

Communications

## Deuterium-labeling Toward Robust Function of Organic Molecules: Enhanced Photo-stability of Partially Deuterated 1', 3', 3'-Trimethyl-6-nitrospiro[2H-1-benzopyran-2, 2'-indoline]

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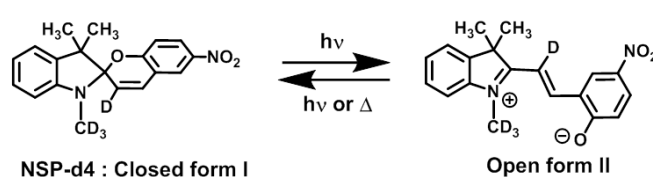
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**ABSTRACT:** Synthesis of a deuterium-labeled derivative of nitrospirobenzopyran (NSP), one of representative photochromic compounds, has been described. Four deuteriums were successfully introduced on 1-methyl and  $\alpha$ -methylene relative to spiro-carbon in the title compound with more than 95atom%D purity. Main photodegraded products of NSP were two oxindoles in acetonitrile, and additional products were formed in poly(isobutyl-methacrylate) films possibly due to restricted molecular motion in polymer matrix. Quantitative HPLC analysis revealed that partial introduction of deuterium to NSP brought a noticeable isotope effect, recognizable enhancement in photo-resistivity of NSP, *i.e.*, 8.3% in solutions and 29% in polymeric films.

Latent durability of synthetic compositions has become a big issue to utilize them in state-of-the-art, optoelectronic devices for stable long-term usage so that technological development toward robustness of molecular based materials is quite important. We focus attention on isotopic derivatization of organic molecules through recently developed catalytic protium(H)-deuterium(D) exchange reactions in D<sub>2</sub>O under microwave irradiation.<sup>1</sup> Hydrogen is the most abundant element of organic molecules and the C-H bond character often governs chemical/physical nature of the molecule. Fluorescence quantum yield of D-aromatic molecules tends to be higher than normal H-derivatives, because high frequency mode of C-H stretching is the most important contributing factor for the non-radiative transition of photoexcited organic molecules (*ex.* S<sub>0</sub> ← S<sub>1</sub>) and heavier D gives less vibronic coupling. We recently revealed photo-physical behaviors of the triplet excited state of deuterated Ir(ppy)<sub>3</sub>-d<sub>24</sub>, which emits green phosphorescence in higher emission quantum yield than Ir(ppy)<sub>3</sub>-h<sub>24</sub> due to reduction of non-radiative transition rate.<sup>2</sup> In terms of chemical stability, bond dissociation rate of C-D becomes slower than C-H due to the difference in zero-point energy when both transition states are similar to the dissociated structures. It is found from light-fastness experiments on some ultraviolet absorbers that D-labeled substances have 1.2 – 1.5 times more durable or longer life, compared to unlabeled ones.<sup>3</sup> We here report synthesis and enhancement of photo-stability of 1', 3', 3'-trimethyl-6-nitrospiro[2H-1-benzopyran-2,2'-indoline]-d<sub>4</sub> (NSP-d<sub>4</sub>, Scheme-1). UV excitation (*e.g.* at 365nm) of colorless closed form I leads photochemical C-O bond rupture at the spiro position, followed by rapid transformation to the open merocyanine form II with characteristic absorption growth in the visible region. II represents a fluxional molecule composed by

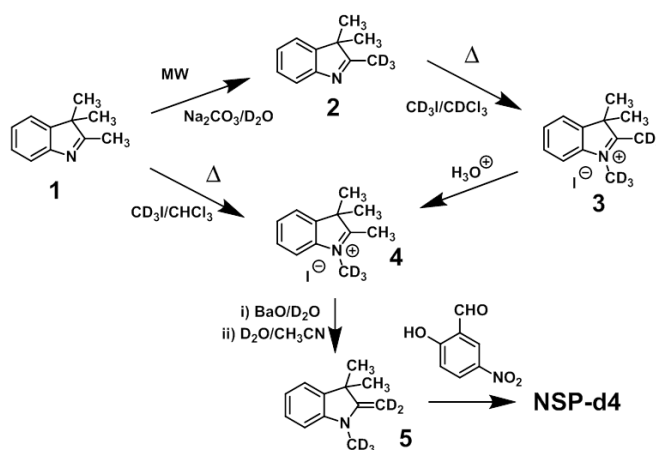
eight conformational isomers with regard to two C=C bonds in the chromophoric conjugation from indoline's N to phenolate's O as long as we concern zwitter-ionic structure.<sup>4</sup> In the present study, consecutive photo-irradiation at 365nm was carried out to the solutions and to the films of NSP, then products were analyzed by reverse phase HPLC (TOSOH TSK-gel ODS-80Ts, H<sub>2</sub>O-acetonitrile (5:95 v/v)), 400MHz <sup>1</sup>H-NMR, GC-MS and ESI-MS to evaluate isotope effect.



