Selective Hydrogenation of Alkene in (3-Trifluoromethyl) Phenyldiazirine Photophor with Wilkinson's Catalyst for Photoaffinity Labeling

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Selective hydrogenation of carbon–carbon double bond in the presence of nitrogen–nitrogen double bond in (3-trifluoromethyl) phenyldiazirine achieved with Wilkinson's catalyst.

Key words photoaffinity labeling; diazirine; hydrogenation; Wilkinson's catalyst

Photoaffinity labeling is a powerful method in the study of biological structures and functions.[1,2] It is suitable for the analysis of biological interactions because it is based on the affinity of the ligand moiety. Various photophors, such as phenyldiazirine, arylazide and benzophenone, were used. Comparative irradiation studies of these three photophors in living cells suggested that a carbene precursor, (3-trifluoromethyl) phenyldiazirine, is the most promising,[3—6] but complicated synthesis of the diazirinyl three-membered ring prevented the application of the photophor. Post-functional synthesis of TPD derivatives is one of problems to be solved.[7—10] It is well known that catalytic transfer hydrogenation followed by Wittig reaction is a useful method for general purpose carbon elongation, but the synthetic route does not apply for diazirinyl compounds, because it was reported that the diazirinyl nitrogen–nitrogen double bond was not tolerated under a hydrogen atmosphere in the presence of Pd–C for more than 1 h.[11,12] Although the selective hydrogenation of alkene in diazirinyl and other photophors containing photo ligand in the presence of Pd/C was reported very recently, the hydrogenation of diazirinyl derivatives is low yield compared with other photophors due to the presence of the homogeneous N=N double bond.[13] Furthermore, the applications of the method were not reported.

Wilkinson's catalyst ($RhCl(PPh_3)_3$) was used as a homogeneous catalyst for alkene hydrogenation. The catalyst seems suitable for catalytic hydrogenation in diazirinyl compounds, because we have already established that the triphenylphosphine moiety does not affect diazirinyl compounds and it was reported as a selective carbon–carbon double bond over a heterogeneous multiple bond (nitro, carboxylic acid, and ester).[14] We will describe selective hydrogenation of the carbon–carbon double bond in the presence of a nitrogen–nitrogen double bond in diazirinyl moiety with Wilkinson's catalyst.

Diazirinyl cinnamyl derivatives were prepared from aldehydes **1**[15,16] and **2**[17] with corresponding Wittig reagents in moderate yield (Fig. 1). The reaction afforded predominantly trans isomer calculated by ^{1}H-NMR signals. Ethyl esters **3a**[15] and **4a**[18] were hydrolyzed with aqueous sodium hydroxide to afford cinnamic acid derivatives Selective hydrogenation of diazirinyl compounds with Wilkinson's catalyst was examined in THF-*tert*-butanol or methanol in a similar manner as described in the reference (Fig. 2). Little difference was observed between these two solvents. The results gave the hydrogenated proportion of the reaction mixture, which was directly monitored by ^{1}H-NMR in CD_3OD. Table 1 shows the degree of hydrogenation of typical compound **3a** with various amounts of Wilkinson's catalyst at room temperature. Although slightly larger amounts of the catalyst than in

Table 1. Proportions of the Hydrogenated Reaction Mixture (**3a**) in the Presence of Various Amounts of Wilkinson's Catalyst at Room Temperature

Wilkinson's catalyst (mol%)	Remaining starting material **3a**	Conversion product **5a**
4	87	13
8	70	30
12	20	80
25	0	100

Proportions were judged by ^{1}H-NMR in CD_3OD.

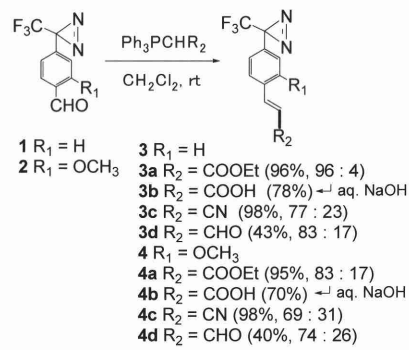

Fig. 1. Synthesis of Unsaturated Diazirinyl Compounds with Wittig Reactions

Each yield and *trans* : *cis* ratio from ^{1}H-NMR are indicated in parentheses.

