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NEW EASY ACCESS TO BENZOCYCLOBUTENONE DERIVATIVES

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Abstract : Benzocyclobutenone derivatives are easily obtained by oxidative transformation of functional polycyclic benzocyclobutenols synthetized by arynic condensations.

Benzocyclobutenones are among the interesting starting materials to obtain benzocyclobutenes. These latter are largely used in the synthesis of a wide range of products.[1]

Benzocyclobutenones substituted on the four membered ring are not easy to obtain. Indeed it necessitates the cyclisation of precursors with the required substituent in the appropriate position.[2] A good starting material could be benzocyclobutanone itself. However its enolization is practically impossible to obtain due to the benzocyclobutadiene form of the potential enolate. Thereby a large number of interesting methods of functionalization of ketones are inapplicable.

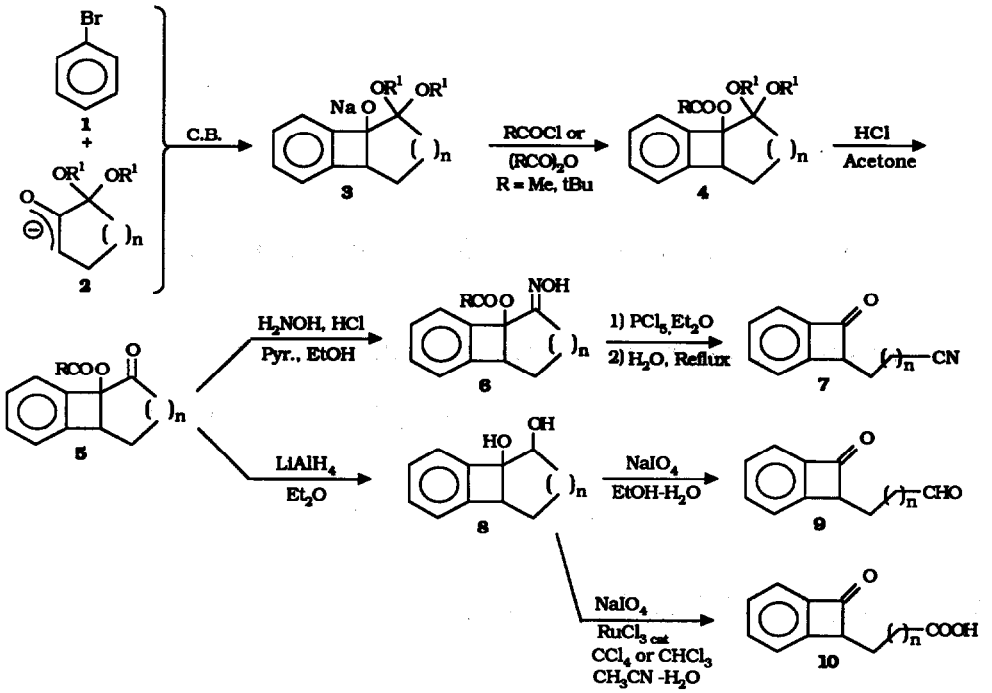
In our laboratory we are working for several years on the synthesis of benzocyclobutene derivatives by arynic condensations of ketone enolates.[3]

Part of the compounds thus prepared lend themselves to be transformed into benzocyclobutenones substituted on the α position of the carbonyl group. If we take into account that arynic condensations of ketone enolates may be performed with substituted aryl halides[4] as well as diversely substituted cyclanones, it may be concluded that the procedure proposed below ought to allow the synthesis of a large number of highly diversified benzocyclobutenones. In this first paper we wish to report the basic statements of this new approach.

Results and discussion

We have reported in the Scheme I the steps involved in the synthesis of the different benzocyclobutenone derivatives.

Scheme I



The results obtained have been gathered in the Table I.

Table I

Entry	n	R^1 R^1	R	4 Yield %[i]	5 Yield %	6 Yield %	7 Yield %	8 Yield % (cis/trans)	9 Yield % (starting isomer 8)	10 Yield % (starting isomer 8)
a	1	CH_3 CH_3	CH_3	50	52	80	88	-	-	-
b	2	-$(CH_2)_3$-	CH_3	83	94	94	73	quant. (40/60)	quant. (each isomer)	75 (trans)
c	3	-$(CH_2)_3$-	CH_3	88	91	96	75	80 (100/0)	quant. (cis)	85 (cis)
d	3	CH_3 CH_3	tBu	82	92	92	76	93 (100/0)	-	-
e	4	-$(CH_2)_3$-	CH_3	72	98	98	82	85 (19/81)	94 (trans)	90 (trans)
f	7	-$(CH_2)_3$-	CH_3	48	94	90	63	70[ii]	96 (mixture)	72 (mixture)
g	8	-$(CH_2)_3$-	CH_3	44	90	86	65	87[iii]	95 (mixture)	82 (mixture)

[i] Yield taking into account recovered unprotected benzocyclobutenols respectively for entry a 16.5 %, b : 10 %, c : 7 %, d : 14 %, e : 18 %, f : 24 %, g : 36 % ; [ii] separable isomers with undetermined stereochemistry (86/14) ; [iii] Isomer ratio determined by ^{13}C NMR (63/37)

The synthesis of **4** has already been published, however, a number of them had never been described before. Protection of the hydroxy group is necessary in order to avoid the formation of a transposed product[5] during the release of the carbonyl group. It was found that direct protection of the intermediate alkoxides was better than hydrolysis which was followed by esterification of the corresponding benzocyclobutenols.

