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SYNTHESIS OF 2,3-DISUBSTITUTED [3-^{13}C]NAPHTHALENES AND [9a-^{13}C]NAPHTHO[2,3-*d*]-1,2,3-OXADIAZOLE **

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Summary

The synthesis of 2-amino-2-hydroxy[3-^{13}C]naphthalene starting from 2-(1,3-dioxolan-2-yl)-benzyl chloride and sodium [^{13}C]cyanide in seven preparative steps is reported. Diazotation of the labelled amino compound followed by deprotonation yields [9a-^{13}C]naphtho[2,3-*d*]-1,2,3-oxadiazole. The β-^{13}C-labelled naphthalenes prepared are characterised by their ^{13}C-chemical shifts and ^{13}C^{13}C spin spin coupling constants.

keywords: 2,3-disubstituted [3-^{13}C]naphthalenes, [9a-^{13}C]naphtho[2,3-*d*]-1,2,3-oxadiazole, ^{13}C-NMR-spectra, ^{13}C^{13}C coupling constants.

Introduction

We have recently reported on the synthesis of naphtho[2,3-*d*]- 1,2,3-oxadiazole **2** (1), the first representative of the 1,2,3-oxadiazole system isolated in crystalline form. Compound **2** is obtained by deprotonation of the *o*-hydroxy-diazonium salt **1**. This is in contrast to the deprotonation of other *o*-hydroxyarene diazonium salts which yield the valence isomeric *o*-quinone diazides (2).

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** Dedicated to Prof. Dr. Ernst Bayer on the occasion of his 65th. birthday.

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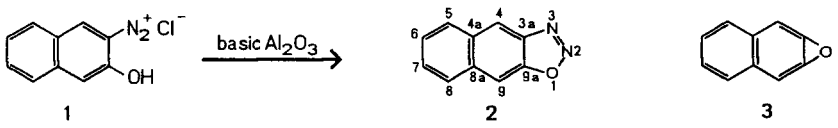


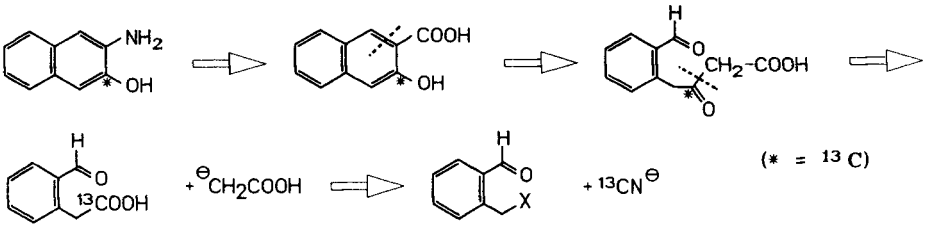
1 2 3

Compound 2 is of interest as potential precursor of naphtho-[2,3-*b*]oxiren 3 (3). In order to investigate the transient existence of 3, the 1,2,3-oxadiazole 2, isotopically labelled at either C-3a or C-9a was required.

In this paper the synthesis of the [*9a*-^{13}*C*]-labelled compound 2 starting from the correspondingly labelled 2-amino-3-hydroxynaphthalene by diazotation followed by deprotonation is described. To the best of our knowledge no methods for the construction of the 2,3-disubstituted naphthalene skeleton labelled at C-3 are given in the literature. Therefore, a reaction sequence leading to 2-amino-3-hydroxy[*3*-^{13}*C*]naphthalene has been developed. This sequence is of general interest since by derivatisation of the compounds described in this paper, access to a variety of labelled and substituted naphthalenes is possible.

Labelling Synthesis

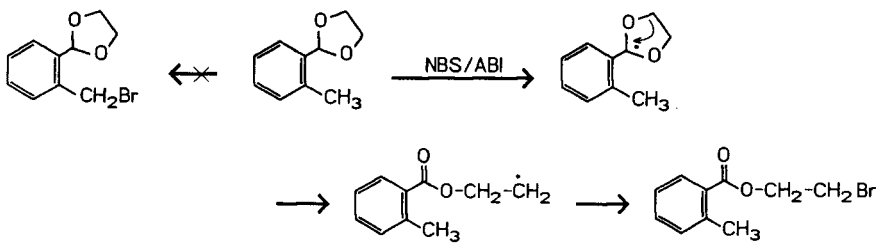
According to the retrosynthetic consideration summarised in scheme 1 2-amino-3-hydroxy[*3*-^{13}*C*]naphthalene should be accessible starting from 2-halomethylbenzaldehyde and sodium [^{13}*C*]cyanide.