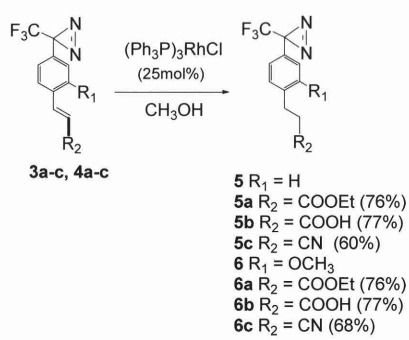

Fig. 2. Selective Hydrogenation of Diazirinyl Cinnamyl Derivatives with Wilkinson's Catalyst

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Table 2. Proportions of the Hydrogenation Reaction Mixture (**3a**) at Various Reaction Times

Time (h)	Remaining starting material **3a**	Conversion product **5a**
1	90	10
3	60	40
5	50	50
10	nd	100

Proportions were judged by ^{1}H-NMR in CD_3OD. nd: no detection.

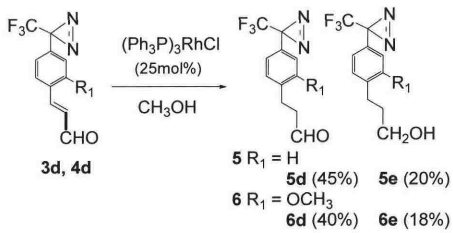

Fig. 3. Selective Hydrogenation of Diazirinyl Cinnamaldehyde Derivatives with Wilkinson's Catalyst

previous reports was needed, the carbon–carbon double bond was reduced by NMR analysis over 25 mol% catalyst. No temperature dependence was observed in this reaction.

Table 2 shows correlations between reaction time and hydrogenation. The reaction was not completed within 5 h. No saturated or unsaturated alcohol was detected in the reaction mixture from cinnamic esters by NMR analysis. These products have characteristic UV adsorption (λ_{max} *ca.* 350 nm), ^{13}C-NMR (for CF_3 125 ppm, q, J=274 Hz, for diazirinyl quaternary carbon 40 ppm, q, $^2J_{CF}$=40 Hz) and ^{19}F-NMR signals (−65 ppm). These results indicated that the reduction proceeded selectively for the carbon–carbon double bond over the nitrogen–nitrogen and carboxyl double bond. Methoxy substituent at *ortho* position of the carbon–carbon double bond did not interfere with the hydrogenation.

Carboxylic acid derivatives (**3b**, **4b**) were reduced in a similar manner as described above without alcohols. The α,β-unsaturated nitriles (**3c**, **4c**) afforded the desired diazirinyl saturated nitriles (**5c**, **6c**, IR *ca.* 2200 cm^{-1}).

Cinnamaldehyde derivatives afforded saturated aldehyde (**5d**, **6d**) and saturated alcohol (**5e**, **6e**). The ratio of saturated aldehyde and saturated alcohol was constant over 12 h incubation (Fig. 3). The results indicated that saturated aldehyde was not reduced to saturated alcohol.

Recent progress of mass spectrometers suggested the application of a stable isotope for photoaffinity labeling.[19—22] The hydrogenation of diazirinyl compounds could also introduce deuterium with commercially available deuterium gas (D_2, 99.8% atom D) in the presence of Wilkinson's catalyst in a similar manner described above. No serious H-D exchange reaction was detected during the reaction (Fig. 4).

It was reported that microwave-assisted catalytic transfer hydrogenation in the presence of Wilkinson's catalyst is more effective, but the diazirinyl moiety does not tolerate microwave conditions, because of the high temperature. Hydrogenation at 1 atm at room temperature was a better method for this purpose. Furthermore we found that hydrogenation of **4a** with Pd/C (5%) in methanol strongly promoted decomposition of diazirinyl moiety within 30 min.