Hydrolysis of **4** must be performed under very mild conditions in order to avoid the transformation into indanone derivatives.[5] Note that most part of ketones **5** were precedently unknown. Oximes **6** were easily obtained and underwent classical second order Beckmann rearrangement[6] to give **7** in good yields.

We did not succeeded in the direct oxidative cleavage of **5**. The quantitative reduction of **5** into **8** allowed to solve our problems. Oxidation of **8** by $NaIO_4$[7] led to the expected ketoaldehyde **9**. Cleavage of the same diol with $NaIO_4$ in presence of a catalytic amount of $RuCl_3,3\ H_2O$ gave the ketoacid **10**.[8]

It must be emphasized that most part of the ketoaldehydes **9** was very air sensitive and that it was necessary to prepare their corresponding dioximes.

In conclusion we have shown that our approach allows the easy preparation of benzocyclobutenones derivatives. One of the interests of this procedure is the simplicity of each step which may be performed on a large scale without problem. We are actively working on the extension of these first results.

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Experimental section

General methods. Melting points were determined on a Kofler melting point apparatus. ^{13}C NMR spectra were recorded on a Bruker AM 400 spectrometer and ^{1}H NMR spectra on a Bruker WP 80 instrument at 80 MHz with Me4Si 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. 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 Petrolum Ether-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.

Materials. Merck or Fluka sodamide washed with appropriate solvents was used.Tetrahydrofuran (THF) was distilled from a benzophenone-sodium couple, dimethoxyethane (DME) from sodium and diethyl ether from diphosphorus pentoxide, acetal cycloalkanones were prepared as previously described.[9]

7,8,9,9a Tetrahydro spiro [5H-benzo[3,4] cyclobuta[1,2] cycloheptene 5,2'[1,3] dioxinan] 4b(6H) (acetyloxy) (4c) (Typical procedure for compounds 4). This compounds was prepared as previously described.[9] Upon completion, the reaction mixture was vigorously stirred under a strong nitrogen stream. The supernatant liquid was then added to a mixture of acetic anhydride

(3 eq), triethylamine (0.5 eq) and 4-(dimethylamino)pyridine (0.15 eq) in THF or DME. After complete reaction, the mass was poured on ice, extracted with diethyl ether, washed twice with water and dried over $MgSO_4$. After evaporation of the solvents under reduced pressure, the different components of the mixture were separated by HPLC. Compound **4f** was purified by semi preparative H.P.L.C. on µporasil® (Physical and spectroscopic data are given in Table II).

Hydrolysis of the acetal group for the synthesis of 3,4,4a,8b Tetrahydro (2H) biphenylenone, 8b (acetyloxy) (5b) (Typical procedure for compounds 5) . To a stirred solution of **4b** (6.8 mmol) in acetone (50 ml) at room temperature was added 5 drops of conc. HCl. After complete reaction (monitored by TLC) the mixture was stirred with solid $NaHCO_3$, filtered and concentrated. The residue was dissolved in water and extracted with diethyl ether then dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue purified by HPLC or flash chromatography (silica) (Physical and spectroscopic data are given in Table III).

Preparation of 4b,6,7,8,9,9a Hexahydro (5H) benzo [3,4] cyclobuta [1,2] cyclohepten-5 (hydroxyimino)-4b(acetyloxy) (6c) (Typical procedure for compounds 6). To a stirred solution of hydroxylamine hydrochloride (1.5-2 eq), pyridine (1.5-2.0 eq) in ethanol (10 ml) maintained at room temperature was added **5c** (1 mmol) dissolved in ethanol (10 ml). After complete reaction (monitored by TLC), the solvent was evaporated under reduced pressure. The mixture was diluted with water and extracted with methylene chloride, washed with 10 % citric acid solution , dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue purified by centrifuge TLC (Chromatotron®) (Physical and spectroscopic data are given in Table IV).

Synthesis of bicyclo [4.2.0] octa 1,3,5-triene 7-(alkylcyanide) 8-oxo (7) (Typical procedure for compounds 7). These derivatives were prepared by the method previously described for the normal Beckmann transposition.[10] To a stirred mixture of **6** (1 mmol) in diethyl ether (10 ml) was added PCl_5 (2.5 mmol). After 15 min the solvent was evaporated under reduced pressure and water was added (10 ml). The mixture was then refluxed for several minutes, cooled to room temperature and extracted with diethyl ether. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure and the products purified by centrifuge TLC (Chromatotron®) (Physical and spectroscopic data are given in Table V).