scheme 1

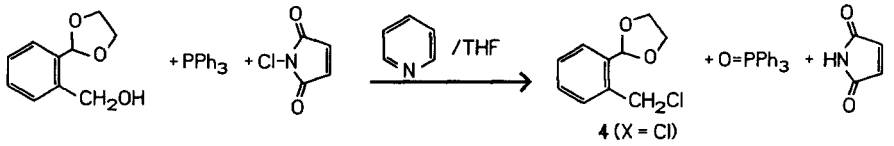
In the first steps of the synthetic sequence the formyl group has to be protected, thus, 2-(1,3-dioxolan-2-yl)-benzylhalide 4 is necessary as starting compound. Acetalisation of 2-bromomethylbenzaldehyde with glycol does not yield 4 since nucleophilic substitution of the bromine at the benzylic position occurs simultaneously by the alcoholic reagent. The attempted bromination of 2-(1,3-dioxolan-2-yl)-toluene by *N*-bromosuccinimide (NBS) in the presence of azo-bis-isobutyronitrile (ABI) also failed. Instead of the expected radical substitution at the

methyl group an intermediate 1,3-dioxolan-2-yl radical is formed. This species rearranges and finally in a clean reaction 2-bromoethyl 2-methylbenzoate is formed (scheme 2).



scheme 2

Substitution of the hydroxy group in 2-(1,3-dioxolan-2-yl)-benzylic alcohol by inorganic acid halides like thionyl chloride or phosphorous tribromide is also not suited to prepare the desired compound, since under the acidic conditions of these reactions the acetal moiety is split. The formation of acids in the OH/halogen exchange and thus concomitant deacetalisation is avoided by application of the *N*-chlorosuccinimide/triphenylphosphane reagent (4) system (scheme 3).

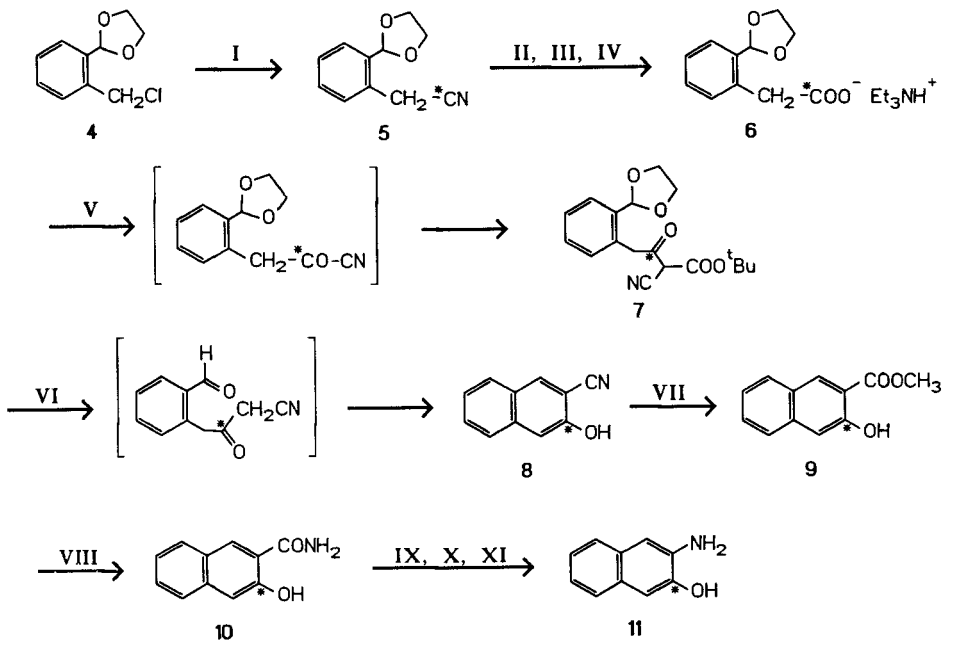


4 (X = Cl)

scheme 3

Starting from 4 (X = Cl) the ^{13}C-labelling synthesis of 2-amino-3-hydroxy[3-^{13}C]naphthalene was accomplished in seven steps as shown in scheme 4.

