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Hydrogen Bonding of Hydroxy Groups to Carbanions in Indenide and Fluorenide Derivatized Alcohols Directly Observed by UV, IR, and NMR Spectroscopy

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Abstract: For investigation of hydrogen bonding to carbanions a number of carbanions containing hydroxy groups have been designed and synthesized. The carbanions were of the type R′-CR_2-CHR-CR_2-OH, with R′ being an indenide or a fluorenide group and R a methyl group or a hydrogen, and were generated from the corresponding indenes and fluorenes. Intramolecular hydrogen bonding was observed by UV, IR, and NMR spectroscopy in both polar [dimethyl sulfoxide (DMSO) and tetrahydrofuran (THF)] and apolar (benzene and toluene) non-hydrogen bond donor solvents with properly designed carbanions. In the latter solvents cryptand 211 was used for complexation of the counter Li^+ cation. For some derivatives the presence of both intramolecular hydrogen bonding to the carbanion and intermolecular hydrogen bonding of the hydroxy group to the solvent was observed. The UV spectroscopy indicated the perturbation of the proton accepting carbanion and IR and NMR spectroscopy showed the effect of the hydrogen bonding on the proton donating OH group.

Introduction

In proton-transfer reactions involving carbon acids hydrogen bonded carbanions are postulated as intermediates.[1] Such species are usually elusive because they are unstable and shortlived and as a consequence little is known about them. The knowledge of specific solvation of carbanions in general is very limited, indeed. There are only a few reports on hydrogen bonding by bulk solvent to carbanions[2] and hydrogen bonding to an isonitrile.[3] In the solid state, crystallographic studies have shown the presence of hydrogen bonding to carbanions,[4] and in the gas phase the strength of hydrogen bonds to acetylides have been measured using ion cyclotron spectroscopy.[5]

We have been designing reaction systems with the potential to yield hydrogen bonded carbanions with life long enough to allow direct observation of such species.[6] In a previous article we have presented results of studies of intramolecular hydrogen bonding of a hydroxy proton to indenide by IR and NMR spectroscopy.[7] In the present paper an extensive study of intramolecular hydrogen bonding of alcohol groups to indenides and fluorenides by means of IR, UV, and ^1H NMR spectroscopy is presented. The UV spectroscopy has been used to investigate the perturbation of the proton accepting carbanion by the hydroxy group, and IR and NMR spectroscopy have been employed for the studies of the perturbation of the proton donor by the carbanion.

In our search for molecular systems having long lived hydrogen bonds to carbanions, we initially used DMSO as solvent and thus took advantage of the extensive knowledge of pK_a values of carbon acids and oxygen acids etc. in this solvent. Indenes and fluorenes are about 10^6–10^9 times stronger acids than alcohols in DMSO.[8]

Molecules were designed with alcohol functional groups linked via three-carbon chains to the five-membered rings of indene and fluorene as shown in Scheme I. The length of the chain was chosen so that the intramolecular hydrogen bond could be a part of a six-membered chelate ring. To further promote the formation of intramolecular hydrogen bonds the chain was substituted with methyl groups in such a way that conformers with the OH group close to the carbanionic five-membered rings of the indenide and fluorenide were favored. Other molecules have been designed with a substitution pattern that disfavor intramolecular hydrogen bonds in the carbanions.

Results and Discussion

In Scheme I all the carbanions together with their precursors that have been studied in the present work are shown. In the experimental section the synthesis of the precursors **3**, **5**, **7**, **13**, **15**, **17**, **19**, and **21** + **22** are reported. The preparation of **1**, **9**, and **11** has been published previously.[6c]

Solutions of the carbanions (<30 mM) were, e.g., made in a screw-cap 5-mm NMR tube by adding *n*-BuLi in hexane to the precursor in the solvent of choice. The solvents used were DMSO, DMF, DMPU, acetonitrile, pyridine, THF, diethyl ether, benzene, and toluene.[9] In THF and the less polar solvents alkoxide rather than carbanion is favored in the equilibrium between these species.

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[1] (a) Cram, D. J. *Fundamentals of Carbanion Chemistry*; Academic Press: New York and London, 1965; pp 86–103. (b) Bell, R. P. *The Proton in Chemistry*, 2nd ed.; Cornell University Press: New York, 1973.

[2] (a) Ford, W. T. *J. Am. Chem. Soc.* **1970**, *92*, 2857. (b) Hogen-Esch, T. E. *J. Am. Chem. Soc.* **1973**, *95*, 639. (c) Greifenstein, L. G.; Pagani, G. A. *J. Org. Chem.* **1981**, *46*, 3336. (d) Mueller-Westerhoff, U. T.; Nazzal, A.; Proessdorf, W. *J. Am. Chem. Soc.* **1981**, *103*, 7678.

[3] (a) Ferstandig, L. L. *J. Am. Chem. Soc.* **1962**, *84*, 1323. (b) Ferstandig, L. L. *J. Am. Chem. Soc.* **1962**, *84*, 3553. (c) Schleyer, P. v. R.; Allerhand, A. *J. Am. Chem. Soc.* **1962**, *84*, 1322. (d) Allerhand, A.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1963**, *85*, 866.

[4] (a) Seebach, D. *Angew. Chem.* **1988**, *27*, 1624. (b) Buchholz, S.; Harms, K.; Massa, W.; Boche, G. *Angew. Chem.* **1989**, *101*, 77.

[5] (a) Caldwell, G.; Rozeboom, M. D.; Kiplinger, J. P.; Bartmess, J. E. *J. Am. Chem. Soc.* **1984**, *106*, 4660.

[6] (a) Ahlberg, P.; Johnsson, B.; Mc Ewen, I.; Rönnqvist, M. *J. Chem. Soc., Chem. Commun.* **1986**, 1500. (b) Ahlberg, P.; Davidsson, Ö. *J. Chem. Soc., Chem. Commun.* **1987**, *623*. (c) Ahlberg, P.; Davidsson, Ö.; Johnsson, B.; Mc Ewen, I.; Rönnqvist, M. *Bull. Soc. Chim. Fr.* **1988**, *2*, 177. (d) Mc Ewen, I.; Ahlberg, P. *J. Chem. Soc., Chem. Commun.* **1989**, *1198*. (e) Mc Ewen, I. *J. Mol. Struct.* (*Theochem.*) **1992**, *276*, 141.

[7] Mc Ewen, I.; Ahlberg, P. *J. Am. Chem. Soc.* **1992**, *114*, 10869.

[8] (a) Matthews, W. S.; Bares, J. E.; Bartmess, J. E.; Bordwell, F. G.; Cornforth, F. J.; Margolin, Z.; McCollum, R. J.; McCollum, G. J.; Vanier, N. R. *J. Am. Chem. Soc.* **1975**, *97*, 7006. (b) Olmstead, W. N.; Margolin, Z.; Bordwell, F. G. *J. Org. Chem.* **1980**, *45*, 3295. (c) Bordwell, F. G.; Drucker, G. E. *J. Org. Chem.* **1980**, *45*, 3225.

[9] The following abbreviations in this paper stand for DMSO = dimethyl sulfoxide; DMF = dimethylformamide; DMPU = (*N,N*′-dimethyl-*N,N*′-propyleneurea)1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone; THF = tetrahydrofurane; AcCN = acetonitrile; cryptand C211 = 4,7,13,18-tetraoxa-1,10-diazabicyclo-(8.5,5)eicosane; IPA = isopropyl alcohol.

