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Diastereomeric Enols and Enol Derivatives of 8-Fluoro-5,11-dihydro-10*H*-dibenzo[*a*,*d*]cyclohepten-10-one with a Chiral 11-Substituent

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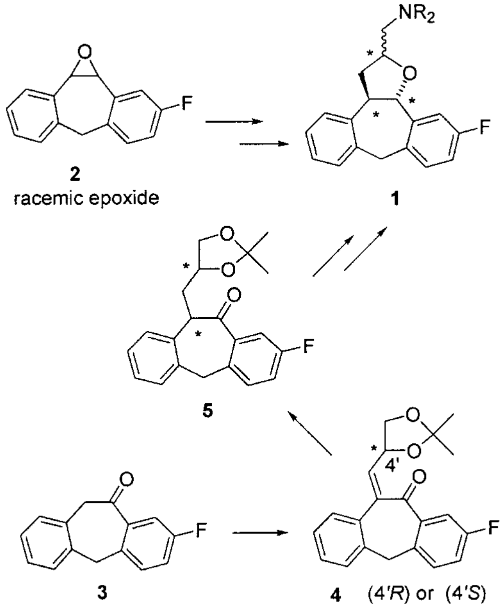
Aldol condensation of 8-fluoro-5,11-dihydro-10*H*-dibenzo-[*a*,*d*]cyclohepten-10-one and (4*S*)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde provides access to the corresponding (*E*,*Z*)-α,β-unsaturated ketones with a (4*R*)-chiral 11-substituent. Subsequent hydrogenation affords a mixture of (11*R*)/(11*S*)-epimeric ketones, which undergoes base-catalysed equilibration resulting in selective crystallisation of the (11*R*) epimer. The enol intermediate and acyclic enol derivatives are shown to exist as two slowly interconverting conformers with a high inversion barrier of the 10,11-disubstituted ring. (© Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, Germany, 2006)

Introduction

trans-Fused hydrofuran compounds of type **1** were recently found to exhibit potent activity in the central nervous system.[1] Racemic compounds **1** can be accessed by ring opening of the (±)-2-fluoro-10,11-epoxide **2** with allyl- or propargylmagnesium halides and further elaboration of the *trans*-disposed alcohol products (Scheme 1).[2]

We also envisaged a homochiral approach starting with aldol condensation of ketone **3** and either (4*R*)- or (4*S*)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde to form the corresponding unsaturated ketone **4**. The stereogenic centre located in the acetal-protected propanediol side-chain may serve to control the two new centres generated upon reduction of the unsaturated ketone moiety and subsequent ring closure to form the tetrahydrofuran ring.

Herein we describe our results with regard to the aldol condensation of **3** and subsequent reduction of the unsaturated ketone **4**. The resulting epimeric ketones **5** interconvert readily via their common enol intermediate, which can be directly observed by NMR spectroscopy. The NMR spectra, however, reveal the existence of two enolic forms instead of one. To elucidate the nature of this phenomenon various enol ether and enol ester models of enolised ketone **5** were submitted to conformational analysis by NMR spectroscopy and model calculations. This analysis revealed the existence of a high inversion barrier for the 5*H*-dibenzo-[*a*,*d*]cycloheptene ring system of the acyclic enol derivatives.



Scheme 1.

Some previous studies have already dealt with the nonplanarity of 5*H*-dibenzo[*a*,*d*]cycloheptene derivatives and the thermodynamic parameters relevant to ring inversion.[3,4]

Results and Discussion

Starting ketone **3** was accessed by applying a reaction sequence similar to that used for the analogous 8-chloro ketone,[5,6] i.e. Friedel–Crafts reaction of fluorobenzene and

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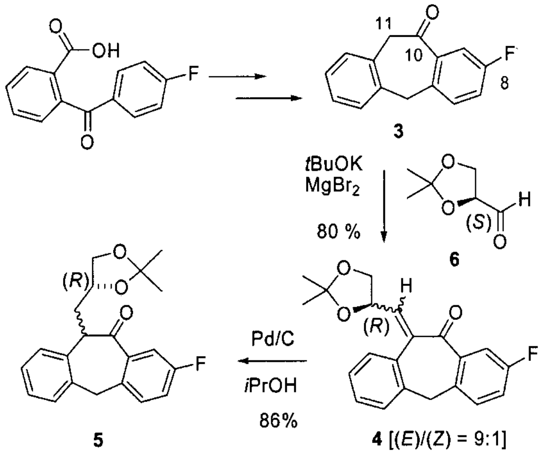
phthalic anhydride, reduction and chain extension of the resulting keto acid, and final acid-catalysed cyclisation.

Both the (4′*R*)-α,β-unsaturated ketone **4** (Scheme 2) and its (4′*S*) enantiomer were obtained by aldol condensation of ketone **3** with the appropriate precursor (4*S*)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde (**6**)[7–10] or its (4*R*) analogue.[11,12] The aldol reaction was carried out in THF using *t*BuOK as a base and $MgBr_2$ as a co-reagent, which led to complete conversion of the initial aldol product into the dehydrated ketone **4**. In contrast, only partial dehydration of the initial aldol product was observed when $MgBr_2$ was omitted. Ketone **4** was formed as an approximate 9:1 mixture of (*E*)- and (*Z*)-isomers that could be separated by column chromatography. The assignment of the structures was based on the characteristic coupling values observed for the carbonyl C-10 atom in the ^{1}H-coupled ^{13}C NMR spectrum. This carbon atom displays two $^3J_{C,H}$ couplings, one with the aromatic H-9 and the other with the vinylic proton, and a $^4J_{C,F}$ coupling with the F atom. While the values of $^3J_{C,H9}$ and $^4J_{C,F}$ are similar for both isomers, those for $^3J_{C,H_{vinyl}}$ are very different [10 Hz for the (*Z*)-isomer and 5 Hz for the (*E*)-isomer (Figure 1)].



Scheme 2.

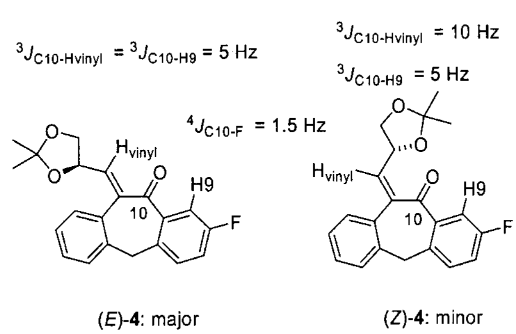


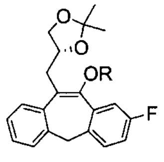
Figure 1. Characteristic coupling constants in the ^{1}H-coupled ^{13}C NMR spectrum of (*E*)- and (*Z*)-isomers **4**.