NSP-d<sub>4</sub> : Closed form I

Open form II

Scheme 1

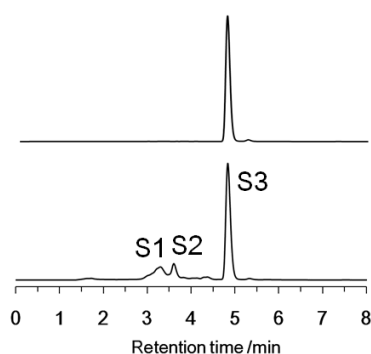


Scheme 2

The synthesis of NSP-d<sub>4</sub> is as follows (Scheme-2). **2-Methyl-d<sub>3</sub>,3,3-dimethylindolenine (2, TMI-d<sub>3</sub>):** Vacuum distilled 1.01g (6.34mmol) of 2,3,3-trimethylindolenine (**1**, TMI), sodium carbonate (11.7mg) and D<sub>2</sub>O (3.04g, 152mmol, ISOTEC 99.9atom%D) were placed in a pressure-tight vessel and heated at 200°C for 60 minutes under microwave irradiation (CEM Discover, 2.45GHz) with stirring. Product was extracted with n-hexane and dried over sodium sulfate. Evaporation gave TMI with weight recovery of 90%. From GC-MS and <sup>1</sup>H-NMR, this reaction condition gave deuteration at 2-methyl position with 93.9 atom%D purity (average of 6 reaction batches), while no other hydrogens were reacted. The isotopic purity almost

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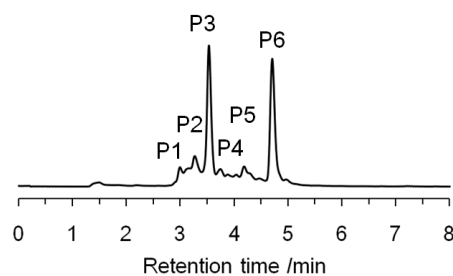
reaches given theoretical abundance,  $100N_D/(N_D + N_H)=94\%$  where  $N_D$  and  $N_H$  are number of deuterium from  $D_2O$  and number of reactive protium from TMI, respectively. 400MHz  $^1H$ -NMR ( $CDCl_3$ ,  $\delta/ppm$ ) 1.30 (6H, s, 3- $CH_3$ ), 7.26-7.53 (4H, m, ring- $H$ ), 2- $CH_3$  undetected. **1-Methyl-*d*3-2-methyl-*d*3,3-dimethylindolenium Iodide (3, MTMI $^+$ -*d*6)**: For quaternization, a solution of 250mg of TMI-*d*3 (1.54mmol), 110 $\mu$ L of iodomethan-*d*<sub>3</sub> (1.77mmol) in 2mL of chloroform-*d* was heated at 80°C for 22hrs in a tight vial (Pierce REACTI-VIAL). Solid products from four batches of the above reaction were collected together by suction filtration, washed with cold chloroform and diethylether, and dried under vacuum. Yield 1.7g (91%).  $^1H$ -NMR measurement suggests that 2-methyl hydrogens partially returned to the protium form by the action of atmospheric moisture during purification processes. 400MHz  $^1H$ -NMR ( $CDCl_3$ ,  $\delta/ppm$ ) 1.54 (6H, s, 3- $CH_3$ ), 6.53-7.31 (4H, m, ring- $H$ ). **1-Methyl-*d*3,3,3-trimethylindolenium Iodide (4, MTMI $^+$ -*d*3)**: Same procedure for MTMI $^+$ -*d*6 was applied except commercial TMI and regular chloroform were used instead. Six batches of the reaction yielded 2.47g of pure product (88%). **1-Methyl-*d*3,3-dimethyl-2-methylene-*d*2-indoline (5, TMMI-*d*5)**: Into a solution of MTMI $^+$ -*d*3 (1.00g, 3.29mmol) in 10mL of  $D_2O$ , BaO (1.49g) was added and the mixture was stirred for 2 hrs. Diethylether extract (5mL x 5times) was dried over sodium sulfate and evaporated to yield 0.484g (84%) of 1-Methyl-*d*3,3-dimethyl-2-methyleneindoline. Final H-D exchange on methylene was done by mixing the indoline with 5.60g of  $D_2O$  in 20mL of dry acetonitrile overnight. This stock solution of TMMI-*d*5 was used for the following coupling reaction. 400MHz  $^1H$ -NMR ( $CDCl_3$ ,  $\delta/ppm$ ) 1.54 (6H, s, 3- $CH_3$ ), 7.26 (4H, m, ring- $H$ ). 1- $CH_3$  and 2- $CH_3$  undetected. **NSP-*d*4**: Into one half of the TMMI-*d*5 stock solution (1.36mmol) was added 241mg of 5-nitrosalicylaldehyde (eq.mol) and the solution was stirred 1 hr at 60°C. Resulted solids were collected, washed with cold acetonitrile and vacuum dried. Yield 394mg (88%), >95atom%D from  $^1H$ -NMR and ESI-MS. More than 99% purity was confirmed by HPLC. 400MHz  $^1H$ -NMR ( $CDCl_3$ ,  $\delta/ppm$ ) 1.56 (6H, s, 3- $CH_3$ ), 6.77 (1H, d, methyne- $H$ ), 6.55 - 8.01 (7H, m, ring- $H$ ). ESI/MS:  $m/z=326.9$  [ $C_{19}H_{14}D_4O_3N_2 + H^+$ ]. Commercial NSP was purified on silica-gel column (dichloromethane as eluent), then recrystallized three times from water-acetonitrile mixture (5:95 v/v) to give final purity of 99% (HPLC).