The labelling is introduced by reaction of 4 with sodium [^{13}C]cyanide in the presence of 15-crown-5 in acetonitrile as solvent (5). The nitrile 5 is hydrolysed and the carboxylic acid formed converted into the triethylammonium salt 6. The corresponding acyl cyanide is prepared in situ (6) by treatment of 6 with diethyl phosphorocyanidate in the presence of triethylamine. The intermediate acyl cyanide reacts with *tert*-butyl cyanoacetate as equivalent of the acetic acid carbanion in a base catalysed C-alkylation step under formation of 7. Treatment of the crude product 7 with trifluoroacetic acid containing a trace of water leads to the deprotection of the acetal function and removal of the *tert*-butoxycarbonyl

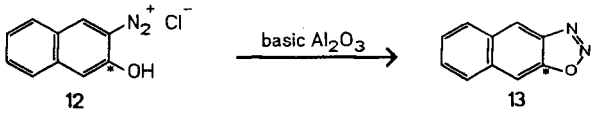


I: $Na^{13}CN$/15-crown-5/CH_3CN, 20°C, 4d; II: NaOH/H_2O, Δ, 20h; III: H^+ (pH 4-5); IV: Et_3N; V: $(EtO)_2P(O)CN$/NC-CH_2-COO^{t}Bu/Et_3N/DMF, 20°C, 3h; VI: F_3C-COOH/H_2O (trace), 20°C, 3h; VII: CH_3OH/HCl/H_2O (1 equ.), Δ, 24h; VIII: NH_3/CH_3OH, 20°C, 20h; IX: 3-(COOH)-C_6H_4-SO_2Cl/NaOH/H_2O; X: NaOCl/H_2O, 40°C; XI: NaOH/H_2O, 75°C, 40 min.

scheme 4

group, followed by intramolecular Knoevenagel condensation. Thus, 2-cyano-2-hydroxy[3-^{13}C]naphthalene 8 is obtained from 7 in a single step. The cyano compound 8 is converted into the carboxamide 10 via the ester 9. As a result of the presence of the activating hydroxyl group, the conventional Hofmann degradation of 10 is accompanied by electrophilic chlorination of the naphthalene system. The activating power of the hydroxyl group can be blocked by intermediate formation of a sulfonic acid ester (7). 3-Carboxybenzene sulfochloride was used as reagent for this purpose. The formed sulfonic acid ester can then be transformed into a soluble sodium salt allowing homogeneous conditions in the Hofmann degradation. Finally the protecting group was split off again by treatment with aqueous sodium hydroxide. The crude product 11 is purified on silica gel with hexane/ethyl acetate (1:1) as eluent.

The diazonium chloride 12 is obtained from the amino derivative 11 by treatment with pentyl nitrite in the presence of hydrogen chloride. Deprotonation of the hydroxyl group in 12 with basic alumina yields [9a-^{13}C]naphtho[2,3-*d*]-1,2,3-oxadiazole 13 (scheme 5).



12 13

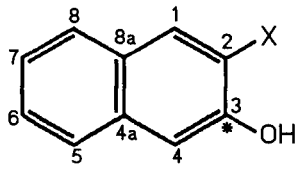
scheme 5

Due to the presence of excess boron trifluoride, the isolation of the corresponding diazonium tetrafluoroborate can become problematic in small scale preparations. Therefore, we recommend the isolation of the chloride and its use in the deprotonation step, instead of the tetrafluoroborate applied earlier (1).

In all labelled naphthalenes reported in this paper the substituents in positions 2 and/or 3 can be derivatised in many ways. Thus, the reported labelling synthesis can be exploited for the preparation of a variety of labelled naphthalenes. Furthermore, by reaction of tert-butyl [2-^{13}C]cyanoacetate with the unlabelled compound **6** a complementary series of 2,3-disubstituted naphthalenes labelled in the neighboured β-position can similarly be obtained.

^{13}C-NMR Spectra

The ^{13}C-chemical shifts of the 2,3-disubstituted [3-^{13}C]naphthalenes prepared have been determined in CD_3OD and are compiled in table 1.