Preparation of 5,6,7,8,9,9a Hexahydro 4bH-benzo [3,4] cyclobuta [1,2] cyclohepten-4b,5 diol (8c) (Typical procedure for compounds 8) . To a stirred mixture of $LiAlH_4$ (2.5 eq) in dry diethyl ether (30 ml) was added compound **5** (4 mmol) dissolved in diethyl ether (15 ml). After complete reaction (monitored by TLC), water was carefully added, the organic layer was washed with 10% HCl solution and dried over $MgSO_4$. The solvent was removed under reduced pressure and the product purified by column chromatography (silica) (Physical and spectroscopic data are given in Table VI).

Synthesis of bicyclo [4.2.0] octa 1,3,5-triene 7-(alkylaldehyde) 8-oxo (9) (Typical procedure for compounds 9) . A solution of sodium metaperiodate (1.5 eq.) in water (10 ml) was added to a stirred solution of diol **8** (2mmol) in ethanol. After complete reaction (monitored by TLC) a thick heavy white precipitate was obtained. The ethanol was evaporated under reduced pressure. The mixture was extracted with methylene chloride and the extract was dried over $MgSO_4$ and concentrated. The product was purified by centrifuge TLC (Chromatotron®) (Physical and spectroscopic data are given in Table VII).

Synthesis of bicyclo [4.2.0] octa 1,3,5-triene 7-(alkylcarboxylic acid) 8-oxo (10) (Typical procedure for compounds 10) . These compounds are prepared by a modified K.B. Sharpless reaction,[8] i.e. the $RuCl_3,3H_2O$ (0.05 eq) is added to the mixture after formation (monitored by T.L.C) of the intermediate compound **9**. The product was purified by flash chromatography on silica gel . (Eluent mixture EtOAc/PE containing 1% AcOH) (physical and spectroscopic data are given in Table VIII).

Table II - Physical and spectroscopic data for compounds 4.

Compound	mp °C (solvent)	IR ν, cm^{-1}	UV (MeOH) λ nm (log ε)	^{1}HNMR (solvent) δ	Analysis (C,H) Calcd. Found
4a	-	(NaCl) 1730 (C=O)	261 (3.84) 267 (3.96) 273 (3.94)	(CCl_4) 0.92-2.64 (7H, m, 2xCH_2 and CH_3CO, s at 1.91), 3.16 (3H, s, OCH_3), 3.19 (3H, s, OCH_3), 4.20-4.40 (1H, m, benzylic H), 6.80-7.72 (4H, m, arom. H)	-
4b	138 (PE/EtOAc)	(KBr) 1780 (C=O)	260 (3.13) 266 (3.21) 272.5 (3.21)	($CDCl_3$) 0.55-2.55 (9H, m, 3xCH_2 and CH_3CO, s at 2.1) 3.70-4.30 (5H, m, benzylic H and $COCH_2$--CH_2O), 7.00-7.58 (4H, m, arom. H)	$C_{17}H_{20}O_4$ 70.81, 6.99 70.63, 6.81
4c	-	(NaCl) 1750 (C=O)	261 (3.18) 267.5 (3.31) 274 (3.28)	(CCl_4) 1.04-2.84 (11H, m, 4xCH_2 and CH_3CO, s at 1.91), 3.15 (3H, s, CH_3O), 3.33 (3H, s CH_3O), 3.56-4.04 (1H, m, benzylic H), 6.78-7.46 (4H, m, arom. H)	$C_{18}H_{22}O_4$ 71.50, 7.33 71.35, 7.33
4d	-	(NaCl) 1770 (C=O)	261 (3.31) 268 (3.35) 274 (3.31)	(CCl_4) 0.90-2.26 (17H, m, 4xCH_2 and $(CH_3)_3CCO$, s at 1.15), 3.12 (3H, s, CH_3O), 3.35 (3H, s CH_3O), 3.56-3.85 (1H, m, benzylic H), 6.76-7.40 (4H, m, arom. H)	-
4e	156 (PE/EtOAc)	(KBr) 1740 (C=O)	261 (3.07) 268 (3.22) 275 (3.20)	($CDCl_3$) 0.99-2.86 (15H, m, 6xCH_2 and CH_3CO, s at 2.01), 2.33-4.22 (5H, m, benzylic H and $COCH_2$--CH_2O), 6.88-7.75 (4H, m, arom. H)	$C_{19}H_{24}O_4$ 72.12, 7.64 72.23, 7.54
4f	150 (PE/EtOAc)	(KBr) 1760 (C=O)	261 (3.63) 267 (3.70) 274 (3.69)	($CDCl_3$) 0.99-2.47 (21H, m, 9xCH_2 and CH_3CO, s at 2.05), 3.46-4.30 (5H, m, benzylic H and $COCH_2$--CH_2O), 6.90-7.70 (4H, m, arom. H)	-
4g	168 (PE/EtOAc)	(KBr) 1765 (C=O)	261 (3.00) 266.5 (3.15) 272 (3.03)	($CDCl_3$) 1.03-2.47 (23H, m, 10xCH_2 and CH_3CO, s at 2.03), 3.26-4.35 (5H, m, benzylic H and $COCH_2$--CH_2O), 6.86-7.69 (4H, m, arom. H)	-

Table III - Physical and spectroscopic data for compounds 5.

