

THE SYNTHESIS AND NMR STUDY OF 2,4-DIARYL-6-(FLUOREN-2-YL)PYRIDINES

Richard HRABAL^a, Pavel LHOTÁK^b and †Antonín KURFÜRST^b

^a NMR Laboratory, Prague Institute of Chemical Technology, 166 28 Prague 6

^b Department of Organic Chemistry,
Prague Institute of Chemical Technology, 166 28 Prague 6

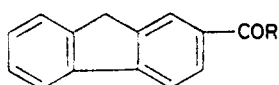
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Dedicated to Professor Miroslav Ferles on the occasion of his 70th birthday.

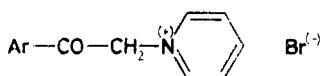
The reaction of 2-cinnamoylfluorene *II* with quaternary pyridinium salts *IIIa*, *IIIb* in the presence of ammonium acetate, gave 2-fluorenyl-2,6-diarylpyridines *IV*. The complete assignment of ¹H and ¹³C resonances by 2D NMR methods is given.

Within the framework of our study^{1,2} of new heteroaromatic luminophores, we have been interested in synthesis of several simple triarylpyridines containing fluorene moiety in a molecule. The only hitherto described method for the preparation of *IVa* is the reaction of benzoylmethylenepyridinium ylide³ with chalcone *II*. We prepared such compounds by Kröhnke's method⁴ consisting in the reaction of chalcone *II* with pyridinium salts *III* in acetic acid–ammonium acetate mixture. Our synthesis started from fluorene which was, after acetylation⁵ to the position 2



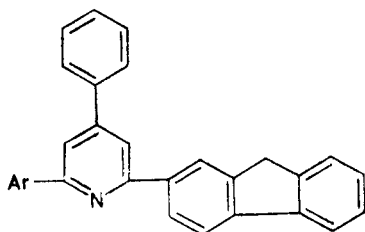
I, R = CH₃

II, R = CH=CH-C₆H₅



IIIa, Ar = phenyl

IIIb, Ar = biphenyl-4-yl



IVa, Ar = phenyl

IVb, Ar = biphenyl-4-yl

and the reaction of the resulting acetyl derivative *I* with benzaldehyde⁶, converted to products *IVa* and *IVb*.

These compounds were prepared as models for the conformational studies of 2,4,6-triarylpyridines by NMR spectroscopy. For this purpose, it was necessary to assign both ¹H and ¹³C resonances of the derivatives *IVa* and *IVb*.

¹H Spectrum of *IVa* is shown in Fig. 1 and ¹³C spectrum in Fig. 2. The assignment was started with H-26, H-26' methylene protons being the most upfield shifted ¹H resonances. From the COSY spectrum (Fig. 3), we were able to detect H-15 and H-16. H-25 is the only resonance in a downfield shifted region of the aromatic part having no vicinal hydrogen neighbour. In spite of that, there is a cross peak connecting H-25 with H-15 via a small four bonds coupling. As ortho-protons of aromatic rings are much more downfield shifted than *meta*- and *para*-protons, especially in the cases of aromatic rings in *ortho* positions of a heterocycle, it is possible to delineate H-3 and H-2. Resonances of H-19, H-20, H-21 and H-22 are characterized by the unique spin pattern easily recognizable in COSY spectrum.

All considerations mentioned above were confirmed by the interpretation of HOHAHA spectrum (not shown). Moreover, other so called relayed cross peaks may be extracted from this spectrum. By the connection of H-3, H-2 and H-1

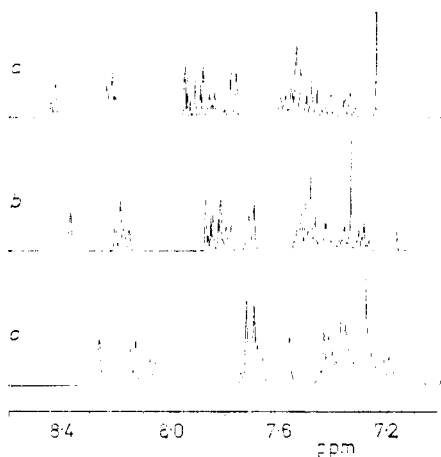


FIG. 1

The concentration dependence of ¹H aromatic proton resonances in *IVa*. a 0.055 mol . l⁻¹; b 0.250 mol l⁻¹; c 0.700 mol l⁻¹ solution in CDCl₃. The displayed region (δ 7.00–8.60) covers only the aromatic part of the spectrum