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Scheme I

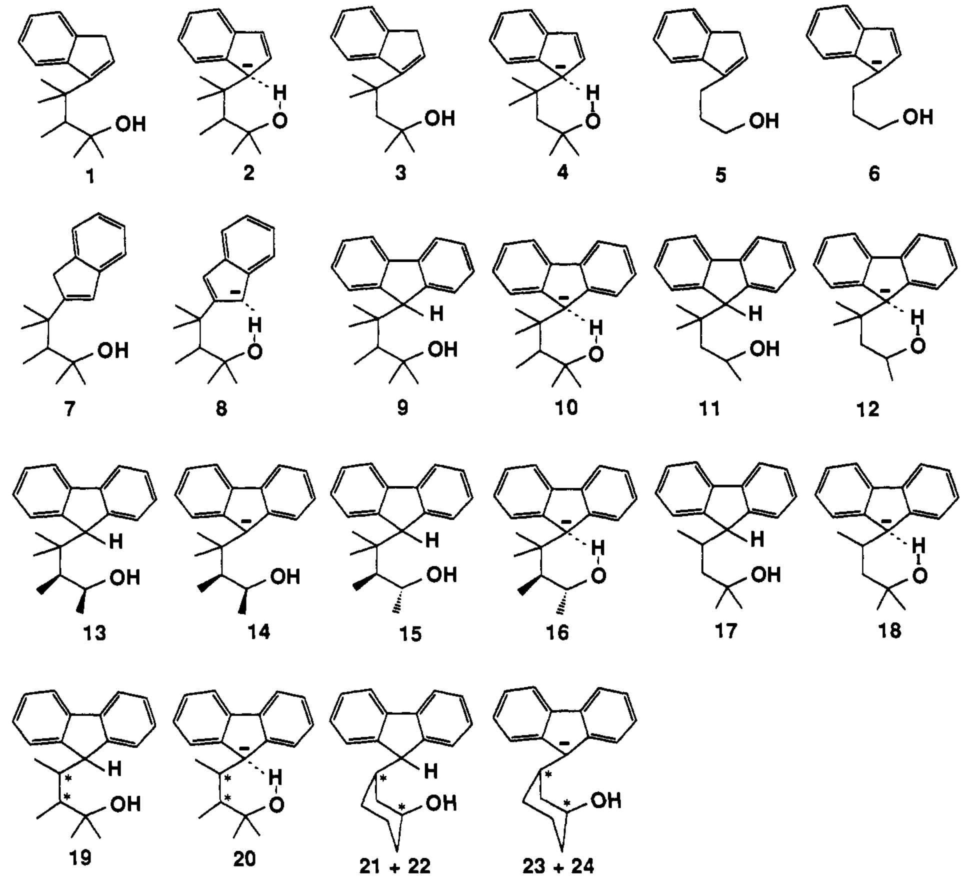

Table I. Stretching Frequencies (cm^{-1}) of the OH Group in Precursors and Carbanions in Different Solvents

	neutral molecules					carbanions[a]			
	DMSO	THF	benzene	toluene		DMSO	THF	benzene	toluene
1	3393	3469	3586		**2**[c]	3316	3324	3310	
3	3385	3470	3586	3585	**4**[c]	3368	3374	3375	3376
5	3358	3468	3607		**6**	3380	3468	3397	
7	3393				**8**[c]	3350			
9	3376				**10**[c]	3301			
11	3372	3464	3593		**12**[c]	3355	3370	3350	
13	3384	3472		3594	**14**	3414	3480		3425
15	3375		3591		**16**[c]	3292[b]		3288	
17	3383				**18**[c]	3370			
19	3390		3584		**20**	3397		3335	
21	3378		3593		**23**	3404		3593	
22	3369		3589		**24**	3384		3589	

[a] In THF, benzene, and toluene, the concentration of C211 was equal to the concentration of the carbanion. [b] Another band was observed as a shoulder on the main band at ca. 3395 cm^{-1}. [c] Intramolecular hydrogen bonding in DMSO.

However, addition of cryptand C211[9] to the solutions of the lithium alkoxides reversed the equilibrium in favor of the carbanions. The explanation of this change is that both the carbanion and the alkoxide are paired with Li$^+$ and that the Li$^+$ alkoxide pair is more stable than the Li$^+$ carbanion pair. Addition of cryptand 211 results in binding of Li$^+$ to the cryptand making the cryptand separated carbanion/Li$^+$ ion pair more stable than the lithium alkoxide.[7,10]

IR Spectroscopy. Benzene, toluene, THF, and DMSO were employed as solvents in the hydrogen bonding investigations of the carbanions and their precursors by IR spectroscopy.[11] Frequency, shape, and intensity of the OH stretching bands were studied. In THF, benzene, and toluene about one carbanion equivalent of C211 was added to the carbanionic solutions. All the indenide or fluorenide alcohols in Table I except for **8**, **10**, and **18** have been studied in benzene and/or toluene and all except for **23** and **24** showed OH stretching bands that had shifted 200–300 cm^{-1} to lower frequencies were broader and more intense relative to their precursors (cf. Figure 1). It is concluded that all the studied carbanions are intramolecularly hydrogen bonded under these conditions except for **23** and **24**, which for sterical reasons avoid such intramolecular hydrogen bonding.

The OH stretching frequencies and thus the shifts ascribed to intramolecular hydrogen bonding were found to be independent of the concentrations of the precursor and the salts of the carbanions, respectively, over large intervals (ca. 10^{-4}–10^{-1} M), indicating that possible aggregation is not influencing the intermolecular hydrogen bonding significantly.

In THF the OH in carbanions is, in part, H-bonded to solvent. Ions **2**, **4**, and **12** show intramolecular hydrogen bonding, but **6** and **14** prefer intermolecular hydrogen bonding to THF molecules, as indicated by the small or absent frequency difference between the OH stretching frequencies of the ions and their precursors, i.e., **5** and **13**.

Also in DMSO, which is a good hydrogen bond acceptor, several of the carbanions in Table I appear to be intramolecularly hydrogen bonded. Only ions **6**, **14**, **23**, and **24** are concluded to be intermolecularly hydrogen bonded to the solvent.

The OH stretching frequencies for those carbanions that have been concluded to be intramolecularly hydrogen bonded are

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[10] (a) Hogen-Esch, T. E.; Smid, J. *J. Am. Chem. Soc.* **1966**, *88*, 307. (b) Hogen-Esch, T. E. In *Advances of Physical Organic Chemistry*; Gold, V., Bethell, D., Eds.; Academic Press: New York, 1977; Vol. 15. (c) Smid, J. In *Ions and Ion-pairs in Organic Reactions*; Szwarc, M., Ed.; Wiley: New York, 1972. (d) Gronert, S.; Streitwieser, A. *J. Am. Chem. Soc.* **1988**, *110*, 2836, and references therein.

[11] Joesten, M. D.; Schaad, L. J. *Hydrogen bonding*; Marcel Dekker, Inc.: New York, 1974; pp 3–7.

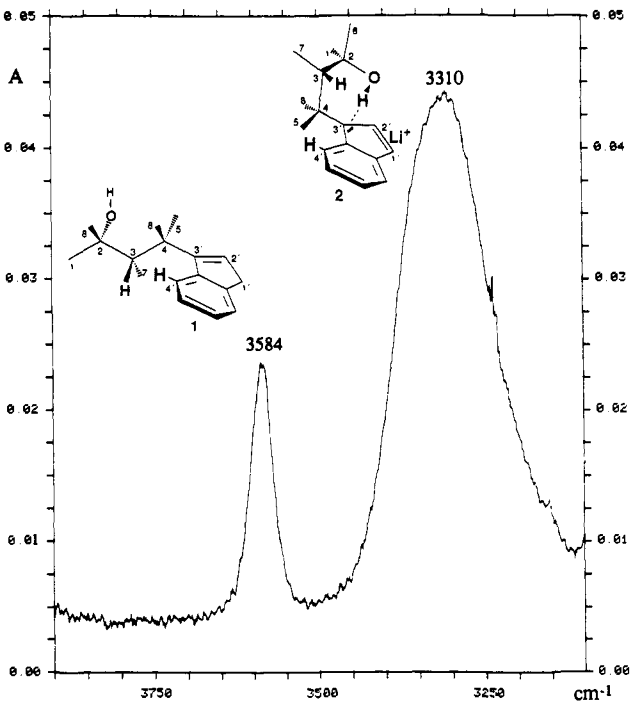

Figure 1. FT-IR absorption spectrum for a mixture of **1** (8.7 mM) and **2** (7.7 mM) with cryptand C211 (10 mM) in benzene at 21 °C.