Compound	mp °C (solvent)	IR ν, cm^{-1}	UV (MeOH) λ nm (log ε)	^{1}HNMR (solvent) δ	MS (m/e) Analysis (C, H) calcd found
5a	-	(CCl4) 1740,1755 (C=O)	268.5 (3.53) 274 (3.54)	(CCl4) 1.03-2.68 (7H, m, 2xCH_2 and CH_3CO, s at 2.04), 3.80-4.00 (1H,m, benzylic H), 6.83-7.91 (4H, m, arom. H)	-
5b	96 (PE/EtOAc)	(KBr) 1715, 1740 (C=O)	263.5 (3.20) 268.5 (3.36) 275 (3.35)	(CCl4) 1.04-2.56 (9H, m, 3xCH_2 and CH_3CO, s at 2.04), 3.71-3.93 (1H, m, benzylic H), 6.98-7.14 (4 H, m, arom. H)	$C_{14}H_{14}O_3$ 230 $(M)^+$, 187 $(M-CH_3CO)^+$ 73.02, 6.12 72.88, 6.25
5c	113 (PE/EtOAc)	(KBr) 1710, 1750 (C=O)	259 (3.13) 267 (3.15) 274 (3.13)	(CCl4) 1.03-2.53 (11H, m, 4xCH_2 and CH_3CO, s at 2.05), 3.71-4.02 (1H, m, benzylic H), 7.02-7.60 (4 H, m, arom. H)	$C_{15}H_{16}O_3$ 244 $(M)^+$ 201$(M-CH_3CO)^+$ 73.75, 6.60 73.93, 6.54
5d	90 (PE/EtOAc)	(KBr) 1720, 1750 (C=O)	261 (3.15) 267 (3.25) 273.5 (3.22)	(CCl4) 1.11-2.37 (17H, m, 4xCH_2 and $(CH_3)_3CCO$, s at 1.22), 3.71-4.02 (1H, m, benzylic H), 6.93-7.55 (4H, m, arom. H)	$C_{18}H_{22}O_3$ 286 $(M)^+$ 201$(M-(CH_3)_3CCO)^+$
5e	76-78 (PE/EtOAc)	(KBr) 1710, 1745 (C=O)	259.5 (3.21) 266 (3.35) 272 (3.34)	(CCl4) 0.96-2.88 (13H, m, 5xCH_2 and CH_3CO, s at 2.08), 3.47-3.92 (1H, m, benzylic H), 6.88-7.56 (4H, m, arom. H)	$C_{16}H_{18}O_3$ 258 $(M)^+$ 215 $(M-CH_3CO)^+$ 74.39, 7.02 73.92, 6.78
5f	122-124 (PE/EtOAc)	(KBr) 1710, 1730 (C=O)	260 (3.76) 266 (3.84) 272.5 (3.82)	(CCl4) 0.80-2.30 (19H, m, 8xCH_2 and CH_3CO, s at 2.03), 3.60-4.08 (1H, m, benzylic H), 6.75-7.70 (4H, m, arom. H)	$C_{19}H_{24}O_3$ 300 $(M)^+$ 257 $(M-CH_3CO)^+$
5g	-	(NaCl) 1715, 1745 (C=O)	260 (3.10) 265.5 (3.26) 272 (3.23)	(CCl4) 1.03-2.50 (21H, m, 9xCH_2 and CH_3CO, s at 2.04), 3.66-4.07 (1H, m, benzylic H), 6.80-7.50 (4 H, m, arom. H)	$C_{20}H_{26}O_3$ 314 $(M)^+$ 271 $(M-CH_3CO)^+$ 76.39, 8.33 76.30, 8.82

Table IV - Physical and spectroscopic data for compounds 6.