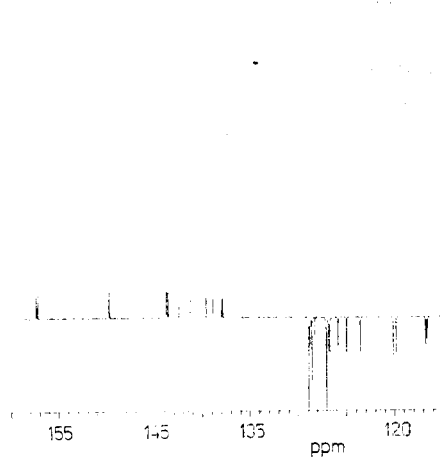


FIG. 2

¹³C Spektrum (Attached Proton Test) of *IVa*. Only the aromatic part (δ 115.00 to 160.00) is displayed

resonances, it is possible to complete one of the aromatic spin systems. The remaining one may also be traced in the spectrum, however H-12 and H-13 (*meta*-, respectively *para*-protons) are nearly degenerated. Both in COSY as in HOHAHA spectrum, the cross peak H-6/H-8 is recognizable, though being very close to the diagonal.

To determine chemical shifts of H-16 and H-22 more accurately, we used the long range COSY taking advantage of a magnetization transfer via more than three bonds couplings. Then it was possible to trace four bonds (H-26, H-26'/H-22; H-26, H-26'/H-25), five bonds (H-26, H-26'/H-16; H-26, H-26'/H-19) and even six bonds (H-26, H-26'/H-15; H-26, H-26'/H-20) cross-peaks. This phenomenon may be explained by the rigidity of the heterocyclic skeleton, pronouncing small proton-proton couplings.

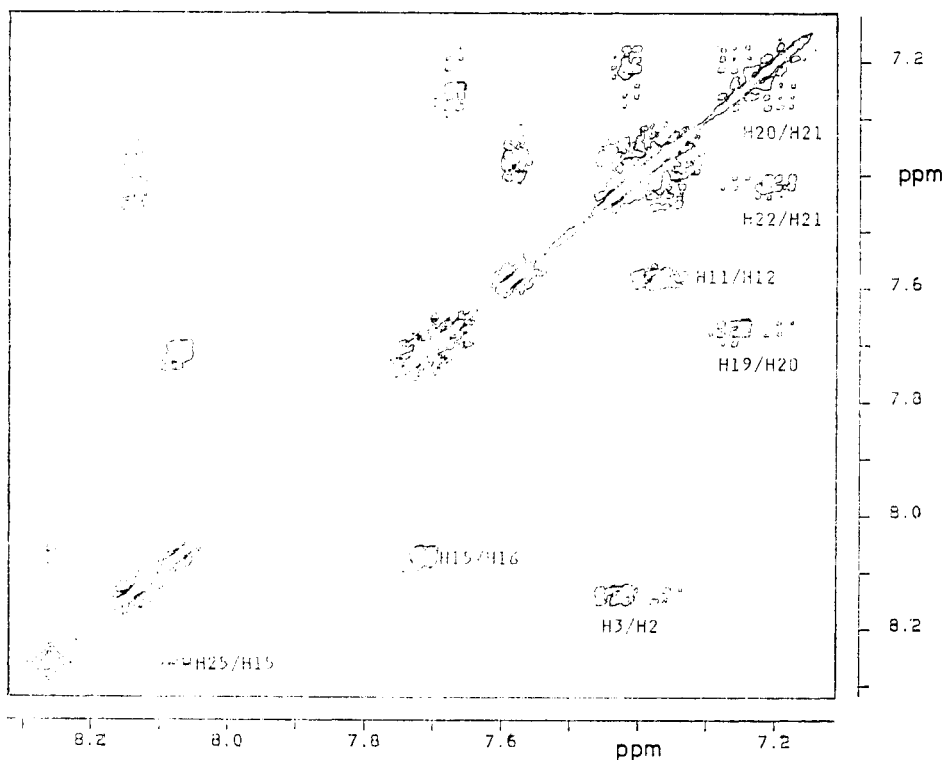


FIG. 3
COSY-45 spectrum of *IVa*

^{13}C Atoms bound directly to hydrogen counterparts were assigned by the interpretation of the heterocorrelated experiment (not shown). The only remaining ambiguity is to determine C-1 and C-13 having similar ^{13}C chemical shifts.