Nr.	X
8	CN
14	COOH
9	$COOCH_3$
10	$CONH_2$
11	NH_2

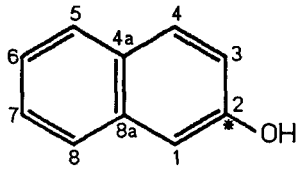
Due to the ^{13}C-enrichment the assignment of C3 is obvious. Furthermore, positions C2, 4, 5, 8a can be assigned on the basis of characteristic ^1J and ^3J coupling constants (8), (9), (10). The only remaining signal for a quarternary carbon in the series of compounds then belongs to C4a. The differentiations between C1 and C8 are possible by means of shift increments given in ref. 11 and have been further assured by selective heteronuclear decoupling experiments. The assignments of positions C6 and C7 have been accomplished on the basis of shift increments (11) and comparision with literature data (12), (13). The ^{13}C-chemical shifts for 2-carboxy-3-hydroxy[3-^{13}C]naphthalene **14** isolated as a by-product (see experimental part) are also given. The values are in agreement with literature data (13).

Table 1. ^{13}C-chemical shifts (δ, ppm) and $^{13}C^{13}C$-coupling constants ($J_{3,i}$, Hz) measured in CD_3OD of 2,3-disubstituted [3-^{13}C]naphthalenes.

Nr., X	C1	C2	C3	C4	C4a	C5	C6	C7	C8	C8a	X
8, CN	136.8	103.5	156.0	110.9	138.2	127.3	130.3	125.5	129.3	128.6	117.7
		(67.7)		(69.6)		(5.6)				(6.7)	
14, COOH*	133.4	116.0	156.2	111.6	138.0	126.8	129.9**	125.1	130.2**	127.5	172.1
		(61.1)		(73.1)		(6.2)				(6.6)	
9, $COOCH_3$	133.5	115.5	157.3	112.2	139.2	127.1	130.2	125.0	130.2	128.5	171.4, 53.0
		(61.4)		(73.8)		(5.6)				(6.7)	
10, $CONH_2$	131.4	118.9	157.0	112.1	138.3	126.9	129.5	124.7	129.9	128.6	173.2
		(62.0)		(72.0)		(5.7)				(6.7)	
11, NH_2	110.6	138.2	147.8	109.3	130.4	126.6	123.3	124.0	126.2	131.2	
	(3.3)	(65.4)		(71.7)		(5.7)				(6.3)	

*in d_6-DMSO/D_2O (1 : 1); **Exchangeable

The $^{13}C^{13}C$-coupling constants found in the routinely measured 250 MHz-^{13}C-NMR-spectra between the labelled position C3 and the carbon atoms Ci are included in table 1. The coupling constants over one bond between C2 and C3 are always lower (61.1-67.7 Hz) compared to the values between C3 and C4 (69.6-73.8 Hz). This is in agreement with 1- and 2-methylnaphthalene (8) and 2-hydroxynaphthalene 15 (14) and has been explained by the lower π-bond order between two adjacent β-positions in the naphthalene skeleton (8).



15

$^1J_{2,1}$ = 71.4 Hz $^1J_{2,3}$ = 63.2 Hz
$^3J_{2,4a}$ = 7.7 Hz $^3J_{2,8}$ = 5.8 Hz

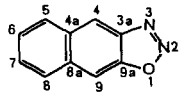
For the vicinal coupling constants $^3J_{3,8a}$ a dual transmitting pathway is feasible and the values found are generally larger (6.3-6.7 Hz) than the $^3J_{3,5}$-coupling constants ranging from 5.6 to 6.2 Hz. Only in the case of the amino compound 13 a small geminal coupling constant $^2J_{3,1}$ = 3.3 Hz could be resolved.

The ^{13}C-NMR-spectrum of [9a-^{13}C]naphtho[2,3-d]-1,2,3-oxadiazole 13 (table 2) has been taken in d_{12}-cyclohexane and similarly assigned as described for the naphthalene derivates.

Table 2. ^{13}C-NMR-data of [9a-^{13}C]Naphtho[2,3-d]-1,2,3-oxadiazol 13

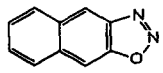
Ci	C3a	C4	C4a	C5	C6	C7	C8	C8a	C9	C9a
δ^{13}C [ppm]	141.5	120.9	131.2	128.7*	125.3	129.4*	128.5	136.6	103.1	148.8
$J_{9a,i}$ [Hz]	56.9	1.7	6.2				6.6		75.4	

*Exchangeable



13 a

⟷



13 b

The $^1J_{9a,3a}$-coupling constant (= 56.9 Hz) is remarkably smaller than $^1J_{9a,9}$ (= 75.4 Hz). If this is again attributed to the π-bond order, it might reflect the marked importance of valence bond structure 13a. The low double bond character

of the C,C-bond in the 1,2,3-oxadiazole subunit could be one of the reasons for the relatively low tendency of valence isomerisation into the corresponding *o*-quinone diazide (1).