Compound	mp °C (solvent)	IR ν, cm^{-1}	UV (MeOH) λ nm (log ε)	^{1}H NMR (solvent) δ	MS (m/e) Analysis (C, H, N) calcd found
6a	131 (PE)	(KBr) 3600, 3100 (OH) 1740 (C=O)	262 (3.94) 268 (4.04) 274 (4.02)	(CDCl3) 1.68-3.43 (7H, m, 2xCH2 and CH3CO, s at 2.06), 3.93-4.20 (1H, m, benzylic H), 6.93-8.03 (4H, m, arom. H), 9.46 (1H, s, NOH exchanged with D2O)	C13H13NO3 231 (M+1)$^+$ 189 (M+1-CH3CO)$^+$
6b	161 (Et2O)	(KBr) 3500-3000 (OH) 1735 (C=O)	262.5 (3.29) 269 (3.44) 275.5 (3.40)	(CCl4) 0.8-3.02 (9H, m, 3xCH2 and CH3CO, s at 2.1), 3.82-4.10 (1H, m, benzylic H), 7.00-7.60 (4H, m, arom. H), 8.90-9.72 (1 H, s, NOH exchanged with D2O)	C14H15NO3 245 (M)$^+$ 68.55, 6.16, 5.71 68.49, 6.03, 5.87
6c	184 (Et2O)	(KBr) 3500-3000 (OH) 1745 (C=O)	259.5 (3.05) 266 (3.20) 272.5 (3.19)	(CDCl3) 1.20-3.11 (11H, m, 4xCH2 and CH3CO, s at 2.00), 3.56-4.00 (1 H, m, benzylic H), 7.03-7.79 (4 H, m, arom. H), 8.59-9.27 (1 H, m, NOH exchanged with D2O)	C15H17NO3 216 (M- CH3CO)$^+$ 69.48, 6.61, 5.40 68.98, 6.51, 5.34
6d	188 (Et2O)	(KBr) 3500-3000 (OH) 1735 (C=O)	260 (3.40) 266 (3.50) 273 (3.49)	(C5D5N) 0.85-3.25 (17H, m, 4xCH2 and (CH3)3C, s at 1.81), 3.62-4.00 (1H, m, benzylic H), 4.60-4.80 (1H, s, NOH exchanged with D2O), 7.00-7.62 (4H, m, arom. H)	C18H23NO3 216 (M-(CH3)3CCO)$^+$
6e	190 (Et2O)	(KBr) 3600-3000 (OH) 1740 (C=O)	260 (3.52) 266.5 (3.60) 272 (3.60)	(C5D5N) 0.70-2.40 (13H, m, 5xCH2 and CH3CO, s at 2.00), 3.40-4.00 (2 H, m, benzylic H and NOH exchanged with D2O), 7.00-7.60 (4 H, m, arom. H)	C16H19NO3 230 (M- CH3CO)$^+$ 70.30, 7.00, 5.12 70.16, 7.17, 5.20
6f	215 (Et2O)	(KBr) 3700-3100 (OH) 1750 (C=O)	260 (2.65) 267 (2.82) 273.5 (2.82)	(C5D5N) 0.60-2.65 (19H, m, 8xCH2 and CH3CO, s at 2.00), 3.80-4.20 (1H, m, benzylic H), 4.60-5.00 (1H, m, NOH exchanged with D2O), 6.90-7.65 (4H, m, arom. H)	C19H25NO3 315 (M)$^+$ 272 (M- CH3CO)$^+$
6g	189 (Et2O)	(KBr) 3500-3000 (OH) 1730 C=O)	259 (2.82) 267 (2.99) 272 (2.96)	(CDCl3) 0.85-2.95 (21H, m, 9xCH2 and CH3CO, s at 2.05), 3.60-4.00 (1H, m, benzylic H), 6.95-7.60 (4H, m, arom. H), 8.40-8.80 (1 H, s, NOH exchanged with D2O)	C20H27NO3 329 (M)$^+$ 286 (M- CH3CO)$^+$

Table V - Physical and spectroscopic data for compounds 7.

Compound	mp °C (solvent)	IR ν, cm^{-1}	UV λ nm (log ε)	^{1}H NMR (CCl4), δ	^{13}C NMR (CDCl3), δ	MS (m/e) Analysis (C,H,N) Calcd. Found
7a	-	(CCl_4)	244 (4.53)	1.87-2.66 (4H, m, 2xCH_2)	190.09 (C=O), 154.29,	$C_{11}H_9NO$
		1720 (C=O)	287.5 (3.95)	4.25 (1H, t, benzylic H,	146.67, 135.77, 129.57,	M^+ = 171
		2215 (C≡N)	295 (3.93)	J=7.2 Hz), 7.20-7.90 (4H,	123.62, 121.34 (arom.C)	
				m,arom. H)	119.03 (C≡N), 63.01 (ben-	
					zylic C), 26.42, 15.50	
					(2xCH_2)	
7b	-	(NaCl)	243 (4.40)	1.46-2.04 (4H, m, 2xCH_2)	191.26 (C=O), 155.37,	$C_{12}H_{11}NO$
		1710 (C=O)	287 (3.99)	2.25 (2H, t, CH_2CN,	146.66, 135.45, 129.40,	$(M-1)^+$ = 184
		2220 (C≡N)	294 (3.97)	J=7.6Hz), 4.10 (1H, t,	123.21, 121.20 (arom.C)	
				benzylic H, J=8.7Hz),	119.20 (C≡N), 63.87(ben-	
				7.16-7.64 (4H, m, arom.H)	zylic C), 29.52, 23.43,	
					17.20 (3xCH_2)	
7c,7d	-	(NaCl)	245 (4.14)	1.33-2.00 (6H, m, 3xCH_2)	192.03 (C=O), 155.79,	$C_{13}H_{13}NO$
		1710 (C=O)	287 (3.79)	2.30 (2H, t, CH_2CN,	146.71, 135.33, 129.32,	$(M-1)^+$ = 199
		2215 (C≡N)	295 (3.75)	J=6.1Hz), 4.14 (1H, t,	123.33, 121.00 (arom.C)	78.36, 6.57, 7.07
				benzylic H, J=7.2Hz),	119.67 (C≡N), 64.48 (ben-	78.56, 6.50, 6.74
				7.14-7.63 (4H, m, arom.H)	zylic C), 29.61, 26.53,	
					25.24, 17.06 (4xCH_2)	
7e	58	(KBr)	243 (4.26)	1.10-1.97 (8H, m, 4xCH_2)	192.53 (C=O), 158.24,	$C_{14}H_{15}NO$
	(PE/Et_2O)	1750 (C=O)	288 (3.89)	2.17 (2H, t, CH_2CN,	148.64, 135.20, 129.16,	$(M-1)^+$ = 212
		2220 (C≡N)	295 (3.88)	J=6.4Hz), 4.60 (1H, t,	123.28, 120.89 (arom.C)	78.84, 7.08, 6.56
				benzylic H, J=7.2Hz),	119.67 (C≡N), 64.68 (ben-	79.11, 6.94, 6.71
				7.20-7.62 (4H, m, arom.H)	zylic C), 30.08, 28.56,	
					26.57, 25.17, 17.08 (5xCH_2)	
7f	-	(NaCl)	244 (4.18)	1.13-2.00 (14H, m, 7xCH_2)	192.89 (C=O), 156.68,	$C_{17}H_{21}NO$
		1760 (C=O)	287.5 (3.64)	2.14 (2H, t, CH_2CN,	146.81, 135.06, 129.26,	M^+ = 255
		2225 (C≡N)	295 (3.63)	J=6.0Hz), 4.07(1H, t,	123.33, 120.55 (arom.C)	
				benzylic H, J=10.2Hz),	119.76 (C≡N), 65.08(ben-	
				7.05-7.57 (4H, m, arom.H)	zylic C), 30.38, 29.73,	
					29.11, 28.66, 28.33,	
					27.33, 25.39, 17.14 (8xCH_2)	
7g	66	(KBr)	244 (4.34)	1.08-2.03 (16H, m, 8xCH_2)	193.04 (C=O), 156.58,	$C_{18}H_{23}NO$
	(PE/Et_2O)	1750 (C=O)	287 (3.95)	2.30 (2H, t, CH_2CN,	146.68, 135.04, 128.99,	M^+ = 269
		2220 (C≡N)	295 (3.93)	J=8.0Hz), 4.23 (1H, t,	123.34, 120.81 (arom.C)	
				benzylic H, J=8.3Hz),	119.83 (C≡N), 65.03(ben-	
				7.27-7.69 (4H, m, arom.H)	zylic C), 30.36, 29.72,	
					29.46, 29.27, 29.21,	
					28.64, 27.34, 25.37,	
					17.13 (9xCH_2)	