Hydrogenation of **4** in the presence of Pd/C as a catalyst afforded a mixture of the epimeric ketones **5a**,**b** in a rather invariant ratio of about 3:2 (86% yield). This ratio could not be changed appreciably by varying the solvent (MeOH, EtOH, *i*PrOH, toluene, THF, EtOAc). When monitoring the hydrogenation in isopropyl alcohol by TLC or HPLC, it was found to proceed by formation of a long-lived, polar intermediate, presumably the enol form resulting from 1,4-addition. This intermediate was not observed when triethylamine was added to the hydrogenation medium. The epimeric ketones **5a** and **5b** could be separated by preparative HPLC but were found to interconvert readily, for example upon treatment with triethylamine. Finally, this epimerisation process could be used to our advantage as the (11*R*) epimer **5a** was found to crystallise selectively under base-catalysed equilibration conditions (isopropyl alcohol containing triethylamine).

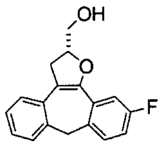
This enolisation/epimerisation process is of crucial importance for the diastereoselectivity of the synthetic sequence leading to target compounds of type **1**, and in this regard we were intrigued by the observation of a long-lived enol intermediate. Thus, when **5a**,**b** was treated with *t*BuOK in THF for 5 min followed by addition of acetic acid (1 equiv.) and immediate TLC analysis, the enol was detected as a transient polar component that quickly disappeared from the THF solution. However, in contrast to the exclusive generation of the ketone tautomers in less polar solvents, ^{1}H NMR analysis of epimeric ketones **5a** or **5b** in [D$_6$]dimethyl sulfoxide revealed partial conversion into two enol components (ratio 1:1). After 15 min, the relative amount of these enols was 25%, and after 1 d, a 33:27:20:20 tautomeric equilibrium containing 60% of ketones **5a**,**b** and 40% of enol forms was established.

The structure of the isomeric enol forms was elucidated by comparing their NMR spectroscopic data with those of the corresponding enol acetate **7** and methoxymethyl enol ether **8** (prepared by acetylation and *O*-alkylation of **5a**,**b**). The NMR spectra of **7** and **8** also reveal the existence of two isomeric components (ratio ca. 1:1), similar to the enolic forms of **5**. In the ^{13}C NMR spectra, this structural relationship clearly appears from the similar double signals and chemical-shift values found for C-10 and C-11 (Table 1). For comparison purposes, Table 1 also lists the chemical-shift values of the single signals observed for C-10 and C-11 in the spectra of the cyclic enol ether **9**, enol acetates **10** and **11**, and the unsubstituted cycloalkene **12**. Cyclic enol ether **9** was obtained by acid hydrolysis of **5a**,**b** while the 11-allyl and 11-propargyl compounds **10** and **11**, respectively, were derived by PCC and Swern oxidation of the corresponding 10-alcohol derivatives,[1,2] followed by treatment with Ac_2O and DMAP.

^{1}H NMR analysis further revealed different geminal coupling constants for the 5-methylene protons of ketone forms **5a**,**b** (–16 Hz) and the enolic species (–13 Hz); the latter value was also observed for enol acetate **10** and dibenzocycloheptatriene **12** (measured at –65 °C). The magnitude of these geminal couplings can be related to the dihedral angle, Φ, between one of the H-C-5 linkages and the π-lobes on the adjacent benzene rings, as exemplified by the large ^2J value reported for planar fluorene (–22.3 Hz; Φ = 30°) and the smaller values for other, non-planar systems (minimal ^2J value for Φ = 90°).[13,14] The lower ^2J values found for enol acetate **10** and cycloalkene **12** (–13 Hz) and



7: R = Ac
8: R = MeOCH$_2$



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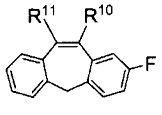

10: R^{10} = OAc; R^{11}= allyl
11: R^{10} = OAc; R^{11}= propargyl
12: R^{10} = R^{11}= H

Table 1. ^{13}C NMR chemical-shift values of C-10 and C-11 (CDCl$_3$, 25 °C).

	5a,**b** (keto)	**5** (enol)	**7**	**8**
C-10 (d)[a]	193.5	148.2	144.5	149.8
	193.2	148.2	144.2	149.7
C-11 (s)	50.0	115.0	128.1	125.6
	49.8	114.6	127.6	124.7
	9	**10**	**11**	**12**
C-10 (d)[a]	150.9[b]	143.8	144.5	130.5
C-11 (s)	114.1[b]	129.6	126.4	132.7

[a] Doublet due to coupling with 8-F. [b] Split values at –65 °C (CD$_2$Cl$_2$: δ = 150.1, 149.6; 113.9, 113.6 ppm).

for ketones **5a**,**b** (–16 Hz) therefore indicate severe bending of the cycloheptatriene and cycloheptadiene ring moieties. In MM+ geometry-optimised models of **10** and a simplified 11-Me analogue of ketone **5** with a favoured equatorial methyl group, this can be seen from the Φ values estimated for H-5$_{eq}$ (ca. 90° for **10**; $\Phi1$, $\Phi2 \approx 100°$ and 95° for the 11-Me analogue of ketone **5**) with respect to the unsubstituted and F-substituted benzene ring.

The above ^{13}C and ^{1}H NMR spectroscopic data suggest the existence of two diastereomeric structures **5**-enol$_1$ and **5**-enol$_2$, which can be attributed to a high inversion barrier of the disubstituted dibenzocycloheptatriene ring system combined with the stereogenic centre already present in the acetal-protected propanediol side-chain. In support of this hypothesis, we unveiled a slow interconversion of the analogous diastereomeric components of enol derivatives **7** and **8** by applying two-dimensional exchange spectroscopy (EXSY).[15–18] From this EXSY analysis and the coalescence experiments carried out for enol acetate **10**, cycloalkene **12** and for the cyclic enol ether **9**, we were able to determine rate constants for the diastereomeric exchange reaction (k_{exch}) and relevant activation parameters $\Delta G^{\ddagger}$ (Table 2).

Table 2. Rate constants and activation parameters ($\Delta G^{\ddagger}$) at temperatures indicated, as derived from ^{1}H NMR EXSY analysis and coalescence experiments.

	T [K]	k_{exch} [s^{-1}]	$\Delta G^{\ddagger}$[a]	Solvent	Method
7	298	0.3	18	CDCl$_3$	EXSY[b]
8	298	0.05	19	C$_6$D$_6$	EXSY[b]
9	248	566	11	CD$_2$Cl$_2$	coalesc.
10	343	85	17	CDCl$_2$CDCl$_2$	coalesc.
12	220	286	10	CD$_2$Cl$_2$	coalesc.