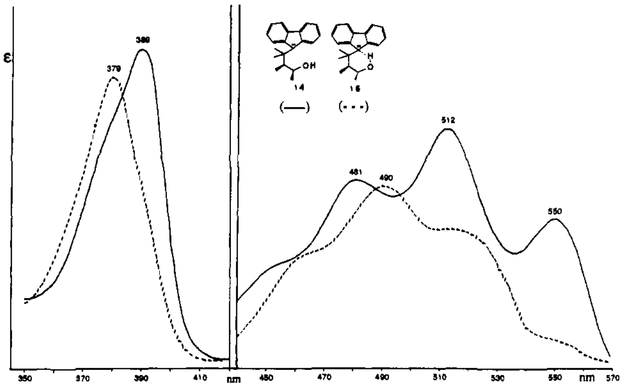

Figure 2. Electronic absorption spectra of the potassium carbanions (ca. 0.75 mM) **14** (- -) and **16** (—) in DMSO at 21 °C.

essentially independent of the solvent. This is consistent with the small solvent interaction of the intramolecularly hydrogen bonded proton.

It is interesting to note that carbanion **16** in DMSO showed two overlapping OH bands. One of these appeared as a shoulder on the main band and at higher frequency than that of the OH band of the precursor **15**. The main carbanion band had a frequency slightly lower than that of **15**. The high-frequency shoulder presumably originates from an intermolecularly hydrogen bonded species and the low-frequency band from carbanions which are intramolecularly hydrogen bonded.

The small increase of the OH stretching frequency on going from precursors to carbanions, which are intermolecularly hydrogen bonded to the solvent in DMSO and THF (5,6; 13,14; 19,20; 21,23; and 22,24), might be due to structural differences in the solvent participation in the hydrogen bonds.

UV Spectroscopy. While IR spectroscopy was a useful tool to study the perturbation of the hydrogen bond donating OH groups by the carbanions, UV spectroscopy has been used to study the perturbation of the carbanions by the hydrogen bonds. The fluorenides were more suitable for such studies than the indenides because the absorption bands of the latter compounds overlapped with bands of the solvent.

Table II. UV Absorption Maxima of the Various Fluorenide Carbanions in DMSO at Room Temperature[a] and Shifts ($\Delta\nu$) of the OH Stretching Bands Observed in DMSO[b]

carbanion	$\Delta\nu$/, cm^{-1}	λ_{max}/, nm	carbanion	$\Delta\nu$/, cm^{-1}	λ_{max}/, nm
10	−75	379	**18**	−13	379
12	−17	379	**20**	+7	379, 389
14	+30	389	**23**	+26	389
16	−83	379	**24**	+15	389

[a] The carbanion concentration was ca. 0.75 mM. The extinction coefficients of the carbanions were ca. 10 000. [b] $\Delta\nu$ is the difference between the OH stretching band frequency of the carbanion and that of its precursor.

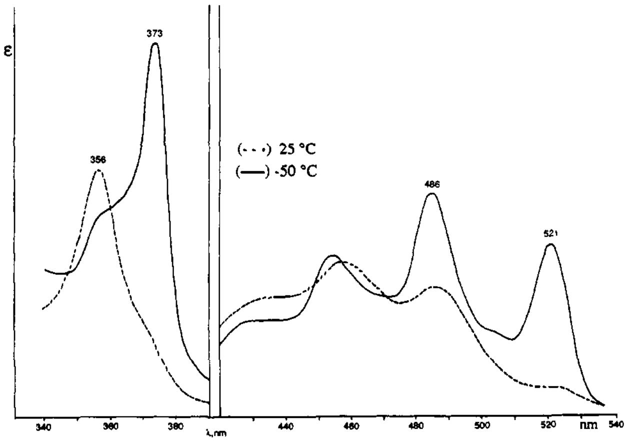

Figure 3. Electronic absorption spectra after Hogen-Esch and Smid[12] of fluorenyl sodium in THF at −50 °C (—), and at 25 °C (- -). At −50 °C, fluorenylsodium exists predominantly as solvent separated ion pairs, while contact ion pairs are dominating at 25 °C.

The UV spectra of the carbanions in the present investigation showed close resemblance with those of unsubstituted fluorenide carbanion reported by Hogen-Esch and Smid.[12] In Figure 2 two representative spectra are shown. Table II lists λ_{max} values for carbanion salts in DMSO. Carbanions **10**, **12**, **16**, and **18** all have maxima at 379 nm, while **14**, **23**, and **24** showed absorption band maxima at 389 nm. Carbanion **20** showed bands at both 379 and 389 nm, the latter one being more intense. The carbanions with bands at 379 nm all showed OH stretching bands at lower frequencies relative to their precursors. Those with maxima at 389 nm all have OH stretching bands at higher frequencies relative to their precursors. Thus the 10 nm blue shift of the absorption maxima observed for **10**, **12**, **16**, **18**, and **20** relative to the 389 nm band are ascribed to perturbation of the carbanions by intramolecular hydrogen bonding.

The UV spectra of the diastereoisomers **14** and **16** in benzene show maxima at 385 nm and 383 nm, respectively. The spectra indicate that **16** is exclusively intramolecularly hydrogen bonded in benzene in contrast to in DMSO, where both intra- and intermolecularly hydrogen bonded species are present. Carbanion **14**, on the other hand, which is not intramolecularly hydrogen bonded in DMSO, appears to be both inter- and intramolecularly hydrogen bonded in benzene.

The 10-nm difference in wavelength between carbanion with OH H-bonded to DMSO and carbanion intraspecies H-bonded resembles Hogen-Esch's observation of the constant wavelength difference solvent separated ion pair minus that for the contact ion pair.[12] In the solvent separated ion pair, the spectral perturbation by the cation is very small indeed, i.e., the spectrum is essentially that of a free carbanion and therefore presumably similar to the spectra of the intermolecularly hydrogen bonded fluorenide carbanions of the present work. Thus, we conclude that the spectral perturbation caused by the hydroxy groups of

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(12) Hogen-Esch, T. E.; Smid, J. *J. Am. Chem. Soc.* **1966**, *88*, 307.

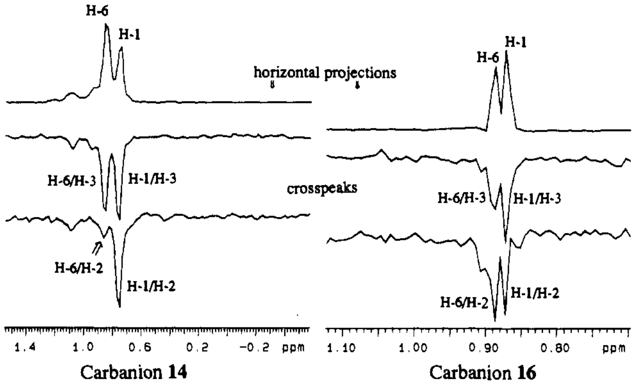
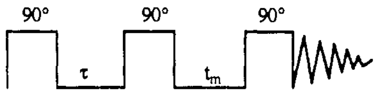


Figure 4. Traces (or skyline projections) extracted from two phase sensitive NOESY spectra at 21 °C.

the intramolecularly hydrogen bonded carbanions are comparable to that caused by K^+ or Cs^+ in contact with fluorenide ion. It is interesting to note that the shift caused by intramolecular specific solvation also is similar to a reported blue shift of 12 nm (from 388 nm to 376 nm) in the fluoradenide carbanion on going from aprotic solvents such as THF or DMSO to protic solvents like methanol. These latter results by Hogen-Esch were interpreted as being due to hydrogen bonding by the bulk hydrocyclic solvent.[2b]

^{1}H NMR Spectroscopy. ^{1}H NMR spectroscopy has also been used to study hydrogen bonding involving the carbanions. It has also been used to study relative configuration and conformation of the side chains. COSY and NOESY were used for the latter determinations. NOESY is commonly used to study NOE effects in macromolecules. However, it has not found such use in studies of small molecules because the growth rate of the NOEs are generally low and the two-dimensional responses are small. The NOESY pulse sequence may be written:



The evolution time is τ and the mixing time is t_m which is kept constant. Short mixing times—less than one second—are normally used for macromolecules. For small molecules the mixing time has to be increased to several seconds and should be as long as the relaxation time T_1 for the protons of interest. In contrast, magnetization transfer due to chemical exchange, which is studied with the same pulse sequence, will show up with very short mixing times.

