Tetrahedron Letters 60 (2019) 59–62

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Fluorometric analysis of borohydrides based on reductive aldehyde-to-alcohol conversion of arylaldehydes

Na Yeong Kim, Ji Hye Baek, Suk-Kyu Chang *

Department of Chemistry, Chung-Ang University, Seoul 06974, Republic of Korea

ARTICLE INFO

Article history:
Received 1 October 2018
Revised 15 November 2018
Accepted 22 November 2018
Available online 23 November 2018

Keywords:
Arylaldehyde
Borohydride assay
Aldehyde-to-alcohol reduction
Reaction-based probe
Fluorescent signaling

ABSTRACT

Fluorometric analysis of borohydride (BH_4^-) species by the reduction of arylaldehydes to the corresponding arylmethanols was investigated. 9-Anthracenecarboxaldehyde (**9-AA**) exhibited pronounced ratiometric fluorescence signaling behavior toward borohydride in alkaline aqueous media. The borohydride-selective signaling of **9-AA** was unaffected by the presence of commonly encountered metal ions and anions. 1-Pyrenecarboxaldehyde (**1-PA**) also showed comparable borohydride signaling behavior. The detection limit was found to be 7.4 μM (0.11 ppm) for **9-AA** and 15.7 μM (0.23 ppm) for **1-PA**. The utility of the probe with μPAD as a convenient tool for the determination of borohydrides was demonstrated.

Borohydrides are valuable reducing agents with extensive applications in inorganic and organic chemistry. In synthetic organic chemistry, borohydrides are widely employed as mild and selective reducing agents for aldehydes, ketones, acid chlorides, and imines [1]. Transformation of aldehydes to alcohols, which is one of the most fundamental and useful processes in the field of synthetic chemistry, is routinely carried out using reductants such as $LiAlH_4$ and other metallic hydrides, hydrogen with platinum and ruthenium catalysts, boranes, hydrazine-KOH, and Zn-Hg/HCl [2]. Besides, most of the alkyl and aryl aldehydes are usually converted to the corresponding alcohols by borohydride under mild conditions [3].

The target-selective reaction of aldehyde-functionalized dyes has been ingeniously used for the construction of reaction-based probes for a number of important chemical species such as cyanide [4], sulfide [5], bisulfite [6], glutathione [7], and hypochlorous acid [8]. In particular, for the visual detection of cysteine and homocysteine, reactions of aldehydes to afford thiazolidine, which are accompanied by a marked fluorescence or color change, have been successfully employed [9]. In addition, fluorogenic aldehydes have been used for monitoring the progress of aldol reactions based on the formation of highly fluorescent aldol products [10]. However, to the best of our knowledge, the afore-mentioned simple but valuable aldehyde-to-alcohol transformation has hardly been used to design probe systems for a specific reducing species.

The development of efficient and practical hydrogen storage methods with high hydrogen densities has recently become imperative for fuel cell technology [11]. In this regard, borohydrides have attracted much research interest as practically viable hydrogen storage systems [12]. However, regeneration of the used borohydride (metaborate, BO_2^-) is the most demanding problem hindering practical application. For this, accurate assay of the regenerated borohydride is required, but the task is especially challenging [13]. Therefore, an easy assay for the rapid and accurate determination of borohydrides is indispensable for chemical as well as industrial applications.

At present, two traditional methods are used for the determination of borohydrides: iodometric titration and volumetric analysis of the evolved hydrogen. In addition, several colorimetric methods based on the reduction of crystal violet [14] and trinitrobenzenesulfonic acid are available [15]. However, there is no report on borohydride-selective fluorescent signaling systems. One thing to note is that the possibility of borohydride signaling by the transformation of 9-anthracenecarboxaldehyde to 9-anthrylmethanol was presented in an earlier literature, but no relevant studies have been conducted [10c].