[a] kcal mol^{-1}. [b] For **7** and **8** no peak broadening was observed at 55 °C in CDCl$_3$; coalescence could not be attained.

These activation parameters reflect the growing barrier to ring inversion with increasing substitution at positions C-10 and C-11 of the cycloheptatriene ring moiety (ca. 18 kcal mol^{-1} for the acyclic enol derivatives **7** and **8**). Interestingly, no splitting of signals was apparent in the NMR spectra of cyclic enol ether **9** at room temperature. For example, the signals for the geminal protons H-5 appear as a simple AB quadruplet, which can be related to the stereocentre in the dihydrofuran ring. However, at –65 °C in CD$_2$Cl$_2$ split signal patterns were observed in both the ^{1}H and ^{13}C NMR spectra, again revealing two diastereomeric conformers (ratio ca. 1:1). In this case the barrier to ring inversion (11 kcal mol^{-1}) could be determined from the coalescence temperature (248 K) observed for one pair of geminal protons in the hydrofuran ring moiety. Clearly, equilibration of the two invertomers is much faster for the cyclic enol ether **9** than for the acyclic analogues **7** and **8**. Hence, inversion of the 5H-dibenzo[a,d]cycloheptene ring system in the latter compounds is impeded by the substituents in positions 10 and 11.

The 11-allyl compound **10** also displays a high inversion barrier (17 kcal mol^{-1}), which was determined by measuring the coalescence temperature (343 K) for conversion of the two AB systems corresponding to CH$_2$-5 and the allyl methylene group into an A$_2$ pattern. This barrier is again much higher than that determined for the 10,11-unsubstituted compound **12** (10 kcal mol^{-1}) and the inversion barrier reported for the non-planar, saddle-shaped monocyclic cycloheptatriene (6 kcal mol^{-1}).[19–22]

Conformational modelling of enol acetates **7**, **10** and **11** has revealed a preferred conformation with an *endo* orientation of the R group attached to the methylene group α to C-11, i.e. this R group points towards the hollow side of the 5H-dibenzo[a,d]cycloheptene ring, away from the axial H atom at C-5 (Figure 2). This orientation also minimizes repulsions of the α-methylene protons with the *peri*-H atom at C-1 and the enolic O atom of the *exo*-oriented acetyl group. Hence, to form a (near) isoenergetic diastereomeric or enantiomeric conformer, ring inversion must be combined with a 180° rotation of the 10- and 11-substituents (**7**, **10**, **11**), and further rotation about the CH$_2$-C-(4′R)

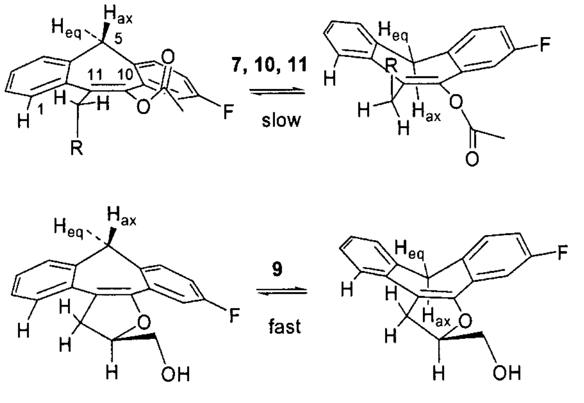

Figure 2. Combined ring inversion and 180° rotation at C-10 and C-11 to form diastereomeric (**7**) or enantiomeric (**10**, **11**) conformers compared to fast ring inversion of cyclic enol ether **9**.

linkage (**7**). The spatial relationship between the invertomers is illustrated in Figure 2. Evidently, the rotational barrier is lifted for ring inversion of the cyclic enol ether **9**, which has the two hydrogen atoms of the α-methylene group in an almost invariant position above and below the plane of the unsubstituted benzene ring.

Presumably, this low conformational mobility of the enol intermediate also accounts for its slow conversion into ketone tautomers **5a**,**b**. Indeed, when protonation occurs from the more accessible *exo* face at C-11 of the enol, the voluminous R group has to move further inside the hollow side of the 5*H*-dibenzo[*a*,*d*]cycloheptene ring system while the α-methylene protons are forced into the plane of the *peri*-H atom and the enolic O atom.

Conclusion

In conclusion, we have developed a suitable approach to prepare a homochiral precursor of target compounds **1**. This involves aldol condensation of the tricyclic ketone **3** with either (4*S*)- or (4*R*)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde to give the (4′*R*)-α,β-unsaturated ketone **4** or its (4′*S*) enantiomer. Hydrogenation of **4** furnishes a mixture of 11-epimeric ketones **5a**,**b**, which interconvert readily via the common enol intermediate. This enol and the corresponding enol derivatives have been shown to exist as two slowly interconverting diastereomeric conformers due to the high inversion barrier of the 10,11-disubstituted 5*H*-dibenzo[*a*,*d*]cycloheptene ring.

Experimental Section

General Remarks: Melting points were determined with a Reichert-Jung Thermovar apparatus or an Electrothermal IA 9000 digital melting point apparatus, and are uncorrected. Infrared spectra were recorded with a Perkin–Elmer 297 grating IR spectrophotometer and a Perkin–Elmer 1720 Fourier transform spectrometer. Mass spectra were recorded with a Hewlett Packard MS-Engine 5989A apparatus for EI and CI spectra, and a Kratos MS50TC instrument for exact mass measurements performed in the EI mode at a resolution of 10000. For the NMR spectra, a Bruker Avance 300 and a Bruker AMX 400 spectrometer were used. Analytical and preparative thin layer chromatography were carried out using Merck silica gel 60 PF-224; for column chromatography 70–230 mesh silica gel 60 (E. M. Merck) was used as the stationary phase.

8-Fluoro-5,11-dihydro-10*H*-dibenzo[*a*,*d*]cyclohepten-10-one (3): Compound **3** was prepared according to the procedure described for the analogous 8-chloro compound.[5,6] M.p. 104–105 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.18 (s, 2 H, CH_2-5 or CH_2-11), 4.24 (s, 2 H, CH_2-11 or CH_2-5), 7.14 (td, J = 8.1, 2.9 Hz, 1 H, H-7), 7.17–7.37 (m, 5 H, H-Ar), 7.79 (dd, J = 9.5, 2.9 Hz, 1 H, H-9) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 42.0 (CH_2-5), 51.1 (CH_2-11), 117.0 (d, $^{2}J_{C,F}$ = 23.0 Hz, *C*H-Ar-F), 120.5 (d, $^{2}J_{C,F}$ = 20.7 Hz, *C*H-Ar-F), 128.0, 128.3, 129.8 (*C*H-Ar), 132.1 (d, $^{3}J_{C,F}$ = 6.9 Hz, *C*H-Ar-F), 132.4 (*C*-Ar), 136.7 (d, $^{3}J_{C,F}$ = 6.9 Hz, *C*-Ar-F), 139.0, 140.0 (*C*-Ar), 162.2 (d, $^{1}J_{C,F}$ = 246.0 Hz, *C*-Ar-F), 193.6 (C=O) ppm. CIMS: *m*/*z* (%) = 227 (100) [MH^{+}].

