMPA was added to a suspension of $NaNH_2$ (2 mmol) in 10 ml of HMPA at room temperature. After 15 min, the reaction was complete and the mixture was poured into ice/water and extracted with diethyl ether. The organic layer was washed successively with water and brine, then dried ($MgSO_4$), and evaporated in vacuo. A rapid filtration on column chromatography gave the benzocyclenone 2.

2a : n = 2 ; mp 54°C (petroleum ether) ; IR (KBr) 1715 $cm^{-1}$ (C=O) ; UV (MeOH) λ nm (log ε) 244 (sh, 3.19) ; $^1H$ NMR ($CCl_4$) δ 1-2.13 (6 H, m, 3 x $CH_2$), 2.36-2.82 (2 H, m, benzylic $CH_2$), 3.17 (6 H, s, 2 x $OCH_3$), 6.86-7.36 (4 H, m, ArH) ; Anal. Calcd. for $C_{14}H_{18}O_3$ : C, 71.77 ; H, 7.74. Found : C, 71.40 ; H, 7.84.

2b : n = 2 ; mp 78°C (ethyl acetate - petroleum ether) ; IR (KBr) 1720 $cm^{-1}$ (C=O) ; UV (MeOH) λ nm (log ε) 245 (sh, 3.25) ; $^1H$ NMR ($CCl_4$) δ 1.41-2.11 (6 H, m, 3 x $CH_2$), 2.51-2.99 (2 H, m, benzylic $CH_2$), 4.00 (4 H, s, $>COCH_2CH_2O$), 6.89-7.51 (4 H, m, ArH) ; Anal. Calcd. for $C_{14}H_{16}O_3$ : C, 72.39 ; H, 6.94. Found : C, 72.38 ; H, 6.85.

2c : n = 3 ; IR (NaCl) 1710 $cm^{-1}$ (C=O) ; UV (MeOH) λ nm (log ε) 247 (3.44) ; $^1H$ NMR ($CCl_4$) δ 1.02-2.09 (8 H, m, 4 x $CH_2$), 2.60-2.93 (2 H, pseudo t, benzylic $CH_2$), 3.24 (6 H, s, 2 x $OCH_3$), 6.89-7.44 (4 H, m, ArH) ; Anal. Calcd. for $C_{15}H_{20}O_3$ : C, 72.55 ; H, 8.11. Found : C, 72.18 ; H, 8.03.

2d : n = 3 ; IR (NaCl) 1710 $cm^{-1}$ (C=O) ; UV (MeOH) λ nm (log ε) 246 (3.21), 321 (sh) ; $^1H$ NMR ($CCl_4$) δ 0.98-1.93 (8 H, m, 4 x $CH_2$), 2.47-2.84 (2 H, pseudo t, benzylic $CH_2$), 3.94 (4 H, s, $>COCH_2CH_2O$), 6.93-7.58 (4 H, m, ArH) ; Anal. Calcd. for $C_{15}H_{18}O_3$ : C, 73.14 ; H, 7.37. Found : C, 72.98 ; H, 7.45.

2e : n = 4 ; IR (NaCl) 1700 $cm^{-1}$ (C=O) ; UV (MeOH) λ nm (log ε) 249 (3.72) ; $^1H$ NMR ($CCl_4$) δ 0.67-2.24 (10 H, m, 5 x $CH_2$), 2.69-3.09 (2 H, pseudo t, benzylic $CH_2$), 3.31 (6 H, s, 2 x $OCH_3$), 6.98-7.56 and 7.67-7.91 (4 H, m, ArH) ; $C_{16}H_{22}O_3$, mass spectrum m/e 262 ($M^+$).

2f : (n = 4) ; mp 100°C (petroleum ether) ; IR (KBr) 1695 $cm^{-1}$ (C=O) ; UV (MeOH) λ nm (log ε) 245 (3.81) ; $^1H$ NMR ($CDCl_3$) δ 0.67-2.27 (10 H, m, 5 x $CH_2$), 2.71-3.06 (2 H, pseudo t, benzylic $CH_2$) 4.13 (4 H, s, $>\overline{COCH_2CH_2O}$), 7.05-7.68 and 7.86-8.14 (4 H, m, ArH) ; Anal. Calcd. for $C_{16}H_{20}O_3$ C, 73.82 ; H, 7.74. Found : C, 73.97 ; H, 7.72.

2g : (n = 5) ; IR (NaCl) 1695 $cm^{-1}$ (C=O) ; UV (MeOH) λ nm (log ε) 252.5 (3.82), 283.5 (sh) ; $^1H$ NMR ($CCl_4$) δ 0.53-2.04 (12 H, m, 6 x $CH_2$), 2.62-3.02 (2 H, m, benzylic $CH_2$), 3.98 (4 H, s, $>\overline{COCH_2CH_2O}$), 6.87-7.33 and 7.77-8.11 (4 H, m, ArH) ; $C_{17}H_{22}O_3$, mass spectrum m/e 274 ($M^+$).