Table VI - Physical and spectroscopic data for compounds 8.

Compound	mp °C (solvent)	IR ν, cm^{-1}	UV λ nm (log ε)	^{1}H NMR (CCl$_4$), δ	MS (m/e) Analysis (C,H,N) Calcd. Found
8b	99	(KBr)	260 (3.05)	(CDCl3) 1.11-2.40 (6H, m, 3xCH2),	$C_{12}H_{14}O_2$
cis	(PE)	3600, 3100	267 (3.23)	2.60-3.40 (2H, m, OH exchanged	
		(OH)	273.5 (3.20)	with D_2O), 3.42-3.69 (1 H, m,	75.76, 7.42
				benzylic H), 4.00-4.27 (1 H, m,	75.68, 7.35
				CHOH), 7.04-7.49 (4 H, m, arom. H)	
8b	107	(KBr)	261 (2.94)	(CD3COCD3) 1.10-2.15 (6H, m,	$C_{12}H_{14}O_2$
trans	(Et_2O)	3500-3100	266 (3.06)	3xCH2), 3.30-3.65 (1H, m, benzylic	190 $(M)^+$
		(OH)	273 (3.06)	H), 3.9-4.70 (3H, m, CHOH and OH	
				exchanged with D_2O), 7.00-7.40 (4H,	
				m, arom. H)	
8c	140	(CCl_4)	260 (3.07)	(CDCl3) 1.09-2.49 (8H, m, 4xCH2),	$C_{13}H_{16}O_2$
	(Et_2O)	3600-3200	267 (3.24)	2.50-3.18 (2H, m, OH exchanged	
		(OH)	273 (3.19)	with D_2O), 3.20-3.64 (1 H, m,	76.44, 7.90.
				benzylic H), 3.65-4.00 (1 H, m,	76.58, 8.00
				CHOH), 6.98-7.40 (4 H, m, arom. H)	
8e	197	(CHCl3)	259 (3.06)	(CD3SOCD3) 1.33-2.60 (10H, m,	$C_{14}H_{18}O_2$
cis	(MeOH)	3580-3240	266 (3.22)	5xCH2), 2.91-3.23 (1H, m, benzy-	
		(OH)	273 (3.18)	lic H), 3.40-3.73 (1H, m, CHOH),	77.03, 8.31
				4.27 (1H, d, OH exchanged with	76.21, 8.30
				D_2O), 5.40 (1H, s, OH), 7.13 (4 H, ps,	
				arom. H)	
8e	121	(KBr)	261.5 (3.52)	(CD3SOCD3) 1.20-2.05 (10H, m,	$C_{14}H_{18}O_2$
trans	(MeOH)	3550-3480	267 (3.61)	5xCH2), 2.80-3.10 (1H, m, benzy-	218 $(M)^+$
		(OH)	373 (3.61)	lic H), 3.95-4.35 (2H, m, CHOH	77.02, 8.31
				and OH exchanged with D_2O),	76.57, 8.27
				5.45-5.70 (1H, m, OH exchanged	
				with D_2O), 6.90-7.35 (4 H, m,	
				arom. H)	
8f	100	(KBr)	261 (3.40)	(CDCl3) 0.65-2.75 (18H, m, 8xCH2	$C_{17}H_{24}O_2$
major	(PE/Et_2O)	3600-3400	268 (3.56)	and 2 OH exchanged with D_2O),	260 $(M)^+$
isomer		(OH)	273.5 (3.54)	3.75-4.30 (2H, m, benzylic H and	
				CHOH), 6.75-7.60 (4H, m, arom. H)	
8g	-	(NaCl)	259 (3.09)	(CCl_4) 0.50-2.20 (18H, m, 9xCH2),	$C_{18}H_{26}O_2$
mixture of		3800-3200	266 (3.31)	3.00-4.00 (4H, m, benzylic H and	274 $(M)^+$
isomers		(OH)	273 (3.31)	CHOH and 2 OH exchanged with	
				D_2O), 6.80-7.45 (4H, m, arom. H)	