(11*E*,*Z*)-11-{[(4*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl]methylene}-8-fluoro-5,11-dihydro-10*H*-dibenzo[*a*,*d*]cyclohepten-10-one (4): Dry DMSO (10.0 mL, 141.5 mmol) was added dropwise to a stirred cold solution (–60 °C) of $(COCl)_2$ (6.17 mL, 70.8 mmol) in CH_2Cl_2 (100 mL). After 10 min, [(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]methanol (4.37 mL, 35.4 mmol) was added dropwise and the mixture was stirred for 10 min. Et_3N (19.7 mL, 141.5 mmol) was added and stirring was continued for another 5 min. The mixture was warmed to room temperature, stirred further for 10 min, filtered through a pad of Celite, and the filter cake washed with CH_2Cl_2 (3 × 20 mL). The filtrate was concentrated at 20 °C to remove CH_2Cl_2 to afford the corresponding aldehyde (4*S*)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde (**6**) as a yellow oil. $MgBr_2$ (3.26 g, 17.7 mmol) and *t*BuOK (2.48 g, 22.1 mmol) were added to an ice-cooled solution of ketone **3** (2.00 g, 8.85 mmol) in THF (30 mL). A solution of the above aldehyde in THF (10 mL) was added dropwise at 0 °C and the mixture was allowed to react at room temperature for 1 h. After disappearance of the starting ketone, NH_4Cl (satd. aq. solution, 20 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The organic phase was dried with $MgSO_4$ and the solvents were evaporated. The residue was purified on a silica gel column using diethyl ether/hexane (25:75) to give 180 mg of the less polar (*Z*)-isomer (6%) and 2.40 g of the more polar (*E*)-isomer (80%). **(*E*)-Isomer:** M.p. 90–92 °C. IR (NaCl): $\tilde{\nu}$ = 3410 (s), 1660 (s), 1600 (s), 1245, 1060 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.33 (s, 3 H, CH_3), 1.48 (s, 3 H, CH_3), 3.82 (t, J = 6.7 Hz, 1 H, CH_2-O), 4.05 (t, J = 6.7 Hz, 1 H, CH_2'-O), 3.86–4.16 (br., 2 H, CH_2-5), 4.58 (dt, J = 8.8, 6.7 Hz, 1 H, CH-O), 7.02 (d, J = 8.8 Hz, 1 H, =CH), 7.05 (dt, J = 8.0, 2.8 Hz, 1 H, Ar-H), 7.18–7.30 (m, 5 H, H-Ar), 7.66 (dd, J = 9.4, 2.7 Hz, 1 H, H-Ar) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 25.8 (*C*H$_3$), 26.0 (*C*H$_3$), 40.0 (*C*H$_2$-5), 69.3 (*C*H$_2$-O), 73.0 (*C*H-O), 110.3 (Me$_2$*C*), 117.6 (d, $^{2}J_{C,F}$ = 22.9 Hz, *C*H-Ar-F), 120.1 (d, $^{2}J_{C,F}$ = 21.4 Hz, *C*H-Ar-F), 126.7, 127.4, 128.9, 130.2 (*C*H-Ar), 130.1 (d, $^{3}J_{C,F}$ = 6.9 Hz, *C*H-Ar-F), 132.7, 139.5 (*C*-Ar), 136.3 (d, $^{4}J_{C,F}$ = 1.5 Hz, *C*-Ar-F), 138.7 (d, $^{3}J_{C,F}$ = 6.1 Hz, *C*-Ar-F), 140.3 (=*C*H), 145.0 (=*C*=), 161.9 (d, $^{1}J_{C,F}$ = 246.4 Hz, *C*-Ar-F), 189.3 (*C*=O) ppm. CIMS: *m*/*z* (%) = 339 (100) [MH^{+}], 281 (96) [MH^{+} – acetone], 263 (45) [MH^{+} – acetone – H_2O]. EIMS: *m*/*z* (%) = 338 (2) [M$^{+\cdot}$], 280 (100) [M$^{+\cdot}$ – acetone]. HRMS calcd. for $C_{21}H_{19}FO_3$ [M$^{+\cdot}$]: 338.1318; found 338.1306. **(*Z*)-Isomer:** ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.42 (s, 3 H, CH_3), 1.49 (s, 3 H, CH_3), 3.73 (d, J = 14.0 Hz, 1 H, CH_2-5), 3.86 (dd, J = 8.4, 7.0 Hz, 1 H, CH_2-O), 4.35 (d, J = 14.0 Hz, 1 H, CH_2'-5), 4.61 (dd, J = 8.4, 7.0 Hz, 1 H, CH_2'-O), 5.28 (q, J = 7.0 Hz, 1 H, CH-O), 6.38 (d, J = 7.0 Hz, 1 H, =CH), 7.10–7.27 (m, 6 H, H-Ar), 7.65 (dd, J = 9.6, 2.8 Hz, 1 H, H-Ar) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 25.27 (*C*H$_3$), 26.59 (*C*H$_3$), 39.95 (*C*H$_2$-5), 70.19 (*C*H$_2$-O), 74.84 (*C*H-O), 109.98 (Me$_2$*C*), 117.20 (d, $^{2}J_{C,F}$ = 22.86 Hz, *C*H-Ar-F), 120.05 (d, $^{2}J_{C,F}$ = 21.59 Hz, *C*H-Ar-F), 126.90, 127.30, 128.41, 129.04 (*C*H-Ar), 130.36 (d, $^{3}J_{C,F}$ = 7.20 Hz, *C*H-Ar-F), 136.56, 138.72 (*C*-Ar), 136.70 (d, $^{3}J_{C,F}$ = 6.45 Hz, *C*-Ar-F), 138.76 (d, $^{4}J_{C,F}$ = 3.23 Hz, *C*-Ar-F), 143.07 (=*C*=), 147.86 (=*C*H), 161.84 (d, $^{1}J_{C,F}$ = 246.18 Hz, *C*-Ar-F), 189.25 (*C*=O) ppm.