2h : (n = 7) ; IR (NaCl) 1700 $cm^{-1}$ (C=O) ; UV (MeOH) λ nm (log ε) 253 (3.86), 286 (sh) ; $^1H$ NMR ($CCl_4$) δ 0.91-2.18 (16 H, m, 8 x $CH_2$), 2.67-3.04 (2 H, pseudo t, benzylic $CH_2$), 3.93 (4 H, s, $>\overline{COCH_2CH_2O}$), 6.93-7.51 and 7.82-8.11 (4 H, m, ArH) ; Anal. Calcd. for $C_{19}H_{26}O_3$ : C, 75.46 ; H, 8.67. Found : C, 75.80 ; H, 9.23.

2i : (n = 8) ; mp 70°C (petroleum ether) ; IR (KBr) 1695 $cm^{-1}$ (C=O) ; UV (MeOH) λ nm (log ε) 251 (3.73), 284 (sh) ; $^1H$ NMR ($CDCl_3$) δ 1.00-2.03 (18 H, m, 9 x $CH_2$), 2.49-2.93 (2 H, pseudo t, benzylic $CH_2$), 3.86 (4 H, s, $>\overline{COCH_2CH_2O}$), 6.88-7.44 and 7.64-7.91 (4 H, m, ArH) ; Anal. Calcd. for $C_{20}H_{28}O_3$ : C, 75.91 ; H, 8.91. Found : C, 76.02 ; H, 8.90.

Hydrolysis of the ketal for the synthesis of benzocyclene 1,2-diones 3

Hydrolysis of dimethyl acetal (Method A). To a solution of 2 (1 mmol) in THF (6 ml) was added HCl 4N (6 ml) and the mixture was refluxed for the time indicated in Table I. After complete reaction (monitored by TLC) the solution was diluted with water, extracted with diethyl ether. The organic layer was washed with saturated $NaHCO_3$ solution then dried over $MgSO_4$. After evaporation of the solvents under reduced pressure, the residue was purified by flash chromatography.

Hydrolysis of ethylene acetal (Method B). $H_2SO_4$ 36N (1 ml) was added with continuous magnetic stirring to a suspension of silica gel (3 g silica gel 60 Merck, for column chromatography, 70-230 mesh) in $CH_2Cl_2$ (4 ml). After 2-3 min, the dichloromethane was evaporated. The keto acetal 2 (4 mmol) dissolved in $CH_2Cl_2$ (2 ml) was added and stirring was continued at room temperature for the time given in the Table I. The solid phase was separated by suction filtration on a sintered glass funnel and the solid was washed several times with $CH_2Cl_2$. The combined organic layers were washed successively with saturated $NaHCO_3$ solution then with water. After drying over $MgSO_4$, the solvents were removed in vacuo and the residue purified.

3a : (n = 2) ; IR (NaCl) 1710, 1660 $cm^{-1}$ (C=O) ; UV (MeOH) λ nm (log ε) 296 (3.31) ; $^1H$ NMR ($CCl_4$) δ 1.44-2.09 (4 H, m, 2 x $CH_2$), 2.40-3.11 (4 H, 2 m, benzylic $CH_2$ and $CH_2C$=O), 7.00-7.75 and 7.98-8.27 (4 H, m, ArH) ; $C_{12}H_{12}O_2$, mass spectrum m/e 188 ($M^+$).

3c : (n = 3) ; IR (NaCl) 1700, 1660 $cm^{-1}$ (C=O) ; UV (MeOH) λ nm (log ε) 293 (sh 3.15), 259 (3.71) ; $^1H$ NMR ($CCl_4$) δ 0.73-2.32 (6 H, m, 3 x $CH_2$), 2.56-3.08 (4 H, m, benzylic $CH_2$ and $CH_2C$=O), 7.00-7.67 and 7.73-8.02 (4 H, m, ArH) ; $C_{13}H_{14}O_2$, mass spectrum CI m/e 220 (M+18).

3e : (n = 4) ; IR (NaCl) 1695, 1660 $cm^{-1}$ (C=O) ; UV (MeOH) λ nm (log ε) 290 (sh, 3.03), 259 (3.53) ; $^1H$ NMR ($CCl_4$) δ 0.73-2.11 (8 H, m, 4 x $CH_2$), 2.42-3.15 (4 H, m, benzylic $CH_2$ and $CH_2C$=O), 7.02-7.93 (4 H, m, ArH) ; $C_{14}H_{16}O_2$, mass spectrum CI, m/e 234 (M+18).

3g : (n = 5) ; IR (NaCl) 1705, 1675 $cm^{-1}$ (C=O) ; UV (MeOH) λ nm (log ε) 260 (3.73) ; $^1H$ NMR ($CCl_4$) δ 0.78-2.07 (10 H, m, 5 x $CH_2$), 2.47-3.07 (4 H, m, benzylic $CH_2$ and $CH_2C$=O), 6.96-7.51 and 7.56-7.80 (4 H, m, ArH) ; $C_{15}H_{18}O_2$, mass spectrum m/e 230 ($M^+$).