Quaternary carbons were identified on the basis of long-range interactions from COLOC spectrum. The displayed region in Fig. 4, is a little bit overcrowded because of minor impurities giving rise to additional cross peaks of a comparable intensity. The two, most downfield shifted ^{13}C resonances, may be accounted for C-5 and C-9 determined by C-5/H-6, C-5/H-3, respectively C-9/H-8, C-9/H-15 and C-9/H-25 cross peaks. The less intensive cross peak at 149.70/7.58 ppm characterizes C-7/H-11 magnetization transfer. As in aromatic systems, $^3J(\text{C}, \text{H})$ is larger than $^2J(\text{C}, \text{H})$ and, the latter is often close to zero, the only quaternary carbon interacting both with H-15 and H-25 is C-17 ($\delta = 142.39$), not C-14 displaying only the interaction with H-8 and H-16 (137.82/7.72, respectively 137.82/7.71 ppm). The coherent

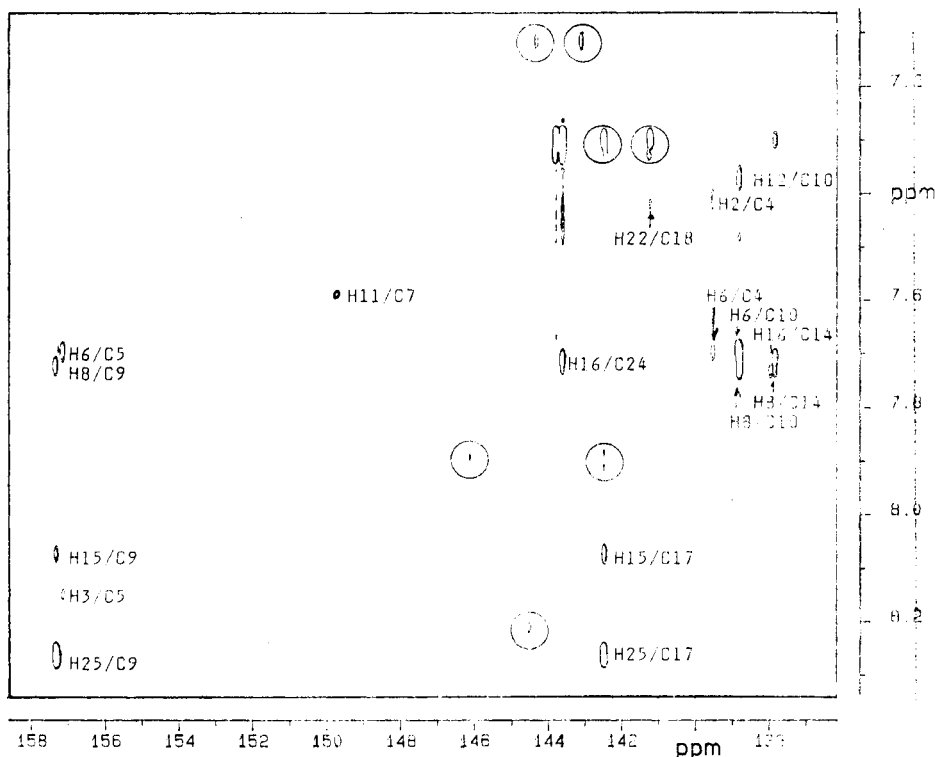


FIG. 4

The region ($\omega_2 = 136.11-158.65$ ppm; $\omega_1 = 7.08-8.34$ ppm) of COLOC spectrum of IVa. Cross-peaks arising from impurities are circled

magnetization transfer from H-26 and/or H-26' was investigated by the long range INEPT. Four quaternary carbon resonances appeared in the spectrum, while H-26, H-26' were saturated. In the case of C-23 and C-24, $^2J(\text{C}, \text{H})$ couplings were active, while the magnetization transfer to C-17 and C-18, respectively, was facilitated by $^3J(\text{C}, \text{H})$ couplings.

C-18 is characterized in COLOC spectrum by C-18/H-20 and C-18/H-22 cross peaks. On the contrary, C-23 and C-24 resonances could not be resolved unambiguously at this stage of the analysis due to a severe overlap of cross peaks in that area. C-4 is then the last unambiguously assignable ^{13}C resonance from COLOC spectrum (Fig. 4), exhibiting two characteristic cross-peaks, namely C-4/H-6 and C-4/H-2, respectively.