The configurations of the two diastereoisomeric carbanions **14** and **16** were determined in DMSO-d_6 by the NOESY procedures. In the spectrum of **16** (Figure 4) the crosspeaks H-6/H-2 and H-1/H-3 were similar in size. This is consistent with **16a** in Scheme II; i.e., we are dealing with the racemic diastereoisomer consisting of the (2*S*,3*R*)/(2*R*/3*S*) pair of enantiomers.

In contrast, the spectrum of **14** showed a crosspeak H-6/H-2 which was much smaller than the H-1/H3 one, indicating the structure **14a** rather than **14b** in Scheme II, i.e., the diastereoisomer consisting of the (2*R*,3*R*)/(2*S*,3*S*) pair. The conformer **14b** is expected to show a larger H-6/H-2 crosspeak. Presumably, conformation **14a** is favored over **14b** because of repulsions between the side chain methyl groups 1 and 6.

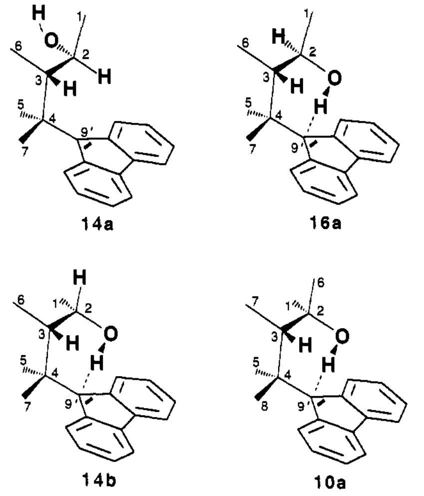
The configuration of **20** could not be assigned because both crosspeaks H-3/H-5 and H-4/H-7 were observed and the other spectroscopic studies indicated the presence of both inter- and intramolecularly hydrogen bonded species in DMSO. No attempts were made to determine the relative configurations of **23** and **24** since none of them showed signs of intramolecular hydrogen bonding in any of the solvents used in the present studies.

Table III. ^{1}H Chemical Shift of the OH Protons of Some of the Precursors and Their Corresponding Carbanions in DMSO, THF,[a] Benzene,[a] and Toluene[a]

	^{1}H chemical shift,[b] ppm					
solvent	1-OH	2-OH	3-OH	4-OH	15-OH	16-OH
DMSO	4.02	3.61	4.01	3.09	4.43	3.60
THF	3.16	3.89				
benzene	1.29	4.53			0.64	4.46
toluene	1.39	4.54	0.97	3.87		

[a] The concentration of cryptand C211 was equal to that of the carbanion. [b] The reference frequencies were set at 2.50 ppm in DMSO-d_6, at 3.58 ppm in THF-d_8, at 7.20 ppm in benzene-d_6 and at 2.30 ppm in toluene-d_8. The chemical shift of the OH proton in the precursors in THF, benzene and toluene was obtained without any cryptand or carbanion present. The ^{1}H NMR spectra were obtained in DMSO at 30 °C and in the other solvents at 21 °C. The solute concentrations were ca. 15 mM.

Scheme II



The ^{1}H NMR spectra of mixtures of fluorenide carbanions and their respective precursors showed broad peaks due to chemical exchange between OH protons and H-9′:s in the five-membered rings. Furthermore, the H-1′ and H-8′ in the fluorenide moieties were equivalent indicating rapid rotation of the side chain around the chain carbon C-9′ bonds.

The ^{1}H NMR studies of the indenide carbanions and their precursors were more informative. Sharp peaks were observed for both precursors and indenide carbanions. The larger reactivity of the fluorenides was also manifested in DMSO-d_6. In this solvent the OH protons were found to be completely exchanged for deuteriums before an ^{1}H NMR spectrum had been obtained. The OH groups of the indenide carbanions were in contrast only slowly deuterated, and complete deuterization was obtained only after several hours of reaction time.

In the ^{1}H NMR spectra of the precursor/carbanion mixtures **1** + **2**, **13** + **14**, and **15** + **16** in DMSO showed carbanion OH peaks upfield relative to the chemical shifts of their respective precursor OH groups. The results are summarized in Table III. The upfield appearance of these intramolecularly hydrogen bonded carbanion OH groups are presumably caused by anisotropy of the aromatic systems[14] counter acting downfield shifts due to the hydrogen bonding. Thus, subtraction of the anisotropy effect would result in an even larger chemical shift of the hydroxy protons of the carbanions. In benzene and toluene the carbanion OH peaks of the above mixtures appeared far downfield of the precursor OH peaks. This is due to the weak intermolecular hydrogen bonding of the precursor hydroxy groups.

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(13) Sanders, J. K. M.; Hunter, B. K. *Mordern NMR Spectroscopy, A guide for Chemists*; Oxford University Press: Oxford, 1987; p 171.

(14) Joesten, M. D., ref 11, p 42.

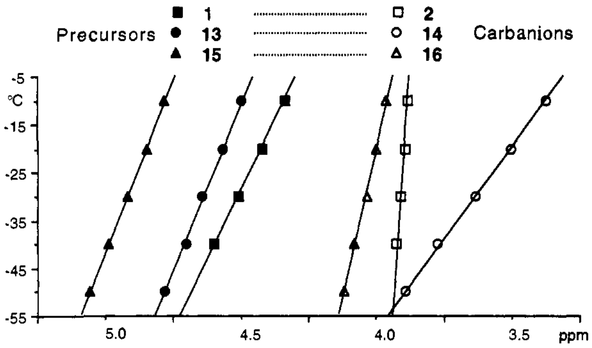

Figure 5. Temperature versus chemical shift of the OH proton in precursors **1**, **13**, and **15** and the OH proton in their corresponding carbanions **2**, **14**, and **16**, respectively, in DMF-d_7.

An equivalent of cryptand 211 was added to the solutions of the carbanions in THF, benzene, and toluene. The chemical shifts of the precursor OH protons were measured in absence of any cryptand or carbanion present in the latter three solvents.

The hydrogen bonding of the carbanions and the precursors has also been investigated by studying the temperature dependence of the ^{1}H NMR chemical shifts of the OH protons. It has been reported that the chemical shift of an intramolecularly hydrogen bonded proton is scarcely temperature dependent in contrast to intermolecularly hydrogen bonded protons.[15] In the latter case a rise in temperature will usually result in a decrease in the concentration of intermolecularly hydrogen bonded species and as a result an upfield shift of the OH signal will be observed.[16]

The ^{1}H NMR spectra were obtained down to −60 °C for the mixtures **1** + **2**, **13** + **14**, and **15** + **16** in DMF-d_7. The results are shown in Figure 5. The OH peak of each of the three precursors **1**, **13**, and **15** shifted strongly downfield upon cooling the solutions. In contrast, the shift of the hydrogen bonded proton in **2** showed only small temperature dependence. The OH peak of the carbanion **14** shifted strongly downfield and that of **16** showed moderate temperature dependence. These results are consistent with the results from the other spectroscopic investigations of these carbanions, i.e., that the OH of **2** is mainly intramolecularly hydrogen bonded and that of **14** is mainly intermolecularly hydrogen bonded. Carbanion **16** is present as a rapidly equilibrating mixture of intra- and intermolecularly hydrogen bonded species.

Experimental Section

Synthetic starting materials and solvents were obtained from commercial suppliers. Nondeuterated DMSO was distilled from NaH_2.[8a] THF-d_8 was stored over Deperox (Fluka AG) and distilled prior to use. Other deuterated solvents were dried over molecular sieves (4Å).

General Procedures. Sample manipulations were carried out in a nitrogen atmosphere and when necessary in a glovebox (Mecaplex GB80) made of stainless steel and equipped with a gas purification system. The water content in the glovebox atmosphere was measured with a Shaw hygrometer (Model SHA-TR) and was 1–2 ppm. All glassware and the syringes were dried in a vacuum oven (3 Pa) at 50 °C over night and introduced into the glovebox avoiding contact with the atmosphere of the room.

The carbanion solutions were prepared by adding a 2.5 M solution of *n*-BuLi in hexane straight into a screw capped 5-mm NMR tube containing the precursor in 0.6 mL of solvent. This procedure was used for preparation of dilute carbanion solutions (<30 mM). The amount of *n*-hexane introduced into the solutions was small and could be further decreased by employing 10 M *n*-BuLi in hexane. The solutions in benzene and toluene had to be <30 mM in carbanion, otherwise two liquid phases were obtained. However, at higher temperatures the solutions became homogeneous.