3h (with enol form) : (n = 7) ; IR (NaCl) 3500-3300 $cm^{-1}$ (OH), 1720, 1670 $cm^{-1}$ (C=O), 1640 $cm^{-1}$ (CH=COH) ; UV (MeOH) λ nm (log ε) 261 (3.67) ; $^1H$ NMR ($CCl_4$) δ 0.73-2.17 (14 H, m, $CH_2$), 2.42-3.06 (3.7 H, m, benzylic $CH_2$ and $CH_2CO$), 5.4 (0.15 H, t, -CH=COH, J = 8 Hz), 6.71 (0.15 H, s, CH=COH, OH exchanged with $D_2O$), 6.95-7.84 (4 H, m, ArH) ; $C_{17}H_{22}O_2$, mass spectrum m/e 258 ($M^+$).

3i (with enol form) : (n = 8) ; IR (NaCl) 3600-3220 $cm^{-1}$ (OH), 1715, 1690, 1670 $cm^{-1}$ (C=O), 1630 $cm^{-1}$ (CH=COH) ; UV (MeOH) λ nm (log ε) 263 (3.85) ; $^1H$ NMR ($CCl_4$) δ 0.77-3.02 (19.4 H, m, $CH_2$, benzylic $CH_2$ and $CH_2CO$), 5.29 (0.3 H, t, CH=COH, J = 8 Hz), 6.53 (0.3 H, s, CH=COH, OH exchanged with $D_2O$), 7.02-7.64 (4 H, m, ArH).

Transposition of 1 under anhydrous conditions (Method C). To a stirred solution of the alcohol 1 (2 mmol) in MeCN (10 ml), was added $Me_3SiCl$ (5 mmol). The reaction was instantaneous (monitored by TLC). After addition of powdered $NaHCO_3$ until neutrality, the solution was filtered off and the solvents evaporated under reduced pression. The keto ether was purified by chromatography.

Method D. To a stirred solution of the alcohol (2 mmol) in $CH_2Cl_2$ (10 ml) maintained at 0-5°C, was slowly added $BF_3$-$OEt_2$ (2.2 mmol) diluted in $CH_2Cl_2$ (5 ml). At the end of the addition, the mixture was allowed to warm to room temperature. At the completion (monitored by TLC), a saturated solution of $NaHCO_3$ (20 ml) was added and the stirring maintained for 10 min. After extraction with $CH_2Cl_2$, drying over $MgSO_4$ and removal of the solvents in vacuo, the products were purified by chromatography.

Transposition of 1 under aqueous conditions (Method E). To a solution of 10 % HCl (20 ml) was added the alcohol 1 (2 mmol) in MeOH (20 ml). The reaction was instantaneous (monitored by TLC) and the mixture was poured into water and extracted with ethyl ether. The organic layer was then washed with a saturated solution of $NaHCO_3$, dried over $MgSO_4$ and evaporated under reduced pressure. A rapid filtration on column chromatography gave the keto alcohol 6.

Method F. To the alcohol 1 (6 mmol) in acetone (20 ml) was added 10 drops of HCl 12N (and 1 or 5 ml of $H_2O$ as mentionned in the Table III). After stirring at room temperature for the time indicated in the Table III, the mixture was poured into water, extracted with ethyl ether. The organic layer was washed with a saturated solution of $NaHCO_3$, dried over $MgSO_4$ and evaporated in vacuo. The products were purified by chromatography.

Spectral data and melting points for indanone derivatives are given in Table V.