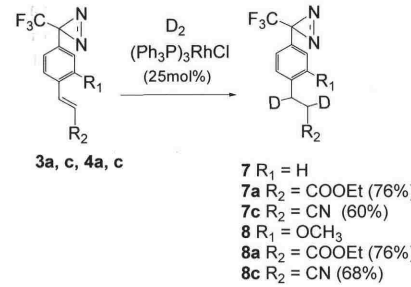

Fig. 4. Selective Hydrogenation of Diazirinyl Cinnamyl Derivatives with Wilkinson's Catalyst in Deuterium Gas

These results indicated that mild selective hydrogenation of the carbon–carbon double bond in the presence of nitrogen–nitrogen double bond (diazirinyl moiety) with Wilkinson's catalyst could be applied to many bioactive compounds for photoaffinity labeling.

Experimental

All NMR spectra were measured using JEOL JNM-FX270 and ECA-500 spectrometers. MS spectra were obtained using JEOL JNM-LA400 spectrometers. IR spectra were obtained using JASCO FT-IR 420. All solvents were of reagent grade and distilled using the appropriate methods.

Typical Experiment for Compounds 3a—d and 4a—d The aldehyde (**1** or **2**) and corresponding Wittig reagent (2.4 eq) are dissolved in CH_2Cl_2. The reaction mixture was stirred at room temperature for 2 h and subjected to silica column chromatography (CH_2Cl_2) to afford pure materials. Compounds **3b** and **4b** were afforded alkaline hydrolysis in aqueous ethanol from correspond ethyl ester **3a** and **4a**.

3-(4-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)acrylic Acid (3b) ^{1}H-NMR ($CDCl_3$) δ: 7.75 (1H, d, J=16.0 Hz), 7.55 (2H, d, J=8.6 Hz), 7.20 (2H, d, J=8.6 Hz), 6.45 (1H, d, J=16.0 Hz), ^{19}F-NMR ($CDCl_3$) δ: −65.0, FAB-MS *m/z*: 257.0546 (Calcd for $C_{11}H_8F_3N_2O_2$: 257.0538).

3-(4-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)acrylonitrile (3c) *trans*-Isomer: ^{1}H-NMR ($CDCl_3$) δ: 7.49 (2H, d, J=8.0 Hz), 7.39 (1H, d, J=16.6 Hz), 7.22 (2H, d, J=8.6 Hz), 5.93 (1H, d, J=16.6 Hz), ^{19}F-NMR ($CDCl_3$) δ: −65.0, *cis*-isomer: ^{1}H-NMR ($CDCl_3$) δ: 7.83 (2H, d, J=8.6 Hz), 7.25 (2H, d, J=8.6Hz), 7.14 (1H, d, J=12.0 Hz), 5.55 (1H, d, J=12.0 Hz), ^{19}F-NMR ($CDCl_3$) δ: −65.0, FAB-MS *m/z*: 238.0602 (Calcd for $C_{11}H_7F_3N_3$: 238.0592), IR (cm^{-1}): 2215.

3-(4-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)acrylaldehyde (3d) *trans*-Isomer: ^{1}H-NMR ($CDCl_3$) δ: 9.72 (1H, d, J=8.0 Hz), 7.60 (2H, d, J=8.6 Hz), 7.47 (1H, d, J=16.0 Hz), 7.24 (2H, d, J=8.6 Hz), 6.74 (1H, m, J=16.0 Hz), ^{19}F-NMR ($CDCl_3$) δ: −64.8, *cis*-isomer: ^{1}H-NMR ($CDCl_3$) δ: 9.72 (1H, d, J=8.0 Hz), 7.75 (1H, d, J=16.0 Hz), 7.57 (2H, d, J=8.6 Hz), 7.22 (1H, d, J=8.0 Hz), 6.48 (1H, m, J=16.0 Hz), ^{19}F-NMR ($CDCl_3$) δ: −64.8, FAB-MS *m/z*: 241.0580 (Calcd for $C_{11}H_8F_3N_2O$: 241.0589).