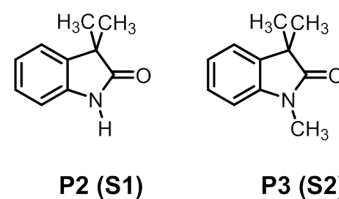
**Figure 1.** HPLC chromatograms of NSP/acetonitrile samples. Before photoirradiation (upper) and after photoirradiation (lower).

Durability tests of NSP and NSP-*d*4 were carried out in their acetonitrile solutions. 3mL of the solutions were placed in fluorescence quvettes (quartz, 10x10mm light-pass-length) and irradiated 24hrs simultaneously under 4 W black-light (UVP UVGL-25 equipped with Hitachi FL4BL Hg lamp) at room temperature. All the solutions were prepared to be equal concentration with OD>2 at 365nm to establish a complete photo-absorbing system. Light

intensities at the settled positions were separately measured by chemical actinometry (Heller's Fluclide) to correct photolysis data. Typical HPLC chromatograms before and after irradiation are shown in Figure 1. The peak at 4.7min (S3) corresponds to NSP. At least two products at 3.3min (S1) and 3.5min (S2) were found after the photolysis. Degraded fractions were 33.6% and 30.8%, for NSP and NSP-*d*4, respectively, averaged values over 9 HPLC analyses for three independent photolytic experiments. This result shows that partial introduction of D improved photo-resistivity of NSP and its apparent degradation yield decreased 8.3% in solution.