TABLE V - PHYSICAL DATA FOR INDANONE DERIVATIVES

| Compounds | mp, °C (solv.) | IR (solv.) $\nu$, $cm^{-1}$ | UV (MeOH) $\lambda$, nm (log $\varepsilon$) | $^1$H NMR (solv.), $\delta$ | $^{13}$C NMR ($CDCl_3$), $\delta$ |
|---|---|---|---|---|---|
| 4a cis | - | (NaCl) 1715 (C=O) | 295 (3.42) 249 (4.14) | ($CCl_4$) 0.97-2.46 (6H, m, 3x$CH_2$), 3.22 (3H, s, $OCH_3$), 3.33-3.69 (1H, m, benzylic H), 7.16-7.95 (4H, m, ArH) | 206.79 (C=O), (arom.C) 155.82, 136.38, 136.29, 127.96, 126.06, 123.67, (aliph.C) 93.91 ($\underline{C}OCH_3$), 53.49 ($OCH_3$), 46.67 (benzylic C), 36.56, 31.98, 24.14 (3x$CH_2$) |
| 4c cis | 90 (petroleum ether) | (NaCl) 1710 (C=O) | 295 (3.40) 248 (4.22) | ($CCl_4$) 0.97-2.29 (8H, m, 4x$CH_2$), 3.11-3.57 (4H, m, benzylic H with s at 3.22, $OCH_3$), 7.12-7.82 (4H, m, ArH) | 205.47 (C=O) (arom.C) 154.64, 135.11, 134.33, 127.55, 124.52, 124.23, (aliph.C) 84.51 ($\underline{C}OCH_3$), 52.06 ($OCH_3$), 40.36 (benzylic C), 29.61, 25.43, 21.02, 20.48 (4x$CH_2$) |
| 4c trans | - | (NaCl) 1720 (C=O) | 295 (3.39) 251 (4.04) | ($CCl_4$) 1.11-2.05 (8H, m, 4x$CH_2$), 2.73-3.22 (4H, m, benzylic H with s at 3.06, $OCH_3$), 7.05-7.75 (4H, m, ArH) | 200.58 (C=O) (arom.C) 156.06, 137.76, 137.46, 126.31, 124.97, 124.61, (aliph.C) 82.75 ($\underline{C}OCH_3$), 50.77 ($OCH_3$), 48.95 (benzylic C), 25.57, 23.75, 21.26, 20.36 (4x$CH_2$) |
| 4e trans | - | (NaCl) 1720 (C=O) | 294 (3.33) 249 (3.98) | ($CCl_4$) 0.78-2.78 (10H, m, 5x$CH_2$), 3.00-3.42 (4H, m, benzylic H with s at 3.13, $OCH_3$), 7.10-7.83 (4H, m, ArH) | 202.35 (C=O) (arom.C) 155.66, 135.03, 134.63, 127.31, 124.28, 124.20, (aliph.C) 84.00 ($\underline{C}OCH_3$), 50.77 ($OCH_3$), 47.64 (benzylic C), 27.70, 26.91, 25.81, 24.34 (5x$CH_2$) |
| 5b cis | - | (NaCl) 3590-3100 (OH) 1710 (C=O) | 295 (3.33) 250 (4.02) | ($CDCl_3$)[a] 1.08-2.30 (7H, m, 3x$CH_2$ and OH exchanged with $D_2O$), 3.46-3.53 (1H, m, $COCH_2\underline{C}H_2OH$), 3.59-3.73 (4H, m, $COCH_2CH_2OH$ and benzylic H), 7.37-7.49 and 7.64-7.75 (4H, 2m, ArH) | 206.97 (C=O) (arom.C) 155.64, 136.36, 136.01, 127.94, 125.97, 123.70, (aliph.C) 93.62 ($\underline{C}OCH_2CH_2OH$), 67.33, 62.17 ($OCH_2CH_2OH$), 47.44 (benzylic C), 36.68, 32.06, 24.12 (3x$CH_2$) |
| 5d cis | - | (NaCl) 3680-3100 (OH) 1710 (C=O) | 295 (3.32) 249 (3.94) | ($CDCl_3$)[a] 1.20-2.09 (8H, m, 4x$CH_2$), 2.37-2.80 (1H, m, OH exchanged with $D_2O$), 3.46-3.51 (1H, pseudo t, benzylic H), 3.51-3.58 and 3.65-3.76 (1H and 3H, 2m, $COCH_2CH_2OH$), 7.36-7.78 (4H, m, ArH) | 206.81 (C=O) (arom.C) 153.72, 135.34, 134.01, 127.69, 124.47, 124.36, (aliph.C) 84.82 ($\underline{C}OCH_2CH_2OH$), 66.33, 62.05 ($OCH_2CH_2OH$), 40.51 (benzylic C), 30.46, 24.61, 20.83, 20.48 (4x$CH_2$) |
| 5f trans | - | (NaCl) 3700-3110 (OH) 1710 (C=O) | 296.5 (3.33) 250 (4.10) | ($CDCl_3$)[a] 1.11-2.58 (11H, m, 5x$CH_2$ and OH, exchanged with $D_2O$), 3.32-3.39 (1H, dd, $J_1$= 6Hz, $J_2$=12Hz, benzylic H), 3.44-3.51 and 3.53-3.65 (1H and 3H, 2m, $COCH_2CH_2OH$), 7.33-7.75 (4H, m, ArH) | 202.80 (C=O) (arom.C) 156.28, 135.87, 135.20, 127.84, 125.16, 124.49, (aliph.C) 84.67 ($\underline{C}OCH_2CH_2OH$), 64.59, 62.55 ($OCH_2CH_2OH$), 48.19 (benzylic C), 28.78, 27.11, 25.77, 24.43 (5x$CH_2$) |
| 5g cis | - | (NaCl) 3700-3120 (OH) 1715 (C=O) | 297 (3.50) 250 (4.16) | ($CDCl_3$)[a] 1.35-2.36 (13H, m, 6x$CH_2$ and OH, exchanged with $D_2O$), 3.25 (1H, d, J=9Hz, benzylic H), 3.38-3.50 and 3.53-3.64 (2x2H, 2m, $COCH_2CH_2OH$), 7.33-7.73 (4H, m, ArH) | 205.12 (C=O) (arom.C) 158.63, 135.73, 133.25, 127.65, 126.00, 124.04, (aliph.C) 85.38 ($\underline{C}OCH_2CH_2OH$), 65.04, 62.03 ($OCH_2CH_2OH$), 50.42 (benzylic C), 32.59, 30.45, 25.73, 25.48, 23.40 (6x$CH_2$) |
| 5h cis | - | (NaCl) 3600-3120 (OH) 1715 (C=O) | 297 (3.38) 250 (4.04) | ($CDCl_3$)[a] 1.31-2.23 (17H, m, 8x$CH_2$ and OH exchanged with $D_2O$), 3.39-3.52 (3H, m, $COCH_2CH_2OH$ and benzylic H), 3.55-3.63 (2H, m, $COCH_2CH_2OH$), 7.34-7.75 (4H, m, ArH) | 205.51 (C=O) (arom.C) 157.24, 135.72, 134.14, 127.71, 125.83, 124.37, (aliph.C) 86.96 ($\underline{C}OCH_2CH_2OH$) 65.31, 62.22 ($OCH_2CH_2OH$), 48.33 (benzylic C), 27.83, 26.86, 26.62, 24.32, 23.71, 22.86, 20.01 (7x$CH_2$) |