Table VII - Physical and spectroscopic data for compounds 9.

Compound	mp °C (solvent)	IR ν, cm^{-1}	UV (MeOH) λ nm (log ε)	^1H NMR (CCl4), δ	^{13}CNMR (CDCl3), δ	MS (m/e) Analysis (C,H,N) Calcd. Found
9b	-	(NaCl)	244 (4.07)	1.39-2.10 (4H, m, 2xCH_2)	201.91(CHO), 192.13	$C_{12}H_{14}N_2O_2$
		1725, 1765	285 (3.71)	2.12-2.65 (2H, m, CH_2CHO)	(C=O) 155.99, 146.62,	218[a]
		(C=O)	294 (3.72)	3.84-4.92 (1H, m, benzylic H), 6.92-7.69 (4H, m, arom. H), 9.22 (1H, t, CHO, J = 2 Hz)	135.30, 129.26, 123.34, 120.94 (arom. C), 64.57 (benzylic C), 43.60, 29.84, 19.91 (3xCH_2)	
9c	166-168[b]	(CCl_4)	243 (4.21)	1.33-2.15 (6H, m, 3xCH_2)	202.25(CHO),192.47	$C_{13}H_{16}N_2O_2$
	(MeOH)	1730, 1770	285.5 (3.71)	2.25-2.39 (2H, m, CH_2CHO)	(C=O) 156.30, 146.66,	232[a]
		(C=O)	294 (3.72)	3.83-4.22 (1H, m, benzylic H), 6.92-7.69 (4H, m, arom. H), 9.22 (1H, t, CHO, J = 2 Hz)	135.19, 129.14, 123.34, 120.87 (arom. C), 64.67 (benzylic C), 43.92, 30.14, 26.90, 21.90 (4xCH_2)	67.22,6.94,13.77[a] 66.86,6.74,13.86
9e	130-132[b]	(NaCl)	244 (4.09)	1.16-2.09 (8H, m, 4xCH_2)	202.48(CHO),192.69	$C_{14}H_{18}N_2O_2$
	(MeOH)	1720, 1760	288 (3.56)	2.16-2.58 (2H, m, CH_2CHO)	(C=O)156.47, 146.71,	246[a]
		(C=O)	294.5 (3.55)	3.94-4.21 (1H, m, benzylic H), 7.19-7.63 (4H, m, arom. H), 9.70 (1H, t, CHO, J = 2.4 Hz)	135.14, 129.08, 123.31, 120.85 (arom. C), 64.87 (benzylic C), 43.76, 30.17, 29.03, 27.13, 21.84 (5xCH_2)	68.26,7.36,11.37[a] 68.17,7.27,11.29
9f	88-90[b]	(NaCl)	245 (3.93)	1.03-2.07 (14H, m, 7xCH_2)	202.79, 192.28 (C=O)	$C_{17}H_{24}N_2O_2$
	(MeOH)	1720, 1760	286 (3.53)	2.15-2.52 (2H, m, CH_2CHO)	156 68, 146.72,	288[a]
		(C=O)	296 (3.42)	3.94-4.30 (1H, m, benzylic H), 7.20-7.62 (4H, m, arom. H), 9.71 (1H, t, CHO, J = 2.6 Hz)	135.04, 128.99, 123.34, 120.80 (arom. C), 65.05 (benzylic C), 43.88, 30.36, 29.43, 29.25, 29.19, 29.11, 27.33, 22.04 (8xCH_2)	
9g	58	(KBr)	244 (4.44)	1.07-2.02 (16H, m, 8xCH_2)	202.86(CHO), 194.68	$C_{18}H_{24}O_2$
	(PE/Et_2O)	1710, 1750	288.5 (3.87)	2.09-2.49 (2H, m, CH_2CHO)	(C=O) 156.69, 146.66,	272
		(C=O)	295 (3.85)	3.90-4.27 (1H, m, benzylic H), 7.20-7.62 (4H, m, arom. H), 9.78 (1H, t, CHO, J = 2.6 Hz)	135.02, 128.96, 123.34, 120.76 (arom. C), 65.03 (benzylic C), 43.69, 30.35, 29.48, 29.315, 29.312, 29.310, 29.11, 27.35, 22.05 (9xCH_2)	

[a]Mass spectrum and analysis of the corresponding bis-oxime ; [b] mp of the corresponding bis-oxime.