3-(2-Methoxy-4-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)acrylic Acid (4b) ^{1}H-NMR ($CDCl_3$) δ: 8.01 (1H, d, J=16.2 Hz), 7.53 (1H, d, J=8.2 Hz), 6.81 (1H, d, J=8.2 Hz), 6.62 (1H, s), 6.55 (1H, d, J=16.2 Hz), 3.84 (3H, s), ^{19}F-NMR ($CDCl_3$) δ: −65.0, FAB-MS *m/z*: 287.0650 (Calcd for $C_{12}H_{10}F_3N_2O_3$: 287.0644).

3-(2-Methoxy-4-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)acrylonitrile (4c) *trans*-Isomer: ^{1}H-NMR ($CDCl_3$) δ: 7.57 (1H, d, J=16.6 Hz), 7.40 (1H, d, J=8.0 Hz), 6.81 (1H, d, J=8.0 Hz), 6.65 (1H, s), 6.09 (1H, d, J=16.6 Hz), 3.90 (3H, s), ^{19}F-NMR ($CDCl_3$) δ: −64.8, *cis*-isomer: ^{1}H-NMR ($CDCl_3$) δ: 8.08 (1H, d, J=8.0 Hz), 7.51 (1H, d, J=12.6 Hz), 6.86 (1H, d, J=8.0 Hz), 6.65 (1H, s), 5.50 (1H, d, J=12.0 Hz), 3.85 (3H, s), ^{19}F-NMR ($CDCl_3$) δ: −64.8, FAB-MS *m/z*: 268.0694 (Calcd for $C_{12}H_9F_3N_2O$: 268.0698), IR (cm^{-1}): 2220.

3-(2-Methoxy-4-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)acrylaldehyde (4d) *trans*-Isomer: ^{1}H-NMR ($CDCl_3$) δ: 9.72 (1H, d, J=8.0 Hz), 7.65 (1H, d, J=16.6 Hz), 7.20 (1H, d, J=8.0 Hz), 6.70 (1H, m, J=8.0 Hz), 6.65 (1H, s), 6.20 (1H, d, J=16.6 Hz), 3.80 (3H, s), ^{19}F-NMR ($CDCl_3$) δ: −64.8, *cis*-isomer: ^{1}H-NMR ($CDCl_3$) δ: 9.72 (1H, d, J=8.0 Hz), 8.00 (1H, d, J=8.0 Hz), 7.45 (1H, d, J=12.0 Hz), 6.85 (1H, d, J=8.0 Hz), 6.65 (1H, s), 6.00 (1H, d, J=12.0 Hz), 3.85 (3H, s), ^{19}F-NMR ($CDCl_3$) δ: −64.8, FAB-MS *m/z*: 271.0690 (Calcd for $C_{12}H_{10}F_3N_2O_2$: 271.0694).

Typical Experiment for Hydrogenation of Diazirinyl Compounds The unsaturated diazirinyl compound and Wilkinson's reagent (25 mol%) were dissolved in CH_3OH. The reaction mixture was stirred at room temperature for 10 h under hydrogen atmosphere and subjected to silica column chromatography (CH_2Cl_2 : *n*-hexane = 1 : 1) to afford pure material.

Ethyl 3-(4-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)propanoate (5a) ^{1}H-NMR ($CDCl_3$) δ: 7.24 (2H, d, J=8.6 Hz), 7.11 (2H, d, J=8.6 Hz), 4.12 (2H, q, J=7.2 Hz), 2.96 (2H, t, J=7.4 Hz), 2.60 (2H, t, J=7.4 Hz), 1.22 (3H, t, J=7.2 Hz), ^{13}C-NMR ($CDCl_3$) δ: 172.5, 142.4, 128.8, 126.6, 126.4, 122.1 (q, J_{CF}=273.9 Hz), 60.5, 35.4, 30.5, 28.3 (q, $^2J_{CF}$=40.4 Hz), 14.2, ^{19}F-NMR ($CDCl_3$) δ: −65.0, FAB-MS *m/z*: 287.1012 (Calcd for $C_{13}H_{14}F_3N_2O_2$: 287.1007).