TABLE V (continued)

| | | | | | |
|---|---|---|---|---|---|
| 5i cis | - | (NaCl) 3590-3200 (OH) 1715 (C=O) | 294 (3.43) 250 (4.10) | ($CDCl_3$)[a] 1.28-2.50 (19H, m, 9x$CH_2$ and s at 2.30, OH exchanged with $D_2O$), 3.29-3.38 (1H, m, benzylic H), 3.40-3.58 and 3.58-3.71 (4H, 2m, $COCH_2CH_2OH$), 7.34-7.74 (4H, m, ArH) | 206.22 (C=O) (arom C) 156.05, 135.55, 133.61, 127.64, 125.43, 124.13, (aliph.C) 89.21 ($\underline{C}OCH_2CH_2OH$) 65.87, 62.10 ($OCH_2CH_2OH$), 47.65 (benzylic C), 30.48, 28.82, 26.81, 26.65, 25.26, 24.10, 21.46, 21.39, 18.74 (9x$CH_2$) |
| 5i trans | - | (NaCl) 3670-3140 (OH) 1715 (C=O) | 295 (3.36) 250.5 (3.99) | ($CCl_4$) 1.03-2.64 (19H, m, 9x$CH_2$ and OH exchanged with $D_2O$), 3.29-3.79 (5H, m, $COCH_2CH_2OH$ and benzylic H), 7.10-7.84 (4H, m, ArH) | 204.44 (C=O) (arom.C) 157.58, 135.61, 134.22, 127.58, 125.17, 124.30, (aliph.C) 84.01 ($\underline{C}OCH_2CH_2OH$) 65.10, 62.40 ($OCH_2CH_2OH$), 46.64 (benzylic C), 30.43, 29.70, 28.39, 26.93, 26.20, 25.98, 24.96, 24.45, 21.02 (9x$CH_2$) |
| 6a cis | 84 (P.E.) | (KBr) 3660-3100 (OH) 1715 (C=O) | 294 (3.39) 248 (4.14) | ($CCl_4$) 0.79-2.71 (6H, m, 3x$CH_2$), 3.33-3.62 (1H, pseudo d, benzylic H), 4.24 (1H, m, OH exchanged with $D_2O$), 6.98-7.78 (4H, m, ArH) | 208.18 (C=O) (arom.C) 155.86, 136.26, 134.80, 127.87, 125.87, 124.11, (aliph.C) 88.34 (COH), 51.90 (benzylic C), 38.82, 31.61, 25.35 (3x$CH_2$) |
| 6c cis | 144 (P.E.) | (KBr) 3570 (OH) 1730 (C=O) | 293 (3.51) 246 (4.13) | ($CDCl_3$) 1.00-2.40 (8H, 2m, 4x$CH_2$), 3.17 (1H, s, OH exchanged with $D_2O$), 3.30 (1H, pseudo t, benzylic H), 7.18-7.89 (4H, m, ArH) | 208.30 (C=O), (arom.C) 153.54, 135.41, 133.83, 127.89, 124.92, 124.25, (aliph.C) 80.10 (COH), 44.60 (benzylic C), 32.70, 23.60, 20.30, (4x$CH_2$) |
| 6f trans | 126 (P.E.-EtOAc) | (KBr) 3410 (OH) 1720 (C=O) | 295 (3.54) 249 (4.20) | ($CCl_4$) 1.02-2.62 (10H, m, 5x$CH_2$), 2.84[a] (1H, pseudo s, OH exchanged with $D_2O$), 3.02-3.53 (1H, m, benzylic H), 7.09-7.93 (4H, m, ArH) | 205.31 (C=O), (arom.C) 155.87, 135.40, 134.00, 127.46, 124.86, 124.45, (aliph.C) 80.45 (COH), 46.59 (benzylic C), 33.56, 27.20, 25.69, 23.93 (5x$CH_2$) |
| 6f cis (= 6e cis) | - | (KBr) 3600-3200 (OH) 1710 (C=O) | 294 (3.45) 248.5 (4.15) | ($CCl_4$) 0.82-2.80 (10H, m, 5x$CH_2$), 2.96-3.62 (2H, m, OH exchanged with $D_2O$, benzylic H), 7.16-7.98 (4H, m, ArH) | 208.64 (C=O), (arom.C) 156.66, 135.88, 133.58, 127.77, 125.52, 124.43, (aliph.C) 82.39 (COH), 51.74 (benzylic C), 34.96, 31.87, 31.26, 26.72, 22.78 (5x$CH_2$) |