(11*R*)-11-{[(4*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl]methyl}-8-fluoro-5,11-dihydro-10*H*-dibenzo[*a*,*d*]cyclohepten-10-one (5a) and (11*S*)-11-{[(4*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl]methyl}-8-fluoro-5,11-dihydro-10*H*-dibenzo[*a*,*d*]cyclohepten-10-one (5b): Et_3N (0.63 mL, 4.50 mmol) and 10% palladium on carbon (150 mg) were added to a solution of α,β-unsaturated ketone (*E*)-**4** (1.00 g, 2.96 mmol) in *i*PrOH (30 mL) and the mixture was hydrogenated at atmospheric pressure in a Parr apparatus for 6 h. The mixture was filtered through a pad of Celite and the catalyst washed with CH_2Cl_2 (4 × 20 mL). After evaporation of the solvent, the residue was purified by column chromatography (CH_2Cl_2) on silica gel. Further HPLC separation (Waters 515 pump, 2-mL injection loop, Merck

Hibar® 250 × 25 mm column LiChrosorb® SI 60 7 µm, Waters 2410 refractive index detector, diethyl ether/hexane = 60:40, 11 mL min^{-1}) gave **5a** (t_R = 13.2 min; 0.61 g, 61 %) as a white crystalline powder and **5b** (t_R = 14.7 min; 0.35 g, 35 %) as a colourless oil.

Selective Crystallisation under Epimerising Conditions: Following hydrogenation of (*E*)-**4** (1.00 g, 2.96 mmol) and workup as described above, the residue consisting of **5a**,**b** was dissolved in *i*PrOH (5 mL), and Et$_3$N (1.20 mL) was added. The mixture was stirred at 40 °C for 1 h and cooled slowly to room temp. The crystallised product was collected by filtration and dried under vacuum to afford pure ketone **5a** as a white powder (0.86 g, 86 %). **5a:** M.p. 144–146 °C. IR (NaCl): $\tilde{\nu}$ = 3434 (s), 2985 (s), 1680 (s), 1415 (s), 1060, 880 cm^{-1}. ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 1.30 (s, 3 H, CH$_3$), 1.37 (s, 3 H, CH$_3$), 2.03 (ddd, *J* = 13.3, 9.1, 2.8 Hz, 1 H, CH$_2$), 2.91 (ddd, *J* = 13.3, 10.7, 3.3 Hz, 1 H, CH$_2'$), 3.71 (dd, *J* = 7.9, 6.4 Hz, 1 H, CH$_2$O), 3.95 (d, *J* = 15.9 Hz, 1 H, CH$_2$-5), 4.17 (dd, *J* = 7.9, 6.1 Hz, 1 H, CH$_2'$O), 4.22–4.27 (m, 1 H, CH-O), 4.70 (dd, *J* = 10.7, 2.8 Hz, 1 H, CH-11), 4.83 (d, *J* = 15.9 Hz, 1 H, CH$_2'$-5), 7.14–7.36 (m, 6 H, H-Ar), 7.77 (dd, *J* = 9.8, 2.9 Hz, 1 H, H-Ar) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 25.6 (*C*H$_3$), 27.1 (*C*H$_3$), 32.2 (*C*H$_2$), 42.0 (*C*H$_2$-5), 50.4 (*C*H-11), 69.9 (*C*H$_2$-O), 74.1 (*C*H-O), 109.1 (Me$_2$*C*), 116.4 (d, $^2J_{C,F}$ = 22.7 Hz, *C*H-Ar-F), 119.8 (d, $^2J_{C,F}$ = 21.5 Hz, *C*H-Ar-F), 125.8, 127.1, 127.9, 128.2 (*C*H-Ar), 131.8 (d, $^3J_{C,F}$ = 7.0 Hz, *C*H-Ar-F), 135.3 (*C*-Ar), 137.0 (d, $^3J_{C,F}$ = 5.9 Hz, *C*-Ar-F), 138.2 (d, $^4J_{C,F}$ = 3.4 Hz, *C*-Ar-F), 140.0 (*C*-Ar), 161.7 (d, $^1J_{C,F}$ = 246.4 Hz, *C*-Ar-F), 193.5 (d, $^4J_{C,F}$ = 1.5 Hz, *C*=O) ppm. CIMS: *m*/*z* (%) = 341 (2) [MH$^+$], 283 (100) [MH$^+$ – acetone]. EIMS: *m*/*z* (%) = 340 (1) [M$^{+\cdot}$], 282 (79) [M$^{+\cdot}$ – acetone], 226 (100). HRMS calcd. for C$_{21}$H$_{21}$FO$_3$ [M$^{+\cdot}$]: 340.1475; found 340.1479. **5b:** Colourless oil. ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 1.35 (s, 3 H, CH$_3$), 1.45 (s, 3 H, CH$_3$), 2.51 (ddd, *J* = 14.2, 8.4, 4.0 Hz, 1 H, CH$_2$), 2.66 (ddd, *J* = 14.2, 8.0, 5.5 Hz, 1 H, CH$_2'$), 3.74 (dd, *J* = 8.0, 7.0 Hz, 1 H, CH$_2$O), 4.03 (d, *J* = 16.1 Hz, 1 H, CH$_2$-5), 4.07 (dd, *J* = 8.0, 6.2 Hz, 1 H, CH$_2'$O), 4.26–4.35 (m, 1 H, CH-O), 4.65 (dd, *J* = 8.0, 5.5 Hz, 1 H, CH-11), 4.75 (d, *J* = 16.1 Hz, 1 H, CH$_2'$-5), 7.14–7.36 (m, 6 H, H-Ar), 7.68 (dd, *J* = 9.8, 2.9 Hz, 1 H, H-Ar) ppm. CIMS: *m*/*z* (%) = 341 (2) [MH$^+$], 283 (100) [MH$^+$ – acetone].