Solutions at higher carbanion concentrations and avoiding the presence of *n*-hexane were prepared in the following way. *n*-BuLi in hexane was introduced into a vessel attached to a vacuum line, and the hexane was evaporated. The precursor solution was then introduced with a gas tight syringe under a flow of nitrogen gas. The carbanions were prepared at room temperature or just above the melting point of the solvent with no noticeable difference.

Some solvents like DMF and pyridine react with *n*-BuLi. Carbanion solutions of these solvents were prepared in the following way. Treatment of the precursor in THF with *n*-BuLi resulted in formation of almost colorless alkoxide. THF was evaporated and the desired solvent was added. The carbanion solution was then transferred to a screw capped 5-mm NMR tube.

The addition of cryptand 211 could be made either before or after the addition of BuLi to the precursors in THF, benzene, or toluene. For the IR spectroscopic studies the fraction of carbanion in the carbanion/precursor solutions was measured by NMR spectroscopy before introducing the solution into the IR cell.

The potassium salts of the carbanions in DMSO were prepared by adding a solution of dimsyl potassium[8a] to the precursors dissolved in DMSO.

IR Spectroscopy. The cell walls of the IR cell were of CaF_2 and separated by a Teflon spacer (0.3 mm). The stop cocks were also made of Teflon. The data were obtained on a Perkin Elmer 1800 FT-IR spectrometer at 21 °C. The number of recorded scans were between 10 and 60, depending on the carbanion and/or precursor concentrations. The carbanion/precursor spectra were obtained by subtracting a spectrum of the pure solvent from the spectra of the solutions. By this procedure all the overtones from the solvent in the region 3000–3700 cm^{-1} were eliminated.

NMR Spectroscopy. The data were acquired and processed using a Varian XL-400 spectrometer equipped with a superconducting magnet operating at a ^{1}H frequency of 399.917 MHz and a ^{13}C frequency of 100.571 MHz. A 5-mm broad band dual probe was employed. TMS has been used as internal reference. The number of transients to obtain a proton spectrum was about 100, and a 16 K transform was carried out over a spectral width of about 4500 Hz. The pulse angle used was between 30° and 60°, but when large proportions of nondeuterated solvents were used, the pulse angle was shortened to less than 3° or a 10 dB attenuator was introduced between the observe amplifier and the observe receiver. ^{13}C NMR spectra were obtained in the usual way.

In all 2D experiments, two dummy transients were dumped before acquiring each new incremental spectrum. The length of the 90° pulse was always checked before any T_1 and 2D experiment. The 90° ^{1}H pulse lasted 32 μs, and the 90° ^{13}C pulse, 14 μs.

The homonuclear ^{1}H shift correlated (COSY) 2D NMR spectra in DMSO-d_6 and DMF-d_7 were obtained with the standard acquisition sequence with a 90° mixing pulse and using phase cycling. The spectral width was 3200 Hz, and the relaxation delay between pulses was 4.5 s. Four 0.5 K transients were acquired for each of the 100 incremental spectra. The whole process took less than 1 h. The FID and the interferogram of the COSY were processed with a Gaussian apodization function.

The NOESY experiments were obtained in the phase sensitive mode with a spectral width of 4500 Hz. Sixteen 1 K transients were acquired for each of the 256 incremental spectra. The mixing time was set equal to the T_1 relaxation time of the OH protons and was 1–3 s. The relaxation delay was set equal to $2 \times T_1$. The FID and the interferogram were processed with a very mild line broadening function (0.1 Hz) and an apodization function equal to 0.6 × AT seconds (the acquisition time of the interferogram is equal to the number of the increments divided by the sweep width). The NOESY experiments in DMSO were carried out at 30 °C, and, in the case with the solvent partially deuterated, a selective homodecoupling of the solvent signal was performed. The spectral width used to obtain a spectrum from **16** in DMSO-d_6 was 1430 Hz, between 0.5 and 4.1 ppm (the hydroxy group being deuterated). No aliasing was observed. The reason to use this narrow spectral width was to increase the resolution of the methyl groups H-1 and H-6 ($\Delta\delta = 0.02$ ppm).

The sample temperature in the probe was measured using a calibrated thermocouple of type K. A resistance temperature detector Pt 100 DIN 1/10 was used as a reference. The thermocouple was introduced in a 5-mm NMR tube.

Synthesis. The indenyl alcohols, except **5** and **7**, and the fluorenyl alcohols were synthesized by 1,4-addition of indenyl- or fluorenyllithium to the proper α,β-unsaturated ketone. The resulting ketones from the

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first step were transformed to alcohols by reaction with either NaBH$_4$ or methyllithium.

Indenyl- and fluorenyllithium were prepared in situ as follows. Fluorene or indene, usually 5.0 g (30 mmol), was dissolved in 50 mL of sodium dried diethyl ether in a flask equipped with a condenser and a septum under nitrogen atmosphere. *n*-Butyllithium (*n*-BuLi), 18.5 mL of a 1.6 M solution (30 mmol) in hexane, was added at room temperature using a syringe. The strongly colored solution obtained was refluxed for 30 min and then cooled to room temperature.

The synthesis of 4-(3-indenyl)-2,3,4-trimethylpentan-2-ol (**1**), 4-(9-fluorenyl)-2,3,4-trimethylpentan-2-ol (**9**), and 4-(9-fluorenyl)-4-methylpentan-2-ol (**11**) have been reported previously.[6c]

4-Methyl-4-(3-indenyl)-2-pentanone (25). To a 50-mL solution of indenyllithium (50 mmol) at 0 °C was added dropwise 4.9 g (50 mmol) of mesityl oxide dissolved in 20 mL of dimethyl ether, and the mixture was refluxed for 15 min. After cooling the reaction mixture it was poured slowly into a rapidly stirred cold ammonium chloride solution, and the product was extracted with ether. Indene and mesityl oxide in the product mixture was evaporated employing a high vacuum pump. The product ketone was pure enough to be used in the next step.

2,4-Dimethyl-4-(3-indenyl)-2-pentanol (3). To a stirred ether solution of **25** (4.0 g, 17 mmol) under nitrogen atmosphere at 0 °C was added 60 mL of MeLi solution (50 mmol) in ether. After warming to 25 °C the reaction mixture was hydrolyzed. The ether phase was washed with water, and a MeOH solution of three pellets of NaOH was added to the ether extract to isomerize a product isomer to the wanted product **3**. After about 10 min the ether phase was washed again several times with water and finally treated with brine. Almost pure alcohol (**3**) (97%, ~1 g) was obtained by flash chromatography with dichloroethane as eluent. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.62 (d, J = 7.4 Hz, 1H), 7.44 (d, J = 7.4 Hz, 1 H), 7.25 (t, J = 7.4 Hz, 1H), 7.14 (t, J = 7.4 Hz, 1 H), 6.22 (t, J = 2.1 Hz, 1 H), 3.95 (s, O*H*), 3.26 (d, br, J ~ 2 Hz, 1 H), 2.01 (s, 2 H), 1.40 (s, 6 H), 0.95 (s, 6 H).

3-(3-Indenyl)-1-propanol (5). To a 50-mL solution of indenyllithium (50 mmol) at 0 °C was added dropwise 2.8 g (50 mmol) of mesityl oxide dissolved in 20 mL of dimethyl ether, and the mixture was refluxed for 15 min. After the reaction mixture cooled, it was poured slowly into a rapidly stirred cold ammonium chloride solution, and the product was isolated by extraction with ether. After washing twice with water, three pellets of NaOH dissolved in 5 mL of MeOH was added to the ether extract to isomerize a product isomer to the product **5**. After 10 min the ether extract was washed several times with water and lastly with brine. Indene and trimethyleneoxide in the reaction mixture were evaporated by using a high vacuum pump. Almost pure alcohol **5** (95%, ~1 g) was obtained by flash chromatography with dichloroethane/ethyl acetate (9:1) as eluent: ^{1}H NMR (400 MHz, toluene-d_8) δ 7.49 (d, J = 7.4 Hz, 1 H), 7.45 (d, J = 7.4 Hz, 1 H), 7.43 (t, J = 7.4 Hz, 1 H), 7.33 (t, J = 7.4 Hz, 1 H), 6.16 (t, J = 1.6 Hz, 1 H), 3.38 (q, J = 5.3 Hz, 2 H, 3.26 (d, br, J ~ 2 Hz), 2.66 (t, J = 5.3 Hz, 2 H), 1.90 (quintet, J = 5.3 Hz, 2 H), 0.92 (t, J = 5.3 Hz, O*H*).