As has already been mentioned, *ortho*-protons are better resolved than *meta*- and *para*-protons. This phenomenon may be utilized in the unambiguous identifica-

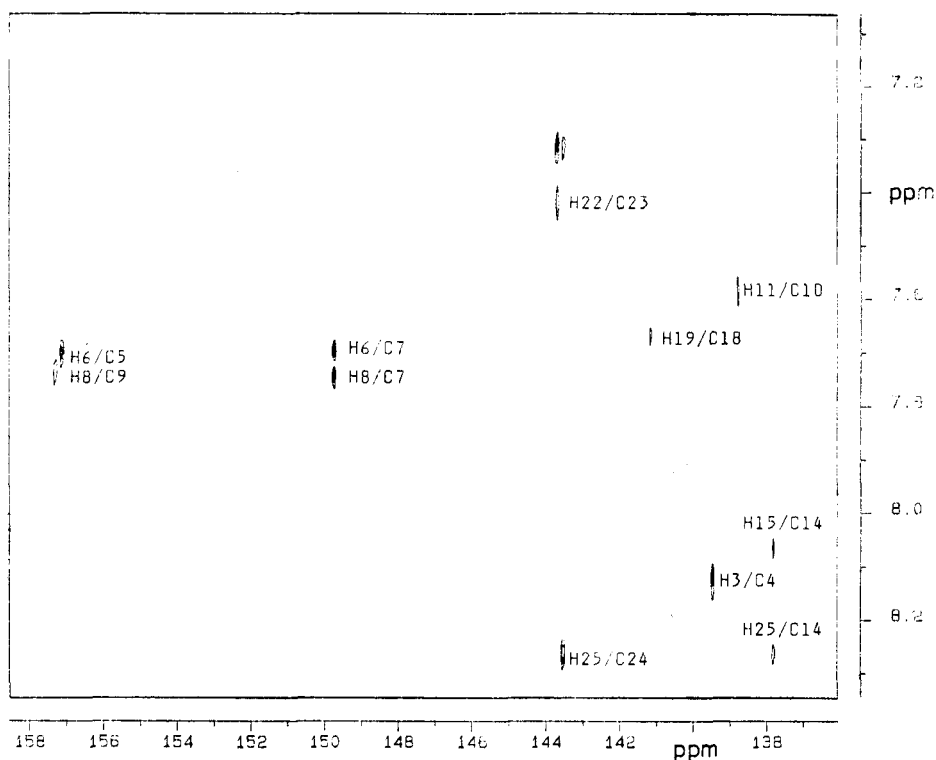


FIG. 5

HOESY spectrum of IVa. The displayed region ($\omega_1 = 7.06\text{--}8.34$ ppm) includes quaternary carbons

tion of remaining quaternary carbons taking advantage of the nuclear Overhauser effect (NOE)⁷. NOE makes possible for quaternary carbons to be connected with their proximal and better resolved *ortho*-protons. For this purpose, 2D version of the heteronuclear NOE experiment, known as HOESY (ref.⁸), was exploited. The results, extracted from Fig. 5, confirm our previous assignments. Furthermore C-23 and C-24 resonances may be resolved. The former is characterized by C-23/H-22 and the latter by C-24/H-25 cross peaks, respectively.

TABLE I
¹H at two different concentrations and ¹³C chemical shifts (ppm) of IVa

Position ^a	¹ H		¹³ C
	0.7 mol l ⁻¹	0.055 mol l ⁻¹	
1	7.38	7.46	128.68 ^b
2	7.44	7.54	128.47
3	8.14	8.23	126.98
4	—	—	139.48
5	—	—	157.10
6	7.70	7.88	116.51
7	—	—	149.70
8	7.72	7.95	116.63
9	—	—	157.30
10	—	—	138.78
11	7.58	7.77	126.93
12	7.36	7.53	128.82
13	7.33	7.48	128.79 ^b
14	—	—	137.82
15	8.07	8.21	125.76
16	7.71	7.90	119.71
17	—	—	142.39
18	—	—	141.15
19	7.67	7.85	120.00
20	7.26	7.41	126.59
21	7.20	7.34	126.71
22	7.42	7.58	124.86
23	—	—	143.69
24	—	—	143.50
25	8.26	8.43	123.48
26, 26r	3.82	4.03	36.83

^a For atom numbering see formula IV; ^b unresolved.