8-Fluoro-11-{[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]methyl}-5*H*-dibenzo[*a*,*d*]cyclohepten-10-yl Acetate (7): Et$_3$N (88 µL, 0.635 mmol), DMAP (20 mg, 0.159 mmol) and Ac$_2$O (60 µL, 0.635 mmol) were added to an ice-cooled solution of ketone **5a** (108 mg, 0.318 mmol) in CH$_2$Cl$_2$ (5 mL). The reaction mixture was stirred at room temp. for 6 h. After disappearance of the ketone (TLC), NH$_4$Cl (satd. aq. solution) was added, the mixture was extracted three times with CH$_2$Cl$_2$ and the organic phase dried with MgSO$_4$, filtered and the solvents were evaporated. The residue was purified by column chromatography on silica gel eluting with CH$_2$Cl$_2$/heptane (1:1) to afford enol acetate **7** as an oil (106 mg, 87 %). ^{1}H NMR (CDCl$_3$, 400 MHz; two isomers): first isomer: δ = 1.26 (s, 3 H, CH$_3$), 1.40 (s, 3 H, CH$_3$), 2.29 (s, 3 H, OAc), 3.10 (dd, *J* = 14.0, 9.5 Hz, 1 H, CH$_2$), 3.18 (dd, *J* = 14.0, 4.6 Hz, 1 H, CH$_2'$), 3.55 (dd, *J* = 8.2, 6.4 Hz, 1 H, CH$_2$-O), 3.63 (d, *J* = 12.9 Hz, 1 H, CH$_2$-5), 3.71–3.83 (m, 2 H, CH$_2'$-O + CH$_2'$-5), 4.11–4.17 (m, 1 H, Σ^3J = 25.7 Hz, CH-O), 6.94 (dt, *J* = 8.4, 2.5 Hz, 1 H, H-Ar), 7.02 (dd, *J* = 9.8, 2.5 Hz, 1 H, H-Ar), 7.17–7.26 (m, 4 H, H-Ar), 7.50 (dd, *J* = 7.8, 2.7 Hz, 1 H, H-Ar) ppm; second isomer: δ = 1.29 (s, 3 H, CH$_3$), 1.37 (s, 3 H, CH$_3$), 2.27 (s, 3 H, OAc), 2.82 (dd, *J* = 13.6, 6.7 Hz, 1 H, CH$_2$), 3.27 (dd, *J* = 13.6, 6.4 Hz, 1 H, CH$_2'$), 3.39 (t, *J* = 7.6 Hz, 1 H, CH$_2$-O), 3.71–3.83 (m, 3 H, CH$_2'$-O + CH$_2$-5), 3.98–4.05 (m, 1 H, Σ^3J = 26.0 Hz, CH-O), 6.94 (dt, *J* = 8.4, 2.5 Hz, 1 H, H-Ar), 7.02 (dd, *J* = 9.8, 2.5 Hz, 1 H, H-Ar), 7.17–7.26 (m, 4 H, H-Ar), 7.50 (dd, *J* = 7.8, 2.7 Hz, 1 H, H-Ar); common signals: δ = 3.71–3.83 (m, 5 H), 6.94 (dt, *J* = 8.4, 2.5 Hz, 1 H, H-Ar), 7.02 (dd, *J* = 9.8, 2.5 Hz, 1 H, H-Ar), 7.17–7.26 (m, 4 H, H-Ar), 7.50 (dd, *J* = 7.8, 2.7 Hz, 1 H, H-Ar) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz; two isomers): δ = 20.8, 20.9 (*C*H$_3$-OAc), 25.7, 25.7, 26.8, 27.0 (*C*H$_3$), 34.5, 35.8 (*C*H$_2$), 40.05, 40.1 (*C*H$_2$-5), 68.6, 69.2 (*C*H$_2$-O), 74.4, 75.4 (*C*H-O), 108.8, 108.9 (Me$_2$*C*), 111.5, 111.6 (d, $^2J_{C,F}$ = 22.9 Hz, *C*H-Ar-F), 116.0, 116.1 (d, $^2J_{C,F}$ = 21.6 Hz, *C*H-Ar-F), 126.1, 126.3, 126.9, 127.1, 127.2, 127.3, 128.6, 128.7 (*C*H-Ar), 127.9, 128.0 (d, $^3J_{C,F}$ = 8.4 Hz, *C*H-Ar-F), 127.6, 128.1 (*C*-11), 133.3, 134.3, 140.6, 140.8 (*C*-Ar), 134.0, 134.2 (d, $^3J_{C,F}$ = 6.9 Hz, *C*-Ar-F), 137.1, 137.3 (d, $^4J_{C,F}$ = 3.1 Hz, *C*-Ar-F), 144.2, 144.5 (d, $^4J_{C,F}$ = 2.1 Hz, *C*-10), 161.2 (d, $^1J_{C,F}$ = 243.4 Hz, *C*-Ar-F), 168.9, 169.0 (*C*=O) ppm. CIMS: *m*/*z* (%) = 383 (12) [MH$^+$], 325 (40) [MH$^+$ – acetone], 265 (100) [MH$^+$ – acetone – AcOH].

(4*R*)-4-{[2-Fluoro-11-(methoxymethoxy)-5*H*-dibenzo[*a*,*d*]cyclohepten-10-yl]methyl}-2,2-dimethyl-1,3-dioxolane (8): CH$_3$OCH$_2$I (0.12 mL, 1.45 mmol) and NaH (0.12 g, 2.90 mmol) were added to an ice-cooled solution of ketone **5a** (247 mg, 0.725 mmol) in THF (5 mL). The reaction mixture was stirred at room temp. for 6 h. After the disappearance of the ketone (TLC), NH$_4$Cl (satd. aq. solution) was added, the mixture was extracted three times with CH$_2$Cl$_2$ and the organic phase was dried with MgSO$_4$, filtered and the solvents were evaporated. The residue was purified by column chromatography on silica gel eluting with diethyl ether/heptane (25:75) to yield enol ether **8** as an oil (190 mg, 68 %). ^{1}H NMR (CDCl$_3$, 400 MHz; two isomers): first isomer: δ = 1.30 (s, 3 H, CH$_3$), 1.40 (s, 3 H, CH$_3$), 2.95 (dd, *J* = 13.6, 6.3 Hz, 1 H, CH$_2$), 3.67–3.85 (m, 5 H, CH$_2$-O + CH$_2$-5 + CH$_2'$), 3.59 (s, 3 H, -OCH$_3$), 4.13–4.17 (m, 1 H, Σ^3J = 25.5 Hz, CH-O), 4.83–4.88 (m, 2 H, O-CH$_2$-O), 6.93–7.54 (m, 7 H, H-Ar) ppm; second isomer: δ = 1.28 (s, 3 H, CH$_3$), 1.43 (s, 3 H, CH$_3$), 3.19 (dd, *J* = 14.2, 4.7 Hz, 1 H, CH$_2$), 3.67–3.85 (m, 5 H, CH$_2$-O + CH$_2$-5 + CH$_2'$), 3.53 (s, 3 H, -OCH$_3$), 4.25–4.28 (m, 1 H, Σ^3J = 26.4 Hz, CH-O), 4.83–4.88 (m, 2 H, O-CH$_2$-O), 6.93–7.54 (m, 7 H, H-Ar) ppm; common signals: δ = 3.67–3.85 (m, 5 H, CH$_2$-O + CH$_2$-5 + CH$_2'$), 4.83–4.88 (m, 2 H, O-CH$_2$-O), 6.93–7.54 (m, 7 H, H-Ar) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz; two isomers): δ = 25.7, 25.8, 26.8, 27.1 (*C*H$_3$), 33.5, 34.8 (*C*H$_2$), 40.2 (*C*H$_2$-5), 57.6, 57.8 (O*C*H$_3$), 68.3, 69.8 (*C*H$_2$-O), 74.8, 76.1 (*C*H-O), 97.2, 97.3 (O-*C*H$_2$-O), 108.5, 109.0 (Me$_2$*C*), 113.1, 113.2 (d, $^2J_{C,F}$ = 22.6 Hz, *C*H-Ar-F), 116.0, 116.2 (d, $^2J_{C,F}$ = 21.6 Hz, *C*H-Ar-F), 124.7, 125.6 (*C*-10), 126.0, 126.2, 126.65, 126.7, 127.1, 127.4, 127.75, 127.8 (*C*H-Ar), 127.9, 128.0 (d, $^3J_{C,F}$ = 8.4 Hz, *C*H-Ar-F), 133.2 (d, $^3J_{C,F}$ = 7.7 Hz, *C*-Ar-F), 134.4, 135.3, 140.1, 140.4 (*C*-Ar), 137.6, 137.7 (d, $^4J_{C,F}$ = 3.1 Hz, *C*-Ar-F), 149.7, 149.8 (d, $^4J_{C,F}$ = 2.1 Hz, *C*-11), 161.2, 161.25 (d, $^1J_{C,F}$ = 243.6 Hz, *C*-Ar-F) ppm. CIMS: *m*/*z* (%) = 385 (5) [MH$^+$], 327 (40) [MH$^+$ – acetone], 295 (100) [MH$^+$ – acetone – MeOH], 265 (61) [MH$^+$ – acetone – CH$_3$OCH$_2$OH].