3-(4-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)propanoic Acid (5b) ^{1}H-NMR ($CDCl_3$) δ: 7.23 (2H, d, J=8.6 Hz), 7.21 (2H, d, J=9.2 Hz), 2.97 (2H, t, J=7.7 Hz), 2.70 (2H, t, J=7.7 Hz), ^{13}C-NMR ($CDCl_3$) δ: 177.5, 142.0, 128.5, 126.3, 126.0, 121.9 (q, J_{CF}=273.9 Hz), 35.4, 30.5, 28.3 (q, $^2J_{CF}$=40.4 Hz), ^{19}F-NMR ($CDCl_3$) δ: −65.0, FAB-MS *m/z*: 259.0698 (Calcd for $C_{11}H_{10}F_3N_2O_2$: 259.0694).

3-(4-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)propanenitrile (5c) ^{1}H-NMR ($CDCl_3$) δ: 7.28 (2H, d, J=8.6 Hz), 7.18 (2H, d, J=8.0 Hz), 2.98 (2H, t, J=7.4 Hz), 2.63 (2H, t, J=7.4 Hz), ^{13}C-NMR ($CDCl_3$) δ: 139.6, 128.8, 128.2, 127.0, 126.5, 122.0 (q, J_{CF}=274.3 Hz), 118.6, 29.7, 28.3 (q, $^2J_{CF}$=40.8 Hz), ^{19}F-NMR ($CDCl_3$) δ: −65.5, FAB-MS *m/z*: 240.0756 (Calcd for $C_{11}H_9F_3N_2$: 240.0749), IR (cm^{-1}): 2218.

Ethyl 3-(2-Methoxy-4-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)-propanoate (6a) ^{1}H-NMR ($CDCl_3$) δ: 7.12 (1H, d, J=8.0 Hz), 6.80 (1H, d, J=8.0 Hz), 6.75 (1H, s), 4.12 (2H, q, J=7.2 Hz), 3.85 (3H, s), 2.92 (2H, t, J=7.7 Hz), 2.59 (2H, t, J=7.7 Hz), 1.23 (3H, t, J=7.2 Hz), ^{13}C-NMR ($CDCl_3$) δ: 173.0, 157.0, 130.9, 130.3, 128.4, 122.1 (q, J_{CF}=274.7 Hz), 118.7, 107.9, 60.4, 55.3, 33.7, 28.5 (q, $^2J_{CF}$=34.8 Hz), 25.8, 14.2, ^{19}F-NMR ($CDCl_3$) δ: −65.0, UV ($CHCl_3$), FAB-MS *m/z*: 317.1120 (Calcd for $C_{14}H_{16}F_3N_2O_3$: 317.1113).

3-(2-Methoxy-4-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)propanoic Acid (6b) ^{1}H-NMR ($CDCl_3$) δ: 7.20 (1H, d, J=8.0 Hz), 6.82 (1H, d, J=8.0 Hz), 6.70 (1H, s), 3.85 (3H, s), 2.97 (2H, t, J=7.7 Hz), 2.72 (2H, t, J=7.7 Hz), ^{13}C-NMR ($CDCl_3$) δ: 177.2, 157.0, 130.5, 130.0, 128.3, 122.0 (q, J_{CF}=274.7 Hz), 118.5, 108.0, 55.3, 33.7, 28.5 (q, $^2J_{CF}$=34.8 Hz), 25.8, ^{19}F-NMR ($CDCl_3$) δ: −65.0, FAB-MS *m/z*: 289.0810 (Calcd for $C_{12}H_{12}F_3N_2O_3$: 289.0800).