At this stage of the analysis, C-10 and C-14 remain unassigned. HOESY experiment provides the unambiguous resolution of both these quaternary carbons, of which C-10 is identified by the interaction with H-11 on one side, and both C-14/H-15 and C-14/H-25 cross peaks determine C-14 resonance, on the other side. The results are summarized in Table I. ^1H Chemical shifts obtained at concentration 0.055 mol . l^{-1} are presented for the comparison with ^1H shifts of *IVb* in Table II.

TABLE II
 ^1H and ^{13}C chemical shifts (ppm) of *IVb*

Position ^a	^1H	^{13}C	Position ^a	^1H	^{13}C
1	—	141.76	16	7.93	120.01
2	7.77	127.43	17	—	142.66
3	8.30	127.56	18	—	141.37
4	—	139.14	19	7.85	120.23
5	—	157.10	20	7.42	126.84
6	7.92	116.86	21	7.34	126.98
7	—	150.17	22	7.59	125.13
8	7.95	117.11	23	—	143.91
9	—	157.73	24	—	143.81
10	—	138.61	25	8.44	123.78
11	7.78	127.21	26, 26'	4.02 ^b	37.08
12	7.55	129.11	27	7.38	127.49
13	7.49	128.96	28	7.49	128.84
14	—	138.15	29	7.69	127.13
15	8.23	126.00	30	—	140.72

^a For atom numbering see formula *V*; ^b unresolved.

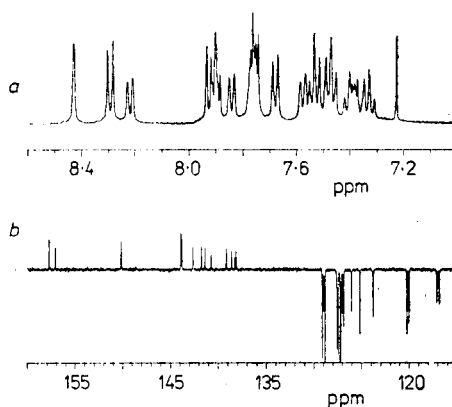
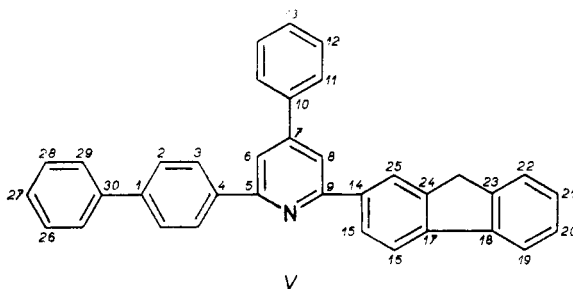


FIG. 6
Aromatic parts of *IVb* NMR spectra. *a* ^1H ;
b ^{13}C (Attached Proton Test). Both regions
are equivalent to the regions in Figs 1 and 2,
respectively



As the structures of both diarylpyridines *IVa* and *IVb* are similar to each other, the assignment of ^1H and ^{13}C resonances of *IVb* (Fig. 6), may be done on the basis of the aforementioned considerations. The meaningful difference between both ^1H spectra is the downfield shift of H-2 of *IVb*, being influenced by another aromatic ring. The ^1H resonance assignments were confirmed by the HOHAHA experiment on one side, and on the other side, the determination of ^{13}C resonances were completed by heterocorrelated experiment (not shown). Table II contains ^1H and ^{13}C resonances in a condensed form.

Large chemical shift differences between ^1H spectra of *IVa* at various concentrations (Fig. 1), may be accounted for local magnetic fields, created by numerous aromatic rings of diarylpyridines *IVa* and *IVb* (Ring Current Shift). This phenomenon can arise either by a change of the distance of aromatic ring systems, caused by concentration changes, or by conformational changes which also alternate their mutual positions. The latter phenomenon is much more interesting, and will be studied later.

EXPERIMENTAL

Melting points were determined on a Boetius block and are uncorrected.

2-Cinnamoylfluorene (*II*)

Dry HCl was passed through the ice cooled solution of 3 g acetylfluorene *I* and 2.3 g benzaldehyde in 200 ml ethanol during 3 h and then the reaction mixture was stirred for other 3 h at 20°C. After pouring it into 300 ml water, the precipitate was filtered off, diluted by hot xylene and filtered. The filtrate was evaporated and the residue (3.84 g, 90%) was chromatographed on SiO_2 in benzene to yield the product *II* melting at 145–147°C (methanol, ref.⁴ m.p. 142–145°C).