In this paper, we report selective and sensitive ratiometric fluorescence signaling probes for borohydride based on the well-established aldehyde-to-alcohol reduction. The fluorescence behavior of typical arylaldehydes and their corresponding reduced

* Corresponding author.
E-mail address: skchang@cau.ac.kr (S.-K. Chang).

https://doi.org/10.1016/j.tetlet.2018.11.056
0040-4039/

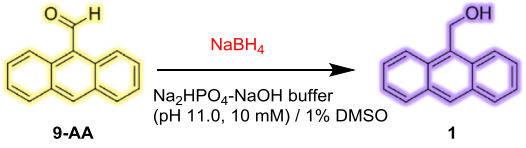
alcohols in aqueous solution was different in terms of quantum yields and emission wavelengths. We exploited this phenomenon to test the selective signaling possibility for an important borohydride reducing agent using the reductive transformation of aldehyde to alcohol. As a practical application, determination of borohydride by means of a microfluidic paper-based analytical device (μPAD) was conducted.

The optimized signaling conditions of the probes for the target borohydride were searched by varying the solvent in phosphate buffer solution (Na_2HPO_4-NaOH buffer, pH 11.0, 10 mM) [16] because borohydride is stable in a strongly alkaline medium and starts to decompose significantly at pH less than 10 [17]. Under the signaling conditions of an alkaline aqueous solution, **9-AA** showed broad absorption bands centered at 365–430 nm (Fig. S1, Supplementary data). Addition of borohydride to the **9-AA** solution resulted in significantly blue-shifted absorption bands at 344, 364, and 383 nm, which are the characteristic vibronic structure of the absorption spectrum of 9-alkylated anthracenes. The observed spectral change was in good agreement with the expected reductive aldehyde-to-alcohol conversion by borohydride (Scheme 1).

Next, the fluorescent borohydride signaling behavior of **9-AA** was investigated. Probe **9-AA** showed a broad emission band near 519 nm, with very weak vibronic emissions at 380–440 nm, in a phosphate buffer solution at pH 11.0 (inset of Fig. 1). The emission behavior of aromatic aldehydes is known to be very weak [18]. Upon reaction with borohydride, the broad band at 519 nm disappeared, and new bands with the characteristic vibronic structure of the anthracene moiety at 392, 409, and 435 nm emerged. The emission profile of the resulting solution was reminiscent of methylanthracene [19]. The fluorescence color concomitantly changed from green to blue under illumination by a hand-held UV lamp.

The large changes in the fluorescence spectrum induced by the borohydride implied the possibility of ratiometric analysis of the signaling behavior. The fluorescence responses were analyzed using the fluorescence intensity ratio of the two diagnostic bands at 519 nm (probe **9-AA**) and 409 nm (alcohol **1**). The fluorescence intensity ratio of the 409 nm and 519 nm bands (I_{409}/I_{519}) changed more than 2000-fold upon the reductive conversion of **9-AA** to alcohol **1** by borohydride. As shown in Fig. 1, the response of **9-AA** toward common alkali, alkaline earth, and transition metal ions is negligible. In the presence of metal ions, the I_{409}/I_{519} ratio changed within a narrow range, between 1.04-fold for Mn^{2+} and 3.47-fold for Zn^{2+} ions. The surveyed anions, too, did not induce any noticeable change in the fluorescence spectra (Fig. S2, Supplementary data).

The borohydride-selective signaling remained unaffected by the presence of most common metal ions as the background (Fig. 2). Actually, borohydride signaling of **9-AA** was irrelevant in the presence of Ag^+ and Hg^{2+} ions owing to the consumption of analyte by redox reaction between these ions and the borohydride [20,21]. However, this interference is not a problem because main purpose of the analytical assay is the determination of analyte concentrations after all possible reactions and interactions with coexisting species have arisen. Common anions also showed nearly no interference with the borohydride-selective signaling of **9-AA** (Fig. S3, Supplementary data). In addition, signaling of borohydride was fast, and a stable response was observed within 10 min (Fig. 3).



Scheme 1. Borohydride signaling by **9-AA**.