3-(2-Methoxy-4-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)propanenitrile (6c) ^{1}H-NMR ($CDCl_3$) δ: 7.21 (1H, d, J=7.4 Hz), 6.78 (1H, d, J=8.0 Hz), 6.6 (1H, s), 3.85 (3H, s), 2.95 (2H, t, J=7.2 Hz), 2.61 (2H, t, J=7.4 Hz), ^{13}C-NMR ($CDCl_3$) δ: 157.0, 130.7, 129.7, 128.3, 122.0 (q, J_{CF}=274.7 Hz), 119.2, 108.2, 55.4, 29.7, 28.4 (q, $^2J_{CF}$=40.4 Hz), 26.7, ^{19}F-NMR ($CDCl_3$) δ: −65.5, FAB-MS *m/z*: 270.0864 (Calcd for $C_{12}H_{11}F_3N_3O$: 270.0854), IR (cm^{-1}): 2220.

3-(4-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)propanal (5d) ^{1}H-NMR ($CDCl_3$) δ: 9.8 (1H, m), 7.23 (2H, d, J=8.6 Hz), 7.12 (2H, d, J=8.6 Hz), 2.97 (2H, t, J=7.4 Hz), 2.79 (2H, m), ^{13}C-NMR ($CDCl_3$) δ: 200.8, 139.5, 128.6, 128.4, 126.7, 123.7 (q, J_{CF}=287.9 Hz), 44.8, 29.7, 29.7, 28.0 (q, $^2J_{CF}$=40.2 Hz), ^{19}F-NMR ($CDCl_3$) δ: −65.0, FAB-MS *m/z*: 243.0755 (Calcd for $C_{11}H_{10}F_3N_2O$: 243.0745).

3-(4-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)propan-1-ol (5e) ^{1}H-NMR ($CDCl_3$) δ: 7.21 (2H, d, J=8.6 Hz), 7.09 (2H, d, J=8.0 Hz), 3.63 (2H, d, J=6.3 Hz), 2.70 (2H, t, J=7.7 Hz), 1.84 (2H, t, J=7.7 Hz), ^{13}C-NMR ($CDCl_3$) δ: 139.0, 128.7, 127.8, 126.5, 123.8 (q, J_{CF}=272.3 Hz), 61.9, 33.8, 31.7, 28.6 (q, $^2J_{CF}$=40.2 Hz), ^{19}F-NMR ($CDCl_3$) δ: −65.0, FAB-MS *m/z*: 245.0910 (Calcd for $C_{11}H_{12}F_3N_2O$: 245.0902).

3-(2-Methoxy-4-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)propanal (6d) ^{1}H-NMR ($CDCl_3$) δ: 9.70 (1H, m), 7.20 (1H, d, J=8.6 Hz), 6.80 (1H, d, J=8.6 Hz), 6.60 (1H, s), 3.85 (3H, s), 2.95 (2H, t, J=7.4 Hz), 2.78 (2H, t, J=7.4 Hz), ^{13}C-NMR ($CDCl_3$) δ: 200.8, 157.0, 1307, 129.5, 127.8, 123.7 (q, J_{CF}=287.9 Hz), 119.0, 108.8, 55.8, 29.7, 29.4, 28.0 (q, $^2J_{CF}$=40.2 Hz), ^{19}F-NMR ($CDCl_3$) δ: −65.0, FAB-MS *m/z*: 273.0860 (Calcd for $C_{12}H_{12}F_3N_2O_2$: 273.0851).

3-(2-Methoxy-4-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)propan-1-ol (6e) ^{1}H-NMR ($CDCl_3$) δ: 7.20 (1H, d, J=7.4 Hz), 7.09 (2H, d, J=8.0 Hz), 6.60 (1H, s), 3.85 (3H, s), 3.63 (2H, d, J=6.3 Hz), 2.70 (2H, t, J=7.7 Hz), 1.84 (2H, t, J=7.7 Hz), ^{13}C-NMR ($CDCl_3$) δ: 156.8, 130.0, 129.6, 127.7, 123.8 (q, J_{CF}=272.3 Hz), 118.9, 109.0, 61.9, 56.0, 33.8, 31.7, 28.6 (q, $^2J_{CF}$=40.2 Hz), ^{19}F-NMR ($CDCl_3$) δ: −65.0, FAB-MS *m/z*: 275.1012 (Calcd for $C_{12}H_{14}F_3N_2O_2$: 275.1007).