Experimental

Melting points are uncorrected. Infrared spectra (IR) were obtained using a Perkin Elmer 281 B spectrophotometer. ^{1}H-NMR and ^{13}C-NMR-spectra were measured on a Bruker WP 250 instrument. Mass spectra were recorded on a TSQ 70, Finnigan MAT.

2-(1,3-Dioxolan-2yl)-benzyl chloride 4.

To a magnetically stirred mixture of 40.5 g (154.4 mmol) triphenylphosphane in 130 ml dry THF and 21.7 g (162.4 mmol) *N*-chlorosuccinimide in 1.22 l dry THF 14.4 g dry pyridine was added under nitrogen. Subsequently, 14.63 g (81.2 mmol) of 2-(1,3-dioxolan-2-yl)-benzylic alcohol (15) in 150 ml dry THF was slowly added. The reaction mixture was stirred at 20°C for 20 h in a nitrogen atmosphere, the precipitate formed filtered off and the filtrate concentrated to ca. 200 ml. After addition of 100 ml ether more precipitate was formed and filtered off. The combined precipitates are washed with a small amount of ether and the combined filtrates concentrated to ca. 50 ml. The solution was purified on a column filled with ca. 400 g basic alumina (4% water). Elution with *n*-hexane/ether (3:1) yields 12.63 g (78.3%) of a colourless oil which solidifies in the cold; mp. 16°C.

^{1}H-NMR ($CDCl_3$): δ (ppm) = 7.61 (m, 1H, arom.); 7.38 (m, 3H, arom.), 6.12 (s, 1H, -O-CH-O-); 4.79 (s, 2H, benzylic CH_2), 4.11 (m, 4H, -O-CH_2-CH_2-O-).

^{13}C-NMR ($CDCl_3$): δ (ppm) = 135.9, 135.8 (C-1, C-2, aromatic ring), 130.4, 129.5, 128.7, 127.3, 126.6 (C-3, C-4, C-5, C-6), 101.3 (-O-CH-O-), 65.3 (-O-CH_2-CH_2-O-), 43.3 (benzylic CH_2).

MS (EI/70 eV): m/z = 198 ($M^{+\cdot}$, 26%), 200 ($M^{+\cdot}$, 9%).

2-(1,3-Dioxolan-2-yl)-benzyl [*cyano*-^{13}*C*]cyanide 5.

A mixture of 7.16 g (30.02 mmol) 4, 1.80 g (36.01 mmol) sodium [^{13}*C*]cyanide (91% ^{13}C-enrichment) and 0.63 mg 15-crown-5 in 85 ml anhydrous acetonitrile was stirred at 20°C for 4 d in a nitrogen atmosphere. The precipitate was filtered off, washed with 10 ml acetonitrile and the filtrate

concentrated. The residue was chromatographed on a short column of alumina with ethyl acetate as eluent yielding 6.48 g (94.7%) of a colourless oil which solidified on standing; mp. 35°C.

^{1}H-NMR ($CDCl_3$): δ (ppm) = 7.51 (m, 2H, arom.); 7.37 (m, 2H, arom.), 5.85 (s, 1H, -O-CH-O-), 4.09 (m, 4 H, -O-CH_2-CH_2-O-), 3.97 (d, $^2J_{CH}$ = 10.6 Hz, 1 H, benzylic CH_2).

^{13}C-NMR ($CDCl_3$): δ (ppm) = 134.8 (s, $^3J_{CC}$ = 3.2 Hz, C-2), 129.4 (d, $^3J_{CC}$ = 2.3 Hz, C-6), 128.9 (d, $^2J_{CC}$ = 2.3 Hz, C-1), 129.9, 128.1, 127.8 (s, C-1, C-4, C-5), 117.9 (s, CN), 102.8 (s, -O-CH-O-), 65.1 (s, -O-CH_2-CH_2-O-), 21.0 (d, $^1J_{CC}$ = 58.2 Hz, benzylic CH_2).

IR (KBr): ν = 2245 (^{12}CN), 2190 (^{13}CN) cm^{-1}.