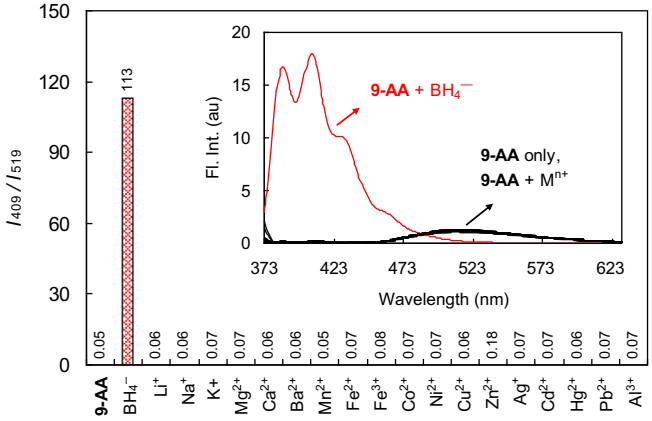


Fig. 1. Selective ratiometric fluorescence signaling of borohydride over metal ions expressed by the I_{409}/I_{519} ratio in phosphate buffer solution (pH 11.0, 10 mM) containing 1% (*v*/*v*) DMSO. Inset: fluorescence spectra of **9-AA** in the presence of borohydride or metal ions. [**9-AA**] = 1.0×10^{-5} M, [BH_4^-] = [M^{n+}] = 1.0×10^{-4} M, [NaOH] = 2.5×10^{-3} M. λ_{ex} = 368 nm.

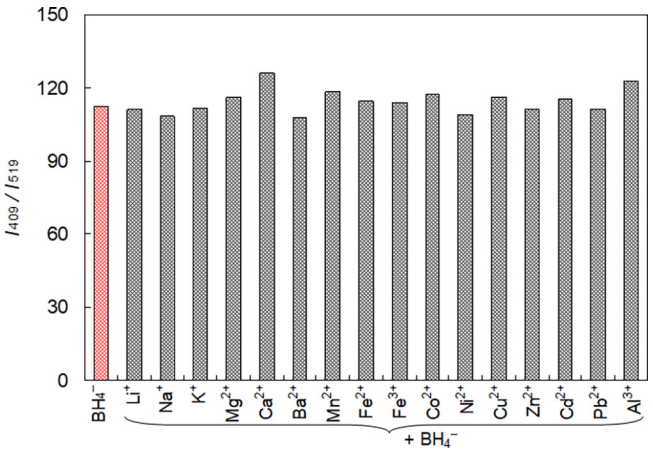


Fig. 2. Competitive fluorescence signaling behavior of **9-AA** for borohydride in the presence of metal ions as the background. [**9-AA**] = 1.0×10^{-5} M, [BH_4^-] = [M^{n+}] = 1.0×10^{-4} M, [NaOH] = 2.5×10^{-3}M. λ_{ex} = 368 nm.

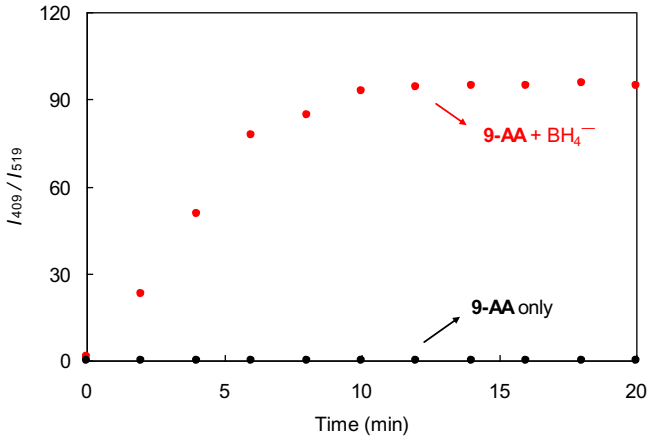


Fig. 3. Time course plot of the fluorescence signaling of borohydride in phosphate buffer solution (pH 11.0, 10 mM) containing 1% (*v*/*v*) DMSO. [**9-AA**] = 1.0×10^{-5} M, [BH_4^-] = 1.0×10^{-4} M, [NaOH] = 2.5×10^{-3} M. λ_{ex} = 368 nm.

The rate constant of borohydride signaling by **9-AA** was calculated to be 0.356 min^{-1} from the time course plot (Fig. S4, Supplementary information).

The quantitative analytical behavior of borohydride signaling by **9-AA** was investigated by fluorescence titration (Fig. 4). As the concentration of borohydride increased, the fluorescence intensity at 409 nm increased steadily, while the intensity at 519 nm decreased. The detection limit for the borohydride signaling of **9-AA** was estimated to be 7.4 μM (0.11 ppm) from the plot of the fluorescence intensity ratio I_{409}/I_{519} vs. log[BH_4^-] following the literature method (Fig. S5, Supplementary data) [22]. We considered that such high analytical sensitivity is not a critical issue for the assay of the borohydride in many practical purposes. However, analysis of low concentration of borohydride would be a requisite for some applications, such as monitoring of the borohydride decomposition in solution and determination of the reduction rate of various organic compounds [23].