| 6g cis | 88 (P.E.) | (KBr) 3520-3200 (OH) 1705 (C=O) | 294 (3.46) 248 (4.12) | ($CDCl_3$) 1.00-2.40 (12H, m, 6x$CH_2$), 2.73 (1H, s, OH exchanged with $D_2O$) 2.94-3.37 (1H, m, benzylic H), 7.19-7.90 (4H, m, ArH) | 208.52 (C=O), (arom.C) 157.63, 135.76, 132.73, 127.70, 125.83, 124.43, (aliph.C) 81.30 (COH), 51.37 (benzylic C), 30.41, 29.93, 29.32, 25.44, 25.02, 23.63 (6x$CH_2$) |
| 6h trans | - | (KBr) 3540-3220 (OH) 1710 (C=O) | 294 (3.38) 249 (4.03) | ($CCl_4$) 1.09-2.89 (17H, m, 8x$CH_2$ with pseudo s at 2.53, OH exchanged with $D_2O$), 3.47-3.78 (1H, m, benzylic H), 7.13-7.91 (4H, m, ArH) | 208.40 (C=O) (arom.C) 159.48, 136.82 133.13, 128.39, 126.41, 125.10, (aliph.C) 80.61 (COH), 43.40 (benzylic C), 36.90, 28.05, 26.23, 23.5[illegible] 22.60, 20.17, 17.45 (8x$CH_2$) |
| 6h cis | 118 (EtOAc-P.E.) | (KBr) 3530-3110 (OH) 1710 (C=O) | 294 (3.41) 248 (4.06) | ($CCl_4$) 1.06-2.41 (16H, m, 8x$CH_2$), 2.69 (1H, pseudo s, OH exchanged with $D_2O$), 3.13-3.53 (1H, m, benzylic H), 7.00-7.91 (4H, m, ArH) | 206.94 (C=O) (arom.C) 154.92, 135.0[illegible] 133.12, 127.09, 125.15, 123.81, (aliph.C) 81.70 (COH), 49.68 (benzylic C), 30.38, 27.11, 25.71, 22.74 22.50, 22.13, 19.50 (8x$CH_2$) |
| 6i trans | - | (KBr) 3560-3160 (OH) 1695 (C=O) | 296 (3.67) 249 (4.24) | ($CCl_4$) 0.89-2.62 (18H, m, 9x$CH_2$), 2.91 (1H, pseudo s, OH exchanged with $D_2O$), 3.42-3.82 (1H, m, benzylic H), 7.15-8.04 (4H, m, ArH) | 209.61 (C=O) (arom.C) 158.34, 136.0[illegible] 133.01, 127.78, 126.10, 124.67, (aliph.C) 80.62 (COH), 45.13 (benzylic C), 36.16, 30.26, 27.87, 27.3[illegible] 26.98, 25.48, 24.21, 22.66, 20.71 (9x$CH_2$) |
| 6i cis | 110 (P.E.) | (KBr) 3580-3110 (OH) 1710 (C=O) | 294 (3.42) 247.5 (4.01) | ($CCl_4$) 0.82-2.13 (18H, m, 9x$CH_2$), 2.73 (1H, pseudo s, OH exchanged with $D_2O$), 3.02-3.31 (1H, s, benzylic H), 7.15-7.85 (4H, m, ArH) | 208.64 (C=O), (arom.C) 155.06, 135.[illegible] 133.04, 127.75, 125.15, 124.34, (aliph.C) 84.73 (COH), 50.94 (benzylic C), 33.77, 27.33, 26.98, 26.4[illegible] 25.04, 24.71, 21.43, 20.70, 18.89 (9x$CH_2$) |

(a) Spectra recorded at 400 MHz.

Alkylation of 6a,c,i cis and 6f trans under phase transfer catalysis. The keto alcohol 6 (4 mmol) was dissolved in $CH_2Cl_2$ (10 ml) with $CH_3I$ (8 mmol, 2 equiv.). 0.5 equivalent of $nBu_4N^+Br^-$ then 50 % aqueous NaOH were added and the mixture was vigorously stirred at room temperature for 24 h. The two phases were decanted and the aqueous layer was extracted twice with $CH_2Cl_2$. After drying over $MgSO_4$ and evaporation of the solvent in vacuo, the corresponding keto ether was rapidly isolated by chromatography on a short column. The respective yields of keto ethers 4a, 4c, 4i and 4e were 80, 60, 93 and 85 %.