[(2*R*)-11-Fluoro-3,8-dihydro-2*H*-dibenzo[3,4:6,7]cyclohepta[1,2-*b*]furan-2-yl]methanol (9): Aqueous HCl (1 N, 3 mL) was added to a solution of ketone **5a** (105 mg, 0.309 mmol) in THF (3 mL). The reaction mixture was stirred at room temp. for 4–5 h. After the disappearance of the ketone (TLC), Na$_2$CO$_3$ (satd. aq. solution) was added, the mixture was extracted three times with CH$_2$Cl$_2$ and the organic phase was dried with MgSO$_4$, filtered and the solvents were evaporated. The residue was purified by column chromatography on silica gel eluting with CH$_2$Cl$_2$. Cyclic enol ether **9** was isolated as an oil (85 mg, 98 %). ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 1.92 (s, 1 H, OH), 3.15 (dd, *J* = 15.2, 7.7 Hz, 1 H, CH$_2$-3), 3.42 (dd, *J* = 15.2, 10.2 Hz, 1 H, CH$_2'$-3), 3.68 (d, *J* = 13.9 Hz, 1 H, CH$_2$-8), 3.72 (d, *J* = 13.9 Hz, 1 H, CH$_2'$-8), 3.87 (dd, *J* = 12.0, 5.8 Hz, 1 H, CH$_2$-OH), 3.91 (dd, *J* = 12.0, 4.1 Hz, 1 H, CH$_2'$-OH), 4.93–5.01 (m, 1 H, Σ^3J = 27.8 Hz, CH-2), 7.03 (dt, J = 8.6, 2.7 Hz, 1 H, H-Ar), 7.22–7.32 (m, 6 H, H-Ar) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 34.9 (*C*H$_2$-3), 41.2 (*C*H$_2$-8), 65.1 (*C*H$_2$-OH), 80.2 (*C*H-2), 111.3 (d, $^2J_{C,F}$ = 23.2 Hz, *C*H-Ar-F), 114.1 (*C*-3a), 116.3 (d, $^2J_{C,F}$ = 21.8 Hz, *C*H-Ar-F), 124.2, 126.5, 127.2, 128.2 (*C*H-Ar), 129.3 (d, $^3J_{C,F}$ = 8.2 Hz, *C*H-Ar-F), 130.5 (d, $^3J_{C,F}$ = 7.6 Hz, *C*-Ar-F), 132.5, 135.1 (*C*-Ar), 132.7 (d, $^4J_{C,F}$ = 3.1 Hz, *C*-Ar-F), 151.0 (d, $^4J_{C,F}$ = 2.9 Hz, *C*-12b), 161.4 (d, $^1J_{C,F}$ = 243.7 Hz, *C*-Ar-F) ppm. CIMS: *m*/*z* (%) = 283 (100) [MH$^+$].

11-Allyl-8-fluoro-5*H*-dibenzo[*a*,*d*]cyclohepten-10-yl Acetate (10): PCC (32 mg, 0.151 mmol) was added to a solution of racemic *trans*-(10*R**,11*S**)-11-allyl-8-fluoro-10,11-dihydro-5*H*-dibenzo[*a*,*d*]-cyclohepten-10-ol (20.2 mg, 0.075 mmol) in CH$_2$Cl$_2$ (1 mL). After reaction at room temp. for 4 h, NH$_4$Cl (satd. aq. solution, 2 mL) was added, the mixture was extracted three times with CH$_2$Cl$_2$ and the organic phase dried with MgSO$_4$, filtered and the solvents were evaporated. The residue was purified by column chromatography on silica gel eluting with CH$_2$Cl$_2$/hexane (50:50) to give the corresponding ketone (±)-11-allyl-8-fluoro-5,11-dihydro-10*H*-dibenzo[*a*,*d*]cyclohepten-10-one. Ac$_2$O (14 µL, 0.151 mmol), DMAP (5 mg, 0.038 mmol) and Et$_3$N (21 µL, 0.151 mmol) were added to a solution of the above 11-allyl ketone in CH$_2$Cl$_2$ (5 mL). After reaction at room temp. for 2 h, NH$_4$Cl (satd. aq. solution, 5 mL) was added, the mixture was extracted three times with CH$_2$Cl$_2$ (5 mL) and the organic phase dried with MgSO$_4$, filtered and the solvents were evaporated. The residue was purified by column chromatography on silica gel eluting with CH$_2$Cl$_2$/hexane (60:40) to yield **10** as an oil (20 mg, 86% over two steps). ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 2.27 (s, 3 H, OAc), 3.42 (ddt, J = 15.5, 5.9, 1.7 Hz, 1 H, CH$_2$), 3.49 (ddt, J = 15.5, 6.5, 1.7 Hz, 1 H, CH$_2'$), 3.73 (d, J = 12.9 Hz, 1 H, CH$_2$-5), 3.78 (d, J = 12.9 Hz, 1 H, CH$_2'$-5), 5.05 (dq, J = 10.1, 1.7 Hz, 1 H, =CH$_{2cis}$), 5.13 (dq, J = 17.1, 1.7 Hz, 1 H, =CH$_{2trans}$), 5.89 (ddt, J = 17.1, 10.1, 6.3 Hz, 1 H, C*H*=CH$_2$), 6.95 (dt, J = 8.4, 2.7 Hz, 1 H, H-Ar), 7.06 (dd, J = 9.9, 2.7 Hz, 1 H, H-Ar), 7.17–7.28 (m, 4 H, H-Ar), 7.48 (d, J = 7.6 Hz, 1 H, H-Ar) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 20.9 (*C*H$_3$), 36.4 (*C*H$_2$), 40.2 (*C*H$_2$-5), 111.6 (d, $^2J_{C,F}$ = 22.9 Hz, *C*H-Ar-F), 116.0 (d, $^2J_{C,F}$ = 21.8 Hz, *C*H-Ar-F), 116.0 (=CH$_2$), 126.1, 126.9, 127.0, 128.4 (*C*H-Ar), 128.0 (d, $^3J_{C,F}$ = 8.3 Hz, *C*H-Ar-F), 129.6 (*C*-11), 134.3 (d, $^3J_{C,F}$ = 8.0 Hz, *C*-Ar-F), 134.9, 140.4 (*C*-Ar), 135.5 (CH=), 137.0 (d, $^4J_{C,F}$ = 3.1 Hz, *C*-Ar-F), 143.8 (d, $^4J_{C,F}$ = 2.85 Hz, *C*-10), 161.2 (d, $^1J_{C,F}$ = 243.1 Hz, *C*-Ar-F), 168.9 (*C*=O) ppm. CIMS: *m*/*z* (%) = 309 (27) [MH$^+$], 267 (100) [MH$^+$ – CH$_2$=C=O], 249 (28) [MH$^+$ – CH$_2$=C=O – H$_2$O].