Borohydride signaling of **9-AA** was attributed to the reduction of the aldehyde functionality of **9-AA** to alcohol of **1** (Scheme 1), as confirmed by ^{1}H NMR measurements. For instance, upon interaction with 2 equiv of borohydride in deuterated DMSO, the resonance of the aldehyde proton in **9-AA** at 11.45 ppm (indicated by a red asterisk) disappeared, and a new resonance ascribable to the characteristic methylene protons of **1** at 5.43 ppm (indicated with a blue asterisk) could be identified (Fig. 5). In the ^{13}C NMR spectrum, the postulated process could be evidenced by the disappearance of the aldehydic carbon resonance at 193 ppm and the appearance of a new peak for the methylene carbon of **1** at 55.8 ppm (Fig. S6, Supplementary data). This conversion was also confirmed by the diagnostic peak at m/z = 208.11 corresponding to signaling product **1** (calcd. for $C_{15}H_{12}O$ = 208.09) in the mass spectrum (Fig. S7, Supplementary data).

To test the generality of the borohydride signaling based on aldehyde-to-alcohol reduction, the fluorescence signaling properties of 1-pyrenecarboxaldehyde (**1-PA**) were evaluated under the optimized conditions using phosphate buffer (Na_2HPO_4-NaOH buffer, pH 11.0, 10 mM) containing 20% DMSO (Scheme 2). Under the signaling conditions in alkaline aqueous solution, **1-PA** exhibited two broad absorption bands centered at 368 and 396 nm (Fig. S8, Supplementary data). Upon treatment with borohydride, **1-PA** revealed significantly blue-shifted absorption bands at 312, 324, and 337 nm at the expense of the original bands at 368 and 396 nm.

In fluorescence measurement, probe **1-PA** showed a broad emission at 473 nm in phosphate buffer solution (pH 11.0, 10 mM). Upon treatment with borohydride, slightly broad but characteristic vibronic emissions of the pyrene fluorophore emerged between 370 nm and 395 nm (inset of Fig. 6). Under the measurement conditions, commonly encountered metal ions and anions gave no responses (Fig. 6 and Fig. S9, Supplementary data). Ratiometric analysis using the emission intensity ratio of the two characteristic wavelengths at 377 nm and 473 nm (I_{377}/I_{473}) for **1-PA** clearly showed the borohydride selectivity of the probe over metal ions and anions. The borohydride-selective signaling of **1-PA**, too, was unaffected by the presence of background metal ions (Fig. S10, Supplementary data) and anions (Fig. S11, Supplementary data), except for Fe^{2} and Fe^{3+}. These two ions induced somewhat reduced borohydride signals (Fig. S10a, Supplementary data), however, such interference was readily circumvented by the ratiometric analysis using the ratio I_{377}/I_{473}. As shown in Fig. S10b

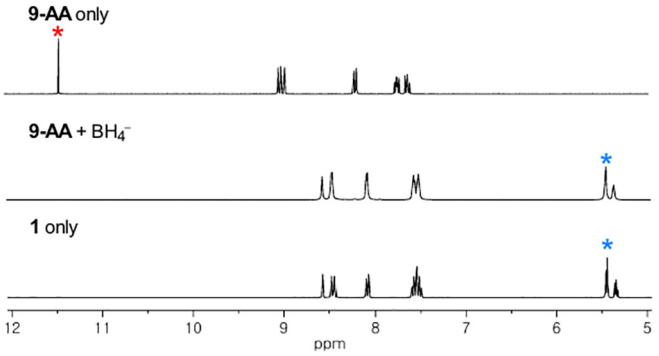
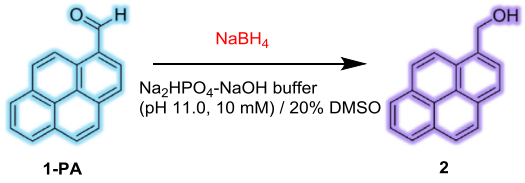


Fig. 5. Partial ^{1}H NMR spectra of **9-AA** before and after treatment with borohydride and reference **1** in DMSO d_6. [**9-AA**] = [**1**] = 5.0 × 10^{-3} M. [BH_4^-] = 1.0 × 10^{-2} M. Peaks indicated by red and blue asterisks are due to the aldehyde and methylene protons of **9-AA** and **1**, respectively.