Degradation of 5b,d,g,h,i cis into the corresponding keto alcohols 6. The methanesulfonate ester was prepared following the procedure described by Crossland et al.[13] The crude mesylate was treated with excess sodium iodide in DMF as described by Yasuda et al.[14] The pure corresponding iodo derivative was obtained by a rapid column chromatography over silica gel (5 % EtOAc in petroleum ether).

n = 2 : 55 % yield ; IR (NaCl) 1700 $cm^{-1}$ (C=O) ; $^1H$ NMR ($CCl_4$) δ 0.75-2.64 (6 H, m, 3 x $CH_2$), 3.02-4.04 (5 H, m, benzylic H, $OCH_2CH_2I$), 7.17-7.89 (4 H, m, ArH).
n = 3 : 63 % yield ; IR (NaCl) 1720 $cm^{-1}$ (C=O) ; $^1H$ NMR ($CCl_4$) δ 1.04-2.30 (8 H, m, 4 x $CH_2$), 3.04-3.59 (3 H, m, benzylic H and $CH_2I$), 3.60-3.93 (2 H, m, $OCH_2$), 7.17-7.86 (4 H, m, ArH).
n = 5 : 62 % yield ; IR (NaCl) 1720 $cm^{-1}$ (C=O) ; $^1H$ NMR ($CCl_4$) δ 0.75-2.60 (12 H, m, 6 x $CH_2$), 2.82-3.89 (5 H, m, benzylic H and $OCH_2CH_2I$), 7.13-7.89 (4 H, m, ArH).
n = 7 : 74 % yield ; IR (NaCl) 1720 $cm^{-1}$ (C=O) ; $^1H$ NMR ($CCl_4$) δ 0.80-2.55 (16 H, m, 8 x $CH_2$), 2.84-3.87 (5 H, m, benzylic H and $OCH_2CH_2I$), 6.89-8.13 (4 H, m, ArH).
n = 8 ; 55 % yield ; IR (NaCl) 1720 $cm^{-1}$ (C=O) ; $^1H$ NMR ($CCl_4$) δ 1.04-2.49 (18 H, m, 9 x $CH_2$), 2.98-3.98 (5 H, m, benzylic H and $OCH_2CH_2I$), 7.27-7.89 (4 H, m, ArH).

The corresponding keto alcohol 6 was obtained from the iodo ether derivative by olefine elimination following two procedures. The first one using magnesium in aprotic medium[15] was applied to the derivative for n = 3 to lead to the keto alcohol 6c cis. The second one with activated Zn in nBuOH[16] allowed the formation of 6a,g,h,i cis with 38, 52, 20 and 8 % yield respectively.

Preparation of compounds 8.

Wolff-Kishner reaction.[17] The benzylic carbonyl reduction of indanonols 6a,c lead to the compound 8
n = 2 : IR (NaCl) 3660-3200 $cm^{-1}$ (OH) ; $^1H$ NMR ($CCl_4$) δ 0.93-2.84 (6 H, m, 3 x $CH_2$), 3.02-3.55 (4 H, m, 3 benzylic H, and OH, exchanged with $D_2O$), 6.82-7.44 (4 H, m, ArH).
n = 3 : IR (NaCl) 3620-3240 $cm^{-1}$ (OH) ; $^1H$ NMR ($CCl_4$) δ 0.93-2.46 (8 H, m, 4 x $CH_2$), 2.55-3.29 (4 H, m, benzylic H with 2.73 and 3.04, AB quartet, J = 15 Hz, benzylic $CH_2$ and OH exchanged with $D_2O$), 7.06-7.53 (4 H, m, ArH).

TABLE VI - ANALYTICAL DATA OF THE INDANONE DERIVATIVES

| Compound | Formula | Analysis (%) Calcd. C | Calcd. H | Found C | Found H | mass spectrometry m/e |
|---|---|---|---|---|---|---|
| 4a cis | $C_{14}H_{14}O_2$ | | - | | | CI, 221 (M+18), 203 (M+1) |
| 4c cis | $C_{14}H_{16}O_2$ | 76.44 | 7.89 | 77.08 | 7.59 | - |
| 4c trans | $C_{14}H_{16}O_2$ | | - | | | 216 ($M^+$) |
| 4e trans | $C_{15}H_{18}O_2$ | | - | | | 230 ($M^+$) |
| 5b cis | $C_{16}H_{15}O_3$ | | - | | | CI, 233 (M+1) |
| 5d cis | $C_{15}H_{18}O_3$ | | - | | | 246 ($M^+$) |
| 5f trans | $C_{16}H_{20}O_3$ | 73.82 | 7.74 | 73.64 | 7.68 | - |
| 5g cis | $C_{17}H_{22}O_3$ | | - | | | 274 ($M^+$) |
| 5h cis | $C_{19}H_{26}O_3$ | | - | | | 302 ($M^+$) |
| 5i cis | $C_{20}H_{28}O_3$ | | - | | | 316 ($M^+$) |
| 5i trans | $C_{20}H_{28}O_3$ | 75.91 | 8.91 | 75.59 | 9.09 | - |
| 6a cis | $C_{12}H_{12}O_2$ | 76.57 | 6.42 | 76.36 | 6.48 | - |
| 6c cis | $C_{13}H_{14}O_2$ | 77.20 | 6.98 | 77.24 | 7.02 | - |
| 6f (=6e cis) | $C_{14}H_{16}O_2$ | | - | | | 216 ($M^+$) |
| 6g cis | $C_{15}H_{18}O_2$ | | - | | | 230 ($M^+$) |
| 6h trans | $C_{17}H_{22}O_2$ | | - | | | 258 ($M^+$) |
| 6h cis | $C_{17}H_{22}O_2$ | 79.03 | 8.58 | 79.82 | 8.80 | - |
| 6i trans | $C_{18}H_{24}O_2$ | 79.37 | 8.88 | 76.50 | 9.05 | - |
| 6i cis | $C_{18}H_{24}O_2$ | | - | | | 272 ($M^+$) |