Ethyl 3-(4-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)[2,3-D_2]propanoate (7a) ^{1}H-NMR ($CDCl_3$) δ: 7.24 (2H, d, J=8.6 Hz), 7.11 (2H, d, J=8.6 Hz), 4.12 (3H, q, J=7.3 Hz), 2.93 (1H, d, J=6.3 Hz), 2.58 (1H, d, J=6.3 Hz), 1.22 (3H, t, J=7.2 Hz), ^{13}C-NMR ($CDCl_3$) δ: 172.5, 142.4, 128.8, 126.6, 120.5 (q, J_{CF}=265.1 Hz), 60.5, 35.1 (t, 19.8 Hz), 30.1 (t, 19.8 Hz), 28.3 (q, $^2J_{CF}$=40.0 Hz), 14.2, ^{19}F-NMR ($CDCl_3$) δ: −65.3, FAB-MS *m/z*: 289.1150 (Calcd for $C_{13}H_{12}D_2F_3N_2O_2$: 289.1133).

3-(4-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)[2,3-D_2]propanenitrile (7c) ^{1}H-NMR ($CDCl_3$) δ: 7.28 (2H, d, J=8.6 Hz), 7.18 (2H, d, J=8.6 Hz), 2.96 (1H, d, J=7.4 Hz), 2.61 (1H, d, J=6.9 Hz), ^{13}C-NMR ($CDCl_3$) δ: 139.6, 128.8, 128.2, 127.0, 120.0, 119.9 (q, J_{CF}=266.3 Hz), 30.7 (t, J=20.4 Hz), 28.0 (q, $^2J_{CF}$=40.2 Hz), 18.8 (t, J=21.0 Hz), ^{19}F-NMR ($CDCl_3$) δ: −65.1, FAB-MS *m/z*: 242.0886 (Calcd for $C_{11}H_7D_2F_3N_3$: 242.0874), IR (cm^{-1}): 2210—2220.

Ethyl 3-(2-Methoxy-4-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)-[2,3-D_2]propanoate (8a) ^{1}H-NMR ($CDCl_3$) δ: 7.17 (1H, d, J=8.0 Hz), 6.72 (1H, d, J=8.6 Hz), 6.57 (1H, s), 4.11 (2H, q, J=7.3 Hz), 3.82 (3H, s), 2.90 (1H, t, J=8.0 Hz), 2.55 (1H, t, J=8.0 Hz), 1.23 (3H, t, J=7.2 Hz), ^{13}C-NMR ($CDCl_3$) δ: 173.0, 157.6, 130.9, 130.3, 128.4, 121.9 (q, J_{CF}=273.5 Hz), 118.7, 107.9, 60.4, 55.3, 33.5 (t, 20.0 Hz), 28.5 (q, $^2J_{CF}$=40.4 Hz), 25.5 (t, 20.0 Hz), 14.2, ^{19}F-NMR ($CDCl_3$) δ: −65.0, FAB-MS *m/z*: 319.1246 (Calcd for $C_{14}H_{14}D_2F_3N_2O_3$: 319.1239).

3-(2-Methoxy-4-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)[2,3-D_2]propanenitrile (8c) ^{1}H-NMR ($CDCl_3$) δ: 7.21 (1H, d, J=8.0 Hz), 6.78 (1H, d, J=6.9 Hz), 6.6 (1H, s), 3.8 (3H, s), 2.9 (1H, d, J=8.0 Hz), 2.59 (1H, d, J=7.4 Hz), ^{13}C-NMR ($CDCl_3$) δ: 157.5, 130.7, 129.6, 128.2, 121.8 (q, J_{CF}=289.5 Hz), 119.1, 108.2, 55.4, 29.7, 28.4 (q, $^2J_{CF}$=40.0 Hz), 26.31 (t, J=21.0 Hz), 16.93 (t, J=21.0 Hz), ^{19}F-NMR ($CDCl_3$) δ: −65.0, FAB-MS *m/z*: 278.0986 (Calcd for $C_{12}H_9D_2F_3N_3O$: 272.0980), IR (cm^{-1}): 2210—2220.

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