Scheme 2. Borohydride signaling by **1-PA**.

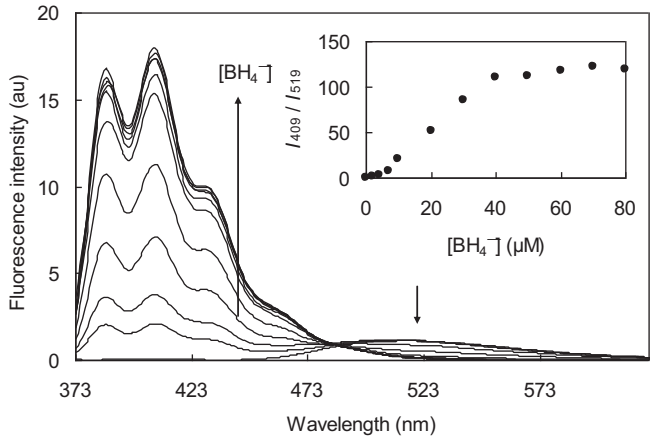


Fig. 4. Fluorescence titration of **9-AA** with borohydride. [**9-AA**] = 1.0 × 10^{-5} M, [BH_4^-] = 0–8.0 × 10^{-5} M, [NaOH] = 2.5 × 10^{-3} M. λ_{ex} = 368 nm.

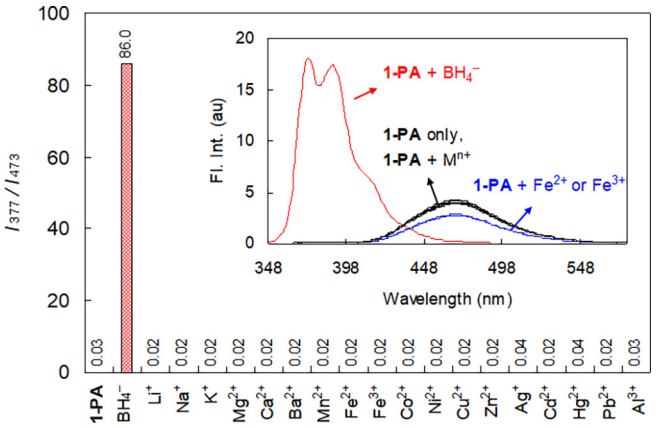


Fig. 6. Selective ratiometric fluorescence signaling of borohydride over other common metal ions by **1-PA**, as expressed by the ratio I_{377}/I_{473}. Inset: fluorescence spectra of **1-PA** in the presence of borohydride or metal ions. [**1-PA**] = 1.0 × 10^{-5} M, [BH_4^-] = [M^{n+}] = 5.0 × 10^{-4} M, [NaOH] = 5.0 × 10^{-3} M in phosphate buffer solution (pH 11.0, 10 mM) containing 20% (*v*/*v*) DMSO. λ_{ex} = 343 nm.

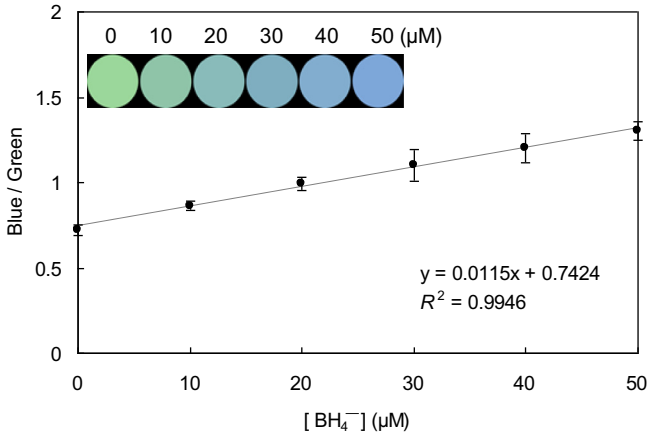


Fig. 7. Plot of fluorescent borohydride signaling with **9-AA