MS (EI/70eV): m/z = 189 ([M - H]$^+$, 100%).

[2-(1,3-Dioxolan-2-yl)-phenyl]-[*1-^{13}C*]acetic acid-triethylammonium salt 6.

6.07 g (31.93 mmol) 5 in 86 ml 20% aqueous sodium hydroxide were refluxed for 20 h. After cooling and dilution with 600 ml water the reaction mixture was extracted with ether. The aqueous phase was adjusted to pH 4.0 - 4.5 with 40% phosphoric acid and then extracted several times with ether. The combined extracts were dried with sodium sulfate. After concentration of the dried etheral solution to ca. 20 ml, 3.07 g (30.3 mmol) of freshly destilled triethylamine was added and the mixture evaporated in vacuo to dryness yielding 8.05 g of an oily residue (89%).

^{1}H-NMR ($CDCl_3$): δ (ppm) = 7.53 (d, $^3J_{HH}$ = 6.8 Hz, 1H, arom.), 7.35 (s, 1H, arom.), 7.27 (m, 2H, arom.), 6.00 (s, 1H, -O-CH-O-), 3.74 (d, $^2J_{CH}$ = 7.4 Hz, 2H, benzylic CH_2), 2.93 (q, $^3J_{HH}$ = 7.3 Hz, 6H, $HN^+(CH_2\text{-}CH_3)_3$), 1.16 (t, $^3J_{HH}$ = 7.3 Hz, 9H, $HN^+(CH_2\text{-}CH_3)_3$.

^{13}C-NMR ($CDCl_3$): δ (ppm) = 135.1, 131.3, 129.1, 128.3, 126.6, 126.4, (s, arom.), 102.3 (s, -O-CH-O), 65.1 (s, -O-CH_2-CH_2-O-), 40.1 (d, $^1J_{CC}$ = 52.9 Hz, benzylic CH_2), 65.1 $HN^+(CH_2\text{-}CH_3)_3$), 8.4 $HN^+(CH_2\text{-}CH_3)_3$.

MS (EI/70 eV): m/z = 208 ([M - H]$^+$ (M = free carboxylic acid), 2%).

tert.-Butyl-2-cyano-1-[2-(1,3-dioxolan-2-yl)-phenyl]-3-oxo-[3-^{13}C]butyrate 7.

To a stirred solution of 8.84 g (28.48 mmol) 6 in 160 ml anhydrous dimethylformamide kept under nitrogen was rapidly added 4.85 g (34.38 mmol) of *tert.*-butyl cyanoacetate, 7.29 g (44.69 mmol) diethyl phosphorocyanidate and 8.25 g (81.53 mmol) triethylamine at 0°C. After 2 h stirring at 0°C and 20 h at 20°C the solvent was removed by an oil pump. The residue was mixed with 250 ml 5% aqueous potassium dihydrogenphosphate and the mixture extracted several times with ether. After drying with sodium sulfate the combined etheral extracts were concentrated on a rotary evaporator yielding 12.3 g (quantitative) of a crude viscous oil which was used in the next step without further purification.

MS (FAB): m/z = 355 ([M + Na^+], 38%).

2-Cyano-3-hydroxy[3-^{13}C]naphthalene 8.

12.32 g (ca. 37 mmol) of crude 8 was dissolved under stirring in 600 ml of freshly distilled trifluoroacetic acid containing 750 µl water. After stirring for 3.5 h at 20°C the solvent was removed on a rotary evaporator, the residue mixed with 150 ml 20% phosphate puffer (potassium dihydrogenphosphate/dipotassium hydrogenphosphate 1:1) and extracted several times with toluene. After drying with sodium sulfate the toluene was removed on a rotary evaporator. The residue was dissolved in the minimum amount of ethyl acetate and chromatographed on a silica gel (60 mesh) column using *n*-hexane/ethyl acetate (1:1) as eluent; yield 1.72 g (27.2%) crystalline product; mp. 183-4°C (ethanol); Lit. (16): 185°C.

^{1}H-NMR ($CDCl_3$): δ (ppm) = 8.18 (d, $^3J_{CH}$ = 8.8 Hz, 1H, H-1), 7.79 (d, $^3J_{HH}$ = 8.3 Hz, 1H, H-8) 7.67 (d, $^3J_{HH}$ = 8.3 Hz, 1H, H-5), 7.50 (t, $^3J_{HH}$ = 7.5 Hz, 1H, H-6*), 7.34 (t, $^3J_{HH}$ = 8.1 Hz, 1H, H-7*), 7.21 (d, $^2J_{CH}$ = 2.1 Hz, 1H, H-4), (*exchangeable).