2,4-Diphenyl-6-(fluoren-2-yl)-pyridin (*IVa*)

The mixture of 0.45 g compound *II*, 0.50 g compound *IIIa* and 2 g ammonium acetate in 15 ml glacial acetic acid was stirred at 80–90°C for 4 h. After pouring into 200 ml water, the precipitate was collected by the suction and twice chromatographed on 50 g SiO_2 (benzene) to yield 0.19 g of *IIIa* (32%) with m.p. 106–107°C (ref.¹ m.p. 112–114°C). For $\text{C}_{30}\text{H}_{21}\text{N}$ (395.5) calculated: 91.10% C, 5.36% H, 3.54% N; found: 91.00% C, 5.63% H, 3.42% N. IR spectrum (CHCl_3): 1 595 s, 1 540 s, 1 403 s cm^{-1} .

2-(Biphenyl-4-yl)-4-phenyl-6-(fluoren-2-yl)-pyridin (*IVb*)

The same synthesis as above with the use of *IIIb*. After the chromatography on SiO_2 and the crystallization from a mixture of ethylacetate-acetone, 60% of the product *IVb*, m.p. 229 to 232°C, was obtained. For $\text{C}_{36}\text{H}_{25}\text{N}$ (471.6) calculated: 91.68% C, 5.36% H, 2.97% N; found: 91.71% C, 5.62% H, 2.80% N. IR spectrum (CHCl_3): 1 595 s, 1 545 s, 1 404 s cm^{-1} .

NMR Spectroscopy

All experiments were carried out on a Bruker AM 400 spectrometer at the ambient temperature. The resonance frequency for ^1H spectroscopy was 400.13 MHz and 100.62 MHz for ^{13}C experiments, respectively. All measurements were done using deuteriochloroform as a solvent with 1% tetramethylsilane as an internal standard. The concentration of *IVa* was either 0.055 mol l^{-1} or 0.7 mol l^{-1} for two reasons: (i) The more concentrated solution enables a shortening of the data acquisition, especially of heterocorrelated experiments: (ii) as it is evident from Fig. 1, the resolution of ^1H spectrum of *IVa* is concentration dependent. Biphenyl derivative *IVb* was used as 0.055M solution and therefore ^1H chemical shifts of *IVa* and *IVb* are comparable.

Spectra were obtained in the absolute value mode. The only exception was the HOHAHA experiment that was processed in a phase sensitive mode using the TPPI method⁹. COSY spectrum¹⁰ was received as 128 t_1 increments of 2 048 data points, multiplied with sine function, shifted by $\pi/10$ in both domains and zero filled to the $(2k) \cdot (1k)$ data points. COSY long range experiment¹¹ was carried out in the same way, the prolonged delay was set to 100 ms to optimize the magnetization transfer via small long range couplings. HOHAHA (Homonuclear Hartman-Hahn) experiment was received along Bax's pulse sequence¹² with the spin lock created by MLEV-17. Heterocorrelated (^1H - ^{13}C) experiment via one bond couplings included polarization transfer, created by the DEPT pulse sequence¹³ and was acquired as 128 t_1 increments of 2 048 data points. After the multiplication of FIDs with Gaussian window function ($\text{LB} = -0.2$, $\text{GB} = 0.3$), data were zero filled to the $(2k) \cdot (1k)$ matrix.

COLOC sequence¹⁴ was used for the assignment of quaternary carbons and the results were confirmed by HOESY experiment¹⁵ (heteronuclear version of NOESY). On one side, COLOC facilitated the magnetization to be transferred from protons to carbons via small two and/or three bond couplings in a coherent way. The magnetization transfer delay was set to $1/2J = 71.5 \text{ ms}$ ($J = 7 \text{ Hz}$) and 64 t_1 increments of 2 048 data points were recorded, processed with unshifted sine bell function in both domains and zero filled to the $(2k) \cdot (1k)$ points matrix. On the other side, HOESY spectrum was used to connect quaternary carbons with their space proximal hydrogen atoms by dipole-dipole interactions. The mixing time was 2 s and the matrix size was the same as for COLOC. Long range INEPT (ref. ¹⁵) was acquired with 32k data points. The decoupler power was set to $\gamma B_1 = 20 \text{ Hz}$ ($P_{90} = 14 \text{ ms}$) and the magnetization transfer delay was 31 ms corresponding to $J(\text{C}, \text{H}) = 8 \text{ Hz}$.

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