1-Hydroxy-2-bromoindane (2b).[17] To a stirred solution of indene (30 mL, 0.26 mol) and water (9 mL, 0.5 mol) in DMSO at 22 °C was added *N*-bromosuccinimide (NBS (47 g, 0.26 mol). After 15 min the reaction mixture was poured into water, and the product was extracted with ether. The crude oil remaining after evaporation of the solvent was crystallized from CHCl$_3$ and afforded 34 g (62%) of the bromohydrin (**26**): mp (after several recrystallizations) 130–131 °C (white needles) (lit. 130–131 °C, 131–132 °C). Only one of the possible isomers appears to have been formed. ^{1}H NMR (100 MHz, C$_6$D$_6$) δ 7.2 (m, 4 H), 5.1 (t, J = 6.4 Hz, 1 H), 4.1 (q, J = 6.4 Hz, 1 H), 3.1 (dd, J = 6.4, 3 Hz, 2 H), 1.7 (d, J = 4.4 Hz, O*H*). The ^{1}H NMR spectrum shows the presence of only one isomer which is probably the trans isomer.[17]

2-Bromoindene (27). The bromohydrin (**26**) (27 g, 0.13 mmol) was refluxed together with *p*-toluene sulfonic acid (PTS) (0.27 g, 3.8 mmol) in 200 mL of toluene using a Dean-Stark water trap for 4 h. After cooling the reaction mixture PTS precipitated and was separated by filtration. The product was crystallized from MeOH. The yield was 90%: mp 38–39 °C; ^{1}H NMR (100 MHz, CDCl$_3$) δ 7.2 (m, 4 H), 6.9 (t, J = 1.46 Hz, 1 H), 3.60 (d, J = 1.46 Hz, 2 H).

4-(2-Indenyl)-3,4-dimethyl-2-pentanone (28).[18] To a stirred suspension of Mg (0.9 g, 33 mmol) in 25 mL of dry THF under an atmosphere of nitrogen was added a portion of 2-bromoindene (**27**) in THF and a few drops of methyl iodide. After the initiation of the Grignard reaction, the rest of the 2-bromoindene (total 6.0 g, 30 mmol) was added dropwise. The reaction mixture adopted a deep red color. After another 15 min of reflux the solution was cooled to 0 °C, and CuCl[19] (0.899 g, 0.899 mmol; 3 mol% of added Mg) was added. Then 3,4-dimethyl-3-pentene-2-one[20] (3.7 g, 33 mmol) was added slowly. After 1.5 h at 0 °C the solution was refluxed for 10 min, and the reaction mixture was then poured slowly into stirred ice-cooled dilute hydrochloric acid, and the product was isolated by extraction with ether. The main product was indene, as has been reported previously.[18] After evaporation of the solvent, purification was made by flash chromatography twice. The first one with petroleum ether/diethyl ether (9:1) and the second one was carried out with methylene chloride/petroleum ether (3:1). By this procedure three ketones with TLC R_f values 0.28, 0.22, and 0.17 (petroleum ether/ether (9:1)) were separated from the byproducts. The yield of **28** was 0.35 g, 5%. An analytical amount was purified by HPLC: ^{1}H NMR (100 MHz, CDCl$_3$) δ 7.25 (m, 4 H), 6.58 (s, 1 H), 3.41 (s, 2 H), 2.90 (q, J = 7.0, 1 H), 2.08 (s, 3 H), 1.30 (s, 6 H), 1.03 (d, J = 7.0, 3 H); MS (70 eV), *m/e* (rel intensity), 157 (100), 156 (18.2), 158 (14.8), 142 (12.1), 141 (10.3), 129 (9.9), 128 (6.3), 115 (9.5), 228 (M$^+$, 6.2).

4-(2-Indenyl)-2,3,4-trimethyl-2-pentanone (7). Avoiding tedious purification of ketone **28** which is a precursor of **7** the following procedure was favored.

Ketone **28** (~0.7 g, 3 mmol) in a mixture with the other ketones (total amount 2 g, 8.7 mmol) in ether was treated with 60 mL of a solution of MeLi in ether (0.8 M, 48 mmol) under an atmosphere of nitrogen at 22 °C. After 10 min of reaction the reaction mixture was poured into an ice–water mixture, and the products were extracted with ether. One pellet of NaOH dissolved in ethanol was added to the ether extract (cf. preparation of **3**). After 5 min the ether extract was washed several times with water and lastly with brine. Partial purification of **7** was made with flash chromatography with hexane/ether (1.3:1). Finally **7** was separated from another alcohol, i.e., **1** and obtained in small amounts using a 25 cm HPLC semipreparative silica column (hexane/THF/IPA (48.8:48.8:0.4%)): MS (70 eV), *m/e* (rel intensity) 157 (100), 158 (14.5), 142 (10.2), 129 (7.1), 115 (6.9), 59 (6.8), 244 (M$^+$, 3.5); ^{1}H NMR (100 MHz, DMSO-d_6) δ 7.1 (m, 4 H), 6.48 (s, 1 H), 3.92 (s, O*H*), 3.41 (dd, J_{AB} = 22.7 Hz, $\delta_A - \delta_B$ = 0.067, 2 H), 1.93 (q, J = 8 Hz, 1 H), 1.32 (s, 3 H), 1.18 (s, 3 H), 1.08 (s, 3 H), 1.06 (s, 3 H), 0.79 (d, J = 8 Hz, 3 H).

4-(Fluoren-9-yl)-3,4-dimethylpentan-2-one (29). To a flask containing a solution of 12 mmol of fluorenyllithium prepared in situ by the normal procedure was added dropwise 0.6 g (6 mmol) of mesityl oxide which had been purified by distillation and dissolved in 10 mL of diethyl ether. After completion of the addition the reaction mixture was refluxed for about 1 h. In order to facilitate the introduction of the methyl group at the 3-position, the solvent was first evaporated at reduced pressure, and the remaining solid residue was dissolved in 20 mL of 1,2-dimethoxyethane (DME) distilled from sodium.[21] Iodomethane, 8.5 g (60 mmol), was added, and the reaction mixture was allowed to stand overnight at room temperature. The reaction mixture was poured into 50 mL of ice-cooled, saturated NaHCO$_3$ solution under vigorous stirring. After separation of the organic phase the aqueous phase was washed with 3 × 20 mL of dichloromethane. The combined organic phases were dried over anhydrous MgSO$_4$ and after evaporation of the solvent the crude product was purified using a flash chromatography column (silica gel) with a mixture of hexane and ethyl acetate (97:3 v/v). Pure compound, as white needle shaped crystals, was obtained by recrystallization once from ethanol: yield 0.5 g, 30%; mp 65–67 °C; ^{1}H NMR (270 MHz, CDCl$_3$, Ciba Geigy) δ 7.2–7.7 (aromatic protons) (m, 8 H), 4.0 (s, 1 H), 3.1 (q, 1 H, J = 7.1 Hz), 2.1 (s, 3 H), 1.2 (d, 3 H, J = 7.1 Hz), 1.1 (s, 3 H), 0.8 (s, 3 H). MS [*m/e* (rel intensity/%)] 278 (0.9, M$^+$), 207 (7.8), 206 (36.1), 192 (5.4), 191 (9.6), 166 (32.5), 165 (100.0), 164 (19.9), 163 (19.3), 139 (12.7), 115 (10.2), 113 (30.1), 89 (4.8), 71 (4.2), 63 (4.8), 55 (11.4), 53 (4.2).