MS (EI/70eV): m/z = 170 ($M^{+\cdot}$, 100%), 141 ([M - ^{13}CO]$^+$, 45%).

2-Carbomethoxy-3-hydroxy[3-^{13}C]naphthalene 9.

A stream of dry hydrogen chloride gas was bubbeled through a refluxing solution of 1.69 g (9.94 mmol) 8 in 280 ml anhydrous methanol under nitrogen for 2 d. The solvent was removed on a rotary evaporator and the residue partitioned between water and ether. The etheral phase was washed with 1% aqueous sodium hydrogen carbonate. The sodium hydrogen carbonate phase was extracted once with ether and the combined etheral phases were dried over sodium sulfate and

then evaporated to dryness. The residue was chromatographed on a silica gel (60 mesh) column with ethyl acetate/petroleum ether (60-90°C) 1:3 yielding 1.73 g (85.8%) product; mp. 73-74°C (ethanol/water); Lit. (17): 74-74.5°C.

^{1}H-NMR ($CDCl_3$): δ (ppm) = 8.47 (d, $^3J_{CH}$ = 8.6 Hz, 1H, H-1), 7.81 (d, $^3J_{HH}$ = 8.6 Hz, 1H, H-8) 7.67 (d, $^3J_{HH}$ = 8.3 Hz, 1H, H-5), 7.48 (t, $^3J_{HH}$ = 7.5 Hz, 1H, H-6*), 7.31 (t, $^3J_{HH}$ = 8.1 Hz, 1H, H-7*), 7.24 (d, $^2J_{CH}$ = 3.2 Hz, 1H, H-4), 3.99 (s, 3H, CH_3), (*exchangeable).

MS (EI/70 eV): m/z = 203 ($M^{+\cdot}$, 45%), 171 ([M - CH_3OH]$^+$, 100%).

The aqueous phase obtained above was adjusted to pH 0-1 and extracted with ether yielding 30 mg 2-carboxy-3-hydroxy[3-^{13}C]naphthalene 14; mp. 223°C (acetone/water); Lit. (18): 224°C.

^{1}H-NMR ($CDCl_3$): δ (ppm) = 8.34 (d, $^3J_{CH}$ = 8.6 Hz, 1H, H-1), 7.74 (d, $^3J_{HH}$ = 8.3 Hz, 1H, H-8) 7.60 (d, $^3J_{HH}$ = 8.4 Hz, 1H, H-5), 7.43 (t, $^3J_{HH}$ = 7.5 Hz, 1H, H-6*), 7.24 (t, $^3J_{HH}$ = 8.5 Hz, 1H, H-7*), 7.15 (d, $^2J_{CH}$ = 2.7 Hz, 1H, H-4), (*exchangeable).

MS (EI/70 eV): m/z = 189 ($M^{+\cdot}$, 55%), 171 (M - H_2O]$^+$, 100%).

2-Aminocarbonyl-3-hydroxy[3-^{13}C]naphthalene 10.

1.72 g (8.47 mmol) of 9 was dissolved in 400 ml of anhydrous methanol saturated with ammonia. The flask was closed with a stop-cock and allowed to stand for 20 h at 20°C. The solvent was removed on the rotary evaporator and the residue partitioned between 200 ml 0.5 normal hydrochloric acid and 400 ml ether. After separation the aqueous phase was extracted several times with ether. The combined etheral phases are washed once with water, dried over sodium sulfate and concentrated to dryness using a rotary evaporator yielding 1.45 g (91.2%) product; mp. 213-14°C (methanol); Lit. (16): 215°C.

^{1}H-NMR ($CDCl_3$): δ (ppm) = 8.43 (d, $^3J_{CH}$ = 9.0 Hz, 1H, H-1), 7.82 (d, $^3J_{HH}$ = 8.2 Hz, 1H, H-8) 7.66 (d, $^3J_{HH}$ = 8.2 Hz, 1H, H-5), 7.46 (t, $^3J_{HH}$ = 7.5 Hz, 1H, H-6*), 7.30 (t, $^3J_{HH}$ = 7.5 Hz, 1H, H-7*), 7.21 (d, $^2J_{CH}$ = 2.9 Hz, 1H, H-4), (*exchangeable).