Table VIII - Physical and spectroscopic data for compounds 10.

Compound	mp °C (solvent)	IR (KBr) ν, cm^{-1}	UV (MeOH) λ nm (log ε)	^{1}HNMR (CDCl$_3$), δ	^{13}C NMR (CDCl$_3$), δ	Analysis (C,H) Calcd. Found
10b	79 (pentane)	1720 1750(C=O) 3400-2800 (OH)	244 (4.04) 289 (3.55) 294.5 (3.55)	1.50-2.05 (4H, m, 2xCH$_2$), 2.40 (2H, t, CH$_2$CO$_2$H, J=6Hz), 4.20 (1H, t, benzylic H, J=6.2H6.97-7.86 (4H, m, arom.H), 10.24 (1H, s, CO$_2$H exchanged with D$_2$O)	192.25 (C=O), 179.28 (CO$_2$H), 155.00, 146.45, 135.22, 129.15, 123.27 120.90 (arom. C), 64.34 (benzylic C) 33.69, 29.62, 22.39 (3xCH$_2$)	C$_{12}$H$_{12}$O$_3$ 70.58, 5.92 70.31, 5.72
10c	58 (PE/Et$_2$O)	1720 1760(C=O) 3400-2500 (OH)	244 (3.89) 286 (3.36) 294.5 (3.36)	1.11-2.14(6H, m, 3xCH$_2$), 2.21 (2H, t, CH$_2$CO$_2$H, J=6Hz), 4.12 (1H, t, benzylic H, J=6.6Hz), 7.00-7.84 (4H, m, arom. H), 10.39 (1H, s, CO$_2$H exchanged with D$_2$O)	192.80(C=O), 178.29 (CO$_2$H), 156.54, 146.64, 135.10, 129.05, 123.34 120.61 (arom. C), 64.85 (benzylic C) 34.14, 30.24, 27.19, 23.36 (4xCH$_2$)	C$_{13}$H$_{14}$O$_3$ 71.87, 6.03 71.36, 6.46
10e	44 (PE/Et$_2$O)	1690 1750(C=O) 3400-2400 (OH)	244 (4.18) 288.5 (3.65) 294 (3.60)	1.05-2.02(8H, m, 4xCH$_2$), 2.26 (2H, t, CH$_2$CO$_2$H, J=6.6Hz), 4.10(1H, t, benzylic H, J=7.6Hz), 6.94-8.01(4H, m, arom. H), 10.85 (1H, s, CO$_2$H exchanged with D$_2$O)	192.88(C=O), 179.79 (CO$_2$H), 156.40, 146.49, 135.06, 128.97, 123.23 120.78 (arom. C), 64.73 (benzylic C) 33.62, 30.02, 28.79, 26.88, 24.34 (4xCH$_2$)	C$_{14}$H$_{16}$O$_3$ 72.39, 6.94 72.14, 7.05
10f	54 (PE/Et$_2$O)	1695 1755(C=O) 3600-2400 (OH)	244 (3.88) 287 (3.38) 295 (3.38)	0.88-2.03 (14H, m, 7xCH$_2$), 2.27 (2H, t, CH$_2$CO$_2$H, J=7.0Hz), 4.20 (1H, t, benzylic H, J=7.0Hz), 6.94-7.87 (4H, m, arom. H), 9.69 (1H, s, CO$_2$H exchanged with D$_2$O)	193.09 (C=O), 179.72 (CO$_2$H), 158.65, 146.59, 135.01, 128.93, 123.29 120.78 (arom. C), 64.97 (benzylic C), 33.95, 30.28, 29.37, 29.13, 29.07, 28.94, 27.87, 24.58 (8xCH$_2$)	C$_{17}$H$_{22}$O$_3$ 74.42, 8.08 74.62, 8.20
10g	65 (PE/Et$_2$O)	1700 1760(C=O) 3300-2500 (OH)	244 (3.86) 289.5 (3.46) 295.5 (3.46)	0.86-2.05 (16H, m, 8xCH$_2$), 2.28 (2H, t, CH$_2$CO$_2$H, J=7.2Hz), 4.20 (1H, t, benzylic H, J=7.0Hz), 7.06-7.82 (4H, m, arom. H), 10.22 (1H, s, CO$_2$H exchanged with D$_2$O)	193.11 (C=O), 179.65 (CO$_2$H), 156.67, 146.12, 134.99, 128.92, 123.89 120.77 (arom. C), 64.99 (benzylic C), 33.94, 30.30, 29.64, 29.42, 29.27, 29.12, 28.96, 27.30, 24.61(9xCH$_2$)	C$_{18}$H$_{24}$O$_3$ 74.96, 8.38 74.86, 8.64

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