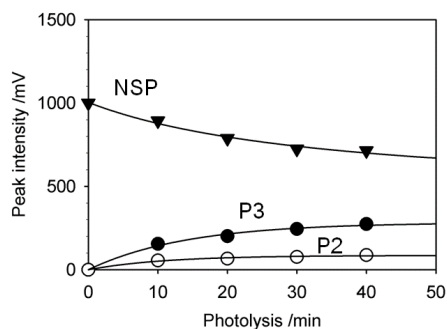


**Figure 2.** HPLC chromatograms of a NSP polymer film after photoirradiation.

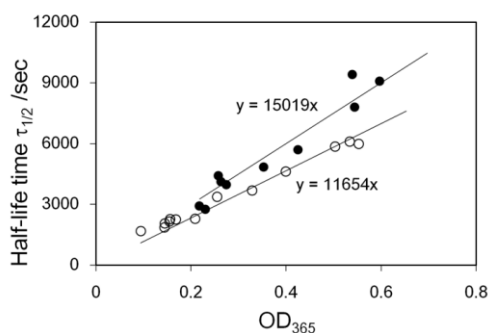


**Figure 3.** Estimated structures of the HPLC fractions P2 and P3 from photodegradation of NSP.

Then, we examined photodegradation of NSP in polymer films. The film was deposited from NSP (NSP-*d*4) solution (1.6mg in 1mL of 5wt% poly(isobutyl methacrylate)/toluene) on a cut slide glass (ca.19x26mm), dried under vacuum, and annealed at 120°C for 1hr before use. Two types of measurements were carried out, i) HPLC analysis of photoproducts and ii) bleaching of photomerocyanine absorption. For photoproduct analysis experiment, samples were arranged on a spinning stage (80rpm) to acquire equal irradiation condition under 500W high-pressure Hg lamp equipped with a bandpass filter for 365nm. A HPLC chromatogram after irradiation is shown in Figure 2 which indicates more variety of side products (P1,P2,...) formed in polymer film than the solution system. Since energy dissipation from photoexcited and vibronic states is limited in the polymer matrix, embedded molecules will suffer more from decomposition reactions than in solution. NSP film and NSP-*d*4 film resembled each other in the product distribution and surviving amount after photolysis. Precise comparison of decomposition rate between two films based on HPLC analysis is rather difficult, since photoreaction of those films depends strongly on the film thickness and O.D. as shown later. Then HPLC fractionation was performed for the THF solutions of photolyzed films, followed by GC-MS and  $^1H$ -NMR analysis. It is known that spiroxan photo-degrades into oxindole and salicylaldehyde in the presence of molecular oxygen.<sup>5</sup> In our analysis, 3.3min component (S1 and P2) is 3,3-dimethyl-2-oxindole [ $m/z=161$ ,  $\delta=1.40ppm$  (6H, s, 3- $CH_3$ )], and 3.5 min component (S2 and P3) is 3,3-dimethyl-1-methyl-2-oxindole [ $m/z=175$ ,  $\delta=1.37ppm$  (6H, s, 3- $CH_3$ ),  $\delta=3.22ppm$  (3H, s, 1- $CH_3$ )], respectively. Time course analysis shows consumption of NSP and formation of oxindoles proceeded in parallel way (Figure 4).



**Figure 4.** Time course of consumption of NSP(P6) and formation of photoproducts P2 and P3 vs. photolytic duration.



**Figure 5.** Plots of half-life time of photoisomer II under continuous photoirradiation on NSP (○) or NP-d4 (●) polymer films at 365nm vs.  $OD_{365}$ . Inset lines and equations were obtained by least square fitting method.

In order to investigate isotope effect in polymer films more precisely, NSP films as well as NSP-d4 films with variety of film thickness (2 - 20  $\mu\text{m}$ ) were prepared. Time course of transmittance change of the sample films was recorded at 633nm by using power-stabilized He-Ne laser under photoirradiation of high-pressure Hg lamp (365nm). Photoirradiation induced intense blue color due to formation of photomerocyanine II at first, but further irradiation caused gradual bleaching. In Figure 5, half-life ( $\tau_{1/2}$ ) of the NSP and NSP-d4 polymer films are plotted versus initial OD at 365nm ( $OD_{365}$ ). Interestingly,  $\tau_{1/2}$  depends almost proportionally on  $OD_{365}$ , i.e.,  $\tau_{1/2} = A \times OD_{365}$  where A is constant. Larger  $OD_{365}$  gave longer lifetime, probably because thick sample has more backup dye molecules behind. More importantly, NSP-d4 films recorded longer half-life than NSP films over the wide range of  $OD_{365}$ . From the ratio of two slopes  $A(\text{NSP-d4})/A(\text{NSP})$  for each set of plots, we evaluate that the isotope effect on photo-resistivity of NSP polymer is as high as 1.29.

In this study, deuteration of NSP was not perfectly done, but only 4 deuteriums were introduced out of 18 hydrogens. Nevertheless, noticeable isotope effect was observed as enhancement of photo-resistivity, 8.3% in solutions and 29% in polymeric films.

Organic molecule will play more important roles in manufacturing future electronic devices which require soft, light-weight, recyclable properties as well as high-performance indices including robustness. Deuteration could be a simple and effective tool to improve strength of molecular framework without changing fundamental optoelectronic features. Thus, chemistry of deuterated molecules is worthy of exploration and further studies are in progress.

**KEYWORDS:** Deuterium labeling, Photochromic spiropyrans, Photo-degradation, Microwave synthesis.

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