MS (EI/70 eV): m/z = 188 ($M^{+\cdot}$, 56%), 171 ([M - NH_3]$^+$, 100%).

2-Amino-3-hydroxy[3-^{13}C]naphthalene 11.

1,44 g (7.70 mmol) of 10 was dissolved in 1.10 ml 30% aqueous sodium hydroxyde and then diluted with 38 ml water. To this mixture 2.01 g (9.10 mmol) 3-carboxybenzene sulfochloride was added in small portions. During the addition the pH was controlled with a pH-meter and continiously adjusted to pH 10.5-12.5 by addition of 30% aqueous sodium hydroxide (total amount necessary ca. 1.05 ml). Towards the end of the procedure the *O*-sulfonic acid ester of 10 precipitated in crystalline form. The precipitate was dissolved by heating to 40°C. After stirring for 15 min. at 40°C the solution was cooled to 18-20°C. As soon as crystallisation starts 23.60 ml 5% aqueous sodium hypochlorite, 2.57 ml 30% aqueous sodium hydroxide and 38 mg gelatine dissolved in little water was added. After stirring for 15 min. at 20°C the mixture was heated to 40°C. After 10 min. 2.57 ml 30% aqueous sodium hydroxide was added and stirring continued for 45 min. Subsequently 2.06 g sodium thiosulfate in a small amount of water were added and the mixture heated to 75°C. At this temperature 7.71 ml 30% aqueous sodium hydroxide was added and the mixture kept with stirring for 40 min. After cooling to 20°C the solution was acidified with 20% hydrochloric acid to pH 0.5-1 yielding a small amount of precipitate which was filtered off. The filtrate contained the product as hydrochloride. By adjusting the pH of the filtrate to 5-6 the neutral product was precipitated and after cooling in an ice bath filtered off by suction. The preciptitate was dried in vacuo and dissolved in the minimum amount of dioxane. The solution was purified on a silica gel column cooled to 10°C by elution with ethyl acetate/petroleum ether (60-90°C) 1:1 yielding 0.83 g (67.3%) of product; mp. 234-5°C (methanol); Lit. (19): 238°C.

^{1}H-NMR ($CDCl_3$): δ (ppm) = 7.47 (d, $^3J_{HH}$ = 7.4 Hz, 1H, H-5*), 7.46 (d, $^3J_{HH}$ = 7.4 Hz, 1H, H-8*), 7.10 (m, 2H, H-6, H-7), 7.03 (d, $^3J_{CH}$ = 5.0 Hz, 1H, H-1), 6.99 (s, 1H, H-4) (*exchangeable).

MS (EI/70 eV): m/z = 160 ($M^{+\cdot}$, 100%).

3-Hydroxy[3-^{13}C]naphthalene-2-diazonium chloride 12.

A stream of dry hydrogen chloride was bubbled through a solution of 183 mg (1.14 mmol) 11 in 8.3 ml anhydrous dioxane for 5 min under a nitrogen atmosphere yielding a finely dispersed precipitate. After dilution with 2.3 ml anhydrous ether and cooling to 0°C 241 mg (2.06 mmol) of isopentyl nitrite in 2.3 ml anhydrous ether was added dropwise within 10 min. Stirring was continued for 1 h at 0°C. Then, 11.4 ml anhydrous ether and 5.5 ml anhydrous *n*-hexane were

added and the precipitate formed was filtered off by suction in a heavy stream of argon to prevent moisture. The precipitate was dried in vacuo yielding 188 mg (79.4%) of microcrystalline yellow to orange coloured product which was immediately used for the next step without further purification.

[9a-^{13}C]Naphtho[2,3-d]-1,2,3-oxadiazole 13.

Under exclusion of light a solution of 183 mg (0.88 mmol) of 12 in 3 ml methanol and 2 ml ethyl acetate was filtered through a column containing ca. 100 g basic alumina (4% water) and rapidly eluted with ethyl acetate/petroleum ether (60-90°C) 1:1. The solvents were removed on a rotary evaporator using a cold water bath. The product was extracted from the residue by treating with ca. 20 ml anhydrous *n*-hexane. The hexane solution was filtered through glass wool and evaporated in vacuo at <20°C affording 25 mg (16.6%) of almost colourless product; mp. 77°C (dec.). The product was stored at -20°C.

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