(2*S,3*R**)-4-(Fluoren-9-yl)-3,4-dimethylpentan-2-ol (13 and 15).** A solution of **29**, 1.2 g (4.3 mmol), and NaBH$_4$, 0.5 g (13 mmol), in 30 mL of 2-propanol, was refluxed overnight in a flask equipped with a condenser under nitrogen atmosphere. The content of the flask was then poured into 50 mL of a saturated, ice-cooled solution of NaHCO$_3$ under vigorous stirring. The organic phase was separated, and the water phase was extracted with 3 × 20 mL of diethyl ether. The combined organic phases

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were dried over anhydrous $MgSO_4$, and the solvent was evaporated under reduced pressure yielding a viscous yellow oil. ^1H NMR showed a diastereoisomer ratio of 1:3. Flash chromatography (silica gel) of the oil using dichloromethane as elutant was performed, and several fractions were collected. Those at the front contained diastereoisomer **13** and those at the end pure **15**. The intermediate fractions contained both isomers. The front and end fractions crystallized upon evaporation of the solvent, and the pure diastereoisomers were obtained after recrystallization twice from hexane. Diastereoisomer **15** was found to be much less soluble than **13** in this medium. The total yield was 0.90 g, 75%: mp of isomer **13** 90–91 °C; mp of isomer **15** 140–142 °C; ^1H NMR (270 MHz, $CDCl_3$, Ciba Geigy), diastereoisomer **13** δ 7.2–7.7 (aromatic protons) (m, 8 H), 4.3 (q, 1 H, $J = 6.3$ Hz), 4.1 (s, 1 H), 1.9 (q, 1 H, $J = 7.1$ Hz), 1.2 (d, 3 H, $J = 6.4$ Hz), 1.05 (d, 3 H, $J = 7.1$ Hz), 0.95 (s, 3 H), 0.83 (s, 3 H); diastereoisomer **15** δ 7.2–7.7 (aromatic protons) (m, 8 H), 4.3 (d of q, 1 H, $J = 6.3$ and 3.6 Hz), 4.2 (s, 1 H), 2.3 (d of q, 1 H, $J = 7.1$ and 3.6 Hz), 1.3 (d, 3 H, $J = 6.3$ Hz), 1.0 (d, 3 H, $J = 7.1$ Hz), 0.9 (s, 3 H), 0.7 (s, 3 H); MS, diastereoisomer **13** [m/e (rel intensity/%)] 280 (1.3, M^+), 207 (4.2), 193 (4.8), 192 (26.5), 191 (13.9), 189 (6.0), 178 (5.4), 167 (12.7), 166 (91.6), 165 (90.4), 164 (19.3), 163 (18.7), 139 (12.0), 115 (20.5), 98 (7.2), 97 (84.3), 89 (4.8), 82 (4.8), 81 (4.2), 72 (6.6), 71 (98.2), 70 (4.8), 69 (19.3), 63 (5.4), 57 (11.4), 56 (5.4), 55 (91.0), 53 (9.6), 45 (83.1), 44 (5.4), 43 (100.0), 42 (6.6), 41 (50.0);. MS, diastereoisomer **15** 280 (1.0, M^+), 192 (9.6), 191 (6.6), 167 (12.0), 166 (88.0), 165 (81.9), 164 (12.7), 163 (12.7), 139 (9.0), 115 (18.1), 97 (17.5), 83 (4.2), 72 (6.0), 71 (100.0), 69 (7.2), 59 (4.2), 57 (4.2), 55 (33.1), 53 (4.2), 45 (63.3).

***trans*-3-Penten-2-one (30).** The solvent of a 187.5-mL 1.6 M solution of methyllithium in diethyl ether was evaporated under reduced pressure leaving a white residue of methyllithium at the bottom of the flask. Sodium dried THF, 200 mL, was then added under a nitrogen atmosphere, and the mixture was stirred until an almost clear solution was obtained. Into a 1-L round-bottomed flask with a nitrogen atmosphere of 13 g (0.15 mol) of crotonic acid was introduced in 200 mL of sodium dried THF. The flask was cooled (0 °C) in an ice bath, and the methyllithium THF solution was added dropwise under vigorous stirring over a period of 1.5 h. After completion of the addition of methyllithium the stirring was continued over night at room temperature. The reaction mixture was then added dropwise under vigorous stirring to 1 L of ice/water. The organic phase was separated, and the aqueous phase was extracted with 3 × 250 mL of dichloromethane. The combined organic phases were dried over anhydrous $MgSO_4$ and the product was distilled. The fraction 115–122 °C was collected (lit.[22] 113–119 °C): yield 3.1 g, 25%; ^1H NMR (400 MHz, $CDCl_3$, Ciba Geigy) δ 6.8–6.9 (m, 1 H), 6.1 (d of q, 1 H, $J = 1.6$ and 16 Hz), 2.4 (s, 3 H), 1.9 (d of d, $J = 1.7$ and 6.9 Hz).

4-(Fluoren-9-yl)-pentan-2-one (31). To a flask containing a solution of 54 mmol of fluorenyllithium prepared in situ according to the normal procedure 3.0 g (36 mmol) of **30** in 25 mL of sodium dried diethyl ether was added by a syringe. The reaction mixture was stirred overnight at room temperature and then refluxed for 1 h. The mixture was poured into 200 mL of an ice-cooled saturated $NaHCO_3$ solution under vigorous stirring. The organic phase was separated, and the aqueous phase was extracted with 3 × 50 mL of dichloromethane. The combined organic phases were dried over anhydrous $MgSO_4$. The oily brown residue obtained after evaporation of the solvent was purified by flash chromatography (silica gel) using a mixture of hexane and ethyl acetate (97:3 v/v). The product was crystallized from hexane and recrystallized once from a mixture of hexane and ethyl acetate (97:3 v/v): yield 2.5 g, 28%; mp 41–42 °C; ^1H NMR (400 MHz, $CDCl_3$, Ciba Geigy) δ 7.2–7.8 (aromatic protons) (m, 8 H), 4.0 (d, 1 H, $J = 3.2$ Hz), 3.0 (m, 1 H), 2.1 (m, 2 H), 2.0 (s, 3 H), 1.0 (d, 3 H, $J = 6.9$ Hz); MS [m/e (rel intensity/%)] 250 (4.2, M^+), 192 (100.0), 191 (25.3), 189 (7.2), 178 (7.8), 166 (14.4), 165 (76.5), 164 (19.3), 163 (21.7), 139 (12.0), 115 (9.0), 89 (4.2), 63 (4.8).

4-(Fluoren-9-yl)-2-methylpentan-2-ol (17). A solution of 2.0 g (8.0 mmol) of **31** in 75 mL of sodium dried diethyl ether was introduced into a flask equipped with a condenser and a septum under nitrogen atmosphere. The flask was cooled to 0 °C in an ice bath and methyllithium; 10 mL (16 mmol) of a 1.6 M solution in diethyl ether was added by a syringe. After stirring the reaction mixture for 2 h at room temperature it was poured into 200 mL of an ice-cold, saturated solution of $NaHCO_3$ in water under vigorous stirring. The organic phase was separated, and the aqueous phase was extracted with 3 × 50 mL of dichloromethane. The combined organic phases were dried over anhydrous $MgSO_4$, and the solvent was evaporated under reduced pressure. The residue was flash chromatographed (silica gel) using dichloromethane as elutant. The crude product obtained (1.4 g) was further purified by preparative straight-phase HPLC using a solvent mixture of hexane and ethyl acetate (70:30): yield 1.1 g, 52%, of a colorless oil; ^1H NMR (400 MHz, $CDCl_3$, Ciba Geigy) δ 7.2–7.8 (aromatic protons) (m, 8 H), 4.0 (d, 1 H, $J = 2.1$ Hz), 2.7 (m, 1 H), 1.4 (m, 2 H), 1.22 (s, 3 H), 1.20 (s, 3 H), 1.0 (d, 3 H, $J = 6.9$ Hz); MS [m/e (rel intensity/%)] 266 (0.9, M^+), 193 (13.9), 192 (54.2), 191 (10.8), 189 (4.8), 178 (13.9), 166 (26.5), 165 (70.5), 164 (17.5), 163 (17.8), 152 (4.2), 139 (12.0), 115 (9.6), 89 (4.8), 84 (6.0), 83 (100.0), 67 (4.2), 63 (6.0), 59 (56.6), 57 (4.8), 56 (4.8), 55 (70.5), 53 (6.0), 45 (6.0).