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## REFERENCES


1) Grégoire, B. ; Carré, M.C. ; Caubère, P., J. Org. Chem. 1986, 51, 1419.
2) a) Trockle, G. ; Catau, G. ; Barberi, C. ; Jacque, M. ; Carré, M.C. ; Caubère, P., Life Sci. 1981, 28, 23 ; b) El Rayyes, N.R. ; Al Jawhary, A., J. Heterocyclic Chem. 1986, 23, 135 ; Jensen, B.L. ; Chockalingam, K., Ibid, 1986, 23, 343 ; Weis, A.L. ; Frolow, F. ; Vishkautsan, R., Ibid, 1986, 23, 705 ; Henin, J. ; Gardent, J., Ibid, 1986, 23, 975 ; Schenone, P. ; Bargagna, A. ; Longobardi, M., Ibid, 1986, 23, 1067 ; Hirota, T. ; Ieno, K. ; Sasaki, K., Ibid, 1986, 23, 1685, and ref. cited therein.
3) Carré, M.C. ; Grégoire, B. ; Caubère, P., J. Org. Chem. 1984, 49, 2050.
4) Tsunetsugu, J. ; Sugahara, M. ; Heima, K. ; Ogawa, Y. ; Kosufi, M. ; Sato, M. ; Ebine, S., J. Chem. Soc., Perkin Trans. I, 1983, 1983.
5) Cava, M.P. ; Muth, K., J. Am. Chem. Soc. 1960, 82, 652 ; Caubère, P. ; Guillaumet, G. ; Mourad M.S., Tetrahedron 1973, 29, 1857 ; Caubère, P. ; Guillaumet, G. ; Mourad, M.S., Bull. Soc. Chim. Fr. 1973, 3493.
6) Tanis, S.P. ; Nakanishi, K., J. Am. Chem. Soc. 1979, 101, 4398.
7) Morita, T. ; Okamoto, Y. ; Sakurai, H., J. Chem. Soc., Chem. Commun. 1978, 874.
8) Lipshutz, B.H. ; Pollart, D. ; Monforte, J. ; Kotsuki, H., Tetrahedron Lett. 1985, 26, 705.
9) Huet, F. ; Lechevallier, A. ; Pellet, M. ; Conia, J.M., Synthesis 1978, 63.
10) Müller, E. Ed. "Methoden der Organischen Chemie" ; Georg Thieme Verlag : Stuttgart, 1973 ; Band VII/2a, Teil 1.
11) Tobe, Y. ; Ueda, Y. ; Nishikawa, H. ; Odaira, Y., J. Org. Chem. 1981, 46, 5009 ; Do Khac Manh Duc ; Fetizon, M. ; Kone, M., Tetrahedron 1978, 34, 3513 ; Pirrung, M.C., J. Am. Chem. Soc. 1981, 103, 82 ; Eaton, P.E. ; Jobe, P.G. ; Nyi, K., J. Am. Chem. Soc. 1980, 102, 6636 ; Do Khac Manh Duc ; Fetizon, M. ; Lazare, S., J. Chem. Soc., Chem. Commun. 1975, 282 ; Peet, N.P. ; Cargill, R.L. ; Bushey, D.F., J. Org. Chem. 1973, 38, 1218 ; Yanagiya, M. ; Kaneko, K. ; Kaji, T. ; Matsumoto, T., Tetrahedron Lett. 1979, 20, 1761.
12) To be published.
13) Crossland, R.K. ; Servis, K.L., J. Org. Chem. 1970, 35, 3195.
14) Yasuda, N. ; Matsuda, K. ; Tsutsumi, H. ; Takaya, T., Chem. Lett. 1984, 10, 1665.
15) Caubère, P., Bull. Soc. Chim. Fr. 1964, 148.
16) Rabjohn, N. "Organic Syntheses" ; Wiley : New York, 1963, Collect. Vol. 4, p. 748.
17) Vogel, A.I., Textbook of Practical Organic Chemistry, 4th ed. ; Longman London and New York, 1978, pp. 600–606.