8-Fluoro-11-(2-propynyl)-5*H*-dibenzo[*a*,*d*]cyclohepten-10-yl Acetate (11): A solution of DMSO (1.69 mL, 23.8 mmol) in CH$_2$Cl$_2$ (15 mL) was added over 5 min to a cooled (–60 °C) solution of oxalyl chloride (1.04 mL, 11.9 mmol) in CH$_2$Cl$_2$ (15 mL) contained in a three-necked flask. The reagent solution was stirred for 10 min, then a solution of *trans*-(10*R**,11*S*)-8-fluoro-11-(2-propynyl)-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cyclohepten-10-ol (1.58 g, 5.94 mmol) in CH$_2$Cl$_2$ (15 mL) was added within about 5 min and the reaction mixture was stirred at –60 °C for 15 min. Et$_3$N (4.97 mL, 35.6 mmol) was added and the cooling bath removed. After reaction at room temp. for 30 min, Na$_2$CO$_3$ (satd. aq. sol., 30 mL) was added. The aqueous phase was extracted with CH$_2$Cl$_2$ (3×25 mL) and the organic phase dried with MgSO$_4$, filtered and the solvents were evaporated. The residue was purified by column chromatography on silica gel eluting with CH$_2$Cl$_2$/hexane (60:40) to afford the 11-propargyl ketone (±)-8-fluoro-11-(2-propynyl)-5,11-dihydro-10*H*-dibenzo[*a*,*d*]cyclohepten-10-one as a white, crystalline product (1.17 g, 75%). Ac$_2$O (0.50 mL, 5.30 mmol), DMAP (0.52 g, 4.24 mmol) and Et$_3$N (0.74 mL, 5.30 mmol) were added to a solution of the above ketone (0.56 g, 2.12 mmol) in CH$_2$Cl$_2$ (40 mL). After reaction at room temp. for 1 h, NH$_4$Cl (satd. aq. solution, 15 mL) was added, the mixture was extracted three times with CH$_2$Cl$_2$ (15 mL) and the organic phase was dried with MgSO$_4$, filtered and the solvents were evaporated. The residue was purified by column chromatography on silica gel eluting with CH$_2$Cl$_2$/hexane (60:40) to yield **11** as a white, crystalline product (0.64 g, 98%). M.p. 151–153 °C. IR (NaCl): $\tilde{\nu}$ = 3304 (s), 1760 (s), 1493, 1370, 1163, 909 cm^{-1}. ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 2.04 (t, J = 2.7 Hz, 1 H, ≡CH), 2.31 (s, 3 H, OAc), 3.55 (dd, J = 17.0, 2.7 Hz, 2 H, CH$_2$), 3.75 (d, J = 13.0 Hz, 1 H, CH$_2$-5), 3.83 (d, J = 13.0 Hz, 1 H, CH$_2'$-5), 6.96 (dt, J = 8.4, 2.6 Hz, 1 H, H-Ar), 7.07 (dd, J = 9.8, 2.6 Hz, 1 H, H-Ar), 7.18–7.27 (m, 4 H, H-Ar), 7.59 (d,J = 7.5 Hz, 1 H, H-Ar) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 20.8 (*C*H$_3$), 21.6 (*C*H$_2$), 40.0 (*C*H$_2$-5), 69.2 (≡*C*H), 81.2 (*C*≡CH), 111.7 (d, $^2J_{C,F}$ = 23.1 Hz, *C*H-Ar-F), 116.3 (d, $^2J_{C,F}$ = 21.7 Hz, *C*H-Ar-F), 126.2, 126.7, 127.0, 128.7 (*C*H-Ar), 126.4 (*C*-11), 128.2 (d, $^3J_{C,F}$ = 8.3 Hz, *C*H-Ar-F), 133.9 (d, $^3J_{C,F}$ = 7.8 Hz, *C*-Ar-F), 134.1, 140.2 (*C*-Ar), 136.8 (d, $^4J_{C,F}$ = 2.6 Hz, *C*-Ar-F), 144.5 (d, $^4J_{C,F}$ = 2.0 Hz, *C*-10), 161.2 (d, $^1J_{C,F}$ = 243.6 Hz, *C*-Ar-F), 168.7 (*C*=O) ppm. CIMS: *m*/*z* (%) = 307 (76) [MH$^+$], 265 (100) [MH$^+$ – ketene], 247 (41) [MH$^+$ – ketene – H$_2$O]. EIMS: *m*/*z* = 306 (18) [M$^+$], 264 (100) [M$^{+\cdot}$ – ketene]. HRMS calcd. for C$_{20}$H$_{15}$FO$_2$ [M$^{+\cdot}$]: 306.1056; found 306.1050.

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