4-(Fluoren-9-yl)-2,3-dimethylpentan-2-ol (19). To a solution of 60 mmol of fluorenyllithium prepared in situ by the normal procedure, a solution of 4.0 g (41 mmol) of 3-methyl-3-penten-2-one[23] in 20 mL of sodium dried diethyl ether was added dropwise under stirring, and the mixture was then refluxed for 5 h. The content of the flask was poured into 400 mL of an ice-cooled saturated $NaHCO_3$ solution under stirring. The organic phase was separated, and the aqueous phase was extracted with 3 × 50 mL of dichloromethane. The combined organic phases were dried over anhydrous $MgSO_4$, and the solvent was evaporated under reduced pressure. The oily residue was partially purified using a flash chromatography column (silica gel) eluted with dichloromethane to remove remaining unreacted fluorene. Upon evaporation of the solvent, 5 g of crude product consisting of a mixture of diastereoisomeric ketones was obtained. The crude product was dissolved, without further purification, in 100 mL of sodium dried diethyl ether under nitrogen atmosphere in a flask equipped with a condenser and a septum. The flask was cooled to 0 °C in an ice bath, and methyllithium, 50 mL (80 mmol) of a 1.6 M solution in diethyl ether, was added by a syringe under vigorous stirring. The mixture was stirred for 5 h at room temperature and then poured into 300 mL of an ice-cooled saturated $NaHCO_3$ solution under stirring. The organic phase was separated, and the aqueous phase was extracted with 3 × 50 mL of dichloromethane. The combined organic phases were dried over anhydrous $MgSO_4$, and the solvent was evaporated under reduced pressure. The oily product was partially purified by flash chromatography (silica gel) using a mixture of hexane and ethyl acetate (90:10 v/v). A pale green oil containing both of the diastereoisomers was obtained as a crude product (1.5 g, 13%) which was further purified by preparative straight phase HPLC, using a mixture of hexane and ethyl acetate (90:10). The ratio between the two diastereoisomers was estimated by HPLC to be 1:10, and only the major product was isolated in pure form as a colorless oil: yield 0.9 g, 8%; ^1H NMR (400 MHz, $CDCl_3$, Ciba Geigy) δ 7.2–7.8 (aromatic protons) (m, 8 H), 4.3 (s, 1 H), 2.5 (m, 1 H), 2.0 (m, 1 H), 1.4 (s, 3 H), 1.37 (d, 3 H, $J = 7.1$ Hz), 1.35 (s, 3 H), 0.5 (d, 3 H, $J = 6.8$ Hz); MS [m/e (rel intensity/%)] 280 (0.8, M^+), 193 (20.5), 192 (60.2), 191 (10.2), 189 (4.8), 179 (4.8), 178 (28.9), 176 (4.2), 167 (4.2), 166 (34.9), 165 (68.1), 164 (17.5), 163 (17.5), 152 (5.4), 139 (11.4), 115 (10.8), 98 (6.0), 97 (66.3), 89 (4.2), 71 (11.4), 69 (40.4), 67 (5.4), 63 (5.4), 59 (84.9), 57 (13.3), 56 (6.0), 55 (100.0), 53 (10.8), 45 (8.4), 43 (46.4), 42 (5.4), 41 (65.7).

3-(Fluoren-9-yl)-cyclohexan-1-one (32). To a solution of 30 mmol of fluorenyllithium prepared in situ by the normal procedure, 2-cyclohexen-1-one, 3.0 g (31 mmol) in 10 mL of diethyl ether was added dropwise under stirring. A white precipitate was instantly formed, and the reaction mixture was stirred for another hour at room temperature. The content of the flask was poured into a saturated, ice-cooled solution of $NaHCO_3$ under vigorous stirring. The organic phase was separated, and the aqueous phase was extracted with 3 × 50 mL of dichloromethane. After drying with anhydrous $MgSO_4$ the solvent was evaporated under reduced pressure. The oily residue was purified by flash chromatography (silica gel) using dichloromethane as eluant. After evaporation of the solvent 4.3 g of crude slightly brown product was obtained. Recrystallization once from hexane gave 4.0 g of white, needle shaped crystals, 51%: mp 103–104 °C; ^1H NMR (400 MHz, $CDCl_3$, Ciba Geigy) δ 7.2–7.7 (aromatic protons) (m, 8 H), δ 4.0 (d, 1 H, $J = 3.1$ Hz), 2.6 (m, 1 H), 2.3 (m, 1 H), 2.15 (m, 1 H), 2.0 (m, 3 H), 1.8 (m, 1 H), 1.6 (m, 2 H). MS [m/e (rel intensity/%)]: 262 (12.1, M^+) 204 (5.5), 189 (4.2), 178 (4.1), 166 (19.3), 165 (75.2), 164 (15.0), 163 (15.1), 139 (9.7), 115 (8.5), 98 (5.4), 97 (71.0), 89 (4.2), 83 (4.2), 70 (7.2), 69 (100.0), 67 (5.4), 63 (6.1), 55 (55.2).

3-(Fluoren-9-yl)cyclohexan-1-ol (21 and 22). A mixture of 1.5 g (5.7 mmol) in 60 mL of 2-propanol and 0.5 g (13 mmol) of $NaBH_4$ was

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refluxed 1.5 h under a nitrogen atmosphere. The reaction mixture was poured into a saturated ice-cold solution of $NaHCO_3$ under vigorous stirring. The organic phase was separated, and the aqueous phase was washed with 3 × 50 mL of dichloromethane. The combined organic phases were dried over anhydrous $MgSO_4$, and the solvent evaporated. The residue, a brown oil, was partially purified by flash chromatography (silica gel) using dichloromethane as elutant. After evaporation of the solvent, 0.83 g of a crude crystalline mixture of the two diastereoisomers was obtained. An analysis by HPLC (silica column, hexane/ethyl acetate (50:50)), showed that the ratio between the two isomers was approximately 1:5. Another flash chromatography was performed, and three fractions were collected. Several recrystallizations from a mixture of hexane and ethyl acetate (90:10) gave 0.12 g of isomer **21** and 0.42 g of isomer **22**. Both isomers were pure. A mixture (0.26 g) of the two isomers was also recovered: total yield 0.80 g, 53%; mp of isomer **21** 131–132 °C: mp of isomer **22** 123–124 °C; ^1H NMR (400 MHz, $CDCl_3$, Ciba Geigy), diastereoisomer **21** δ 7.2–7.7 (aromatic protons) (m, 8 H), 4.05 (m, 1 H), 3.9 (d, 1 H, $J = 3.1$ Hz), 2.7 (m, 1 H), 1.7 (m, 2 H), 1.5 (m, 3 H), 1.3 (m, 2 H), 1.2 (m, 1 H); diastereoisomer **22** δ 7.2–7.7 (aromatic protons) (m, 8 H), 3.95 (d, 1 H, $J = 3.1$ Hz), 3.55 (m, 1 H), 2.2 (m, 1 H), 1.9 (m, 1 H), 1.7 (m, 2 H), 1.45 (m, 1 H), 1.25 (m, 1 H), 1.05 (m, 3 H); MS, diastereoisomer **21** [*m/e* (rel intensity/%)] 264 (11.4, M^+), 191 (4.2), 189 (4.2), 178 (8.4), 167 (14.5), 166 (100.0), 165 (98.8), 164 (15.1), 163 (14.5), 139 (9.6), 115 (10.8), 99 (7.8), 97 (10.2), 82 (8.4), 81 (62.1), 79 (9.0), 69 (18.7), 63 (4.2), 57 (16.3), 55 (33.1), 53 (8.4); MS, diastereoisomer **22** 264 (6.0, M^+), 246 (9.6), 191 (5.4), 179 (6.0), 178 (30.7), 167 (10.2), 166 (76.5), 165 (100.0), 164 (14.5), 163 (13.9), 139 (9.0), 115 (7.2), 97 (10.8), 82 (6.6), 81 (41.0), 79 (7.8), 69 (19.3), 63 (4.2), 57 (13.2), 55 (28.9), 53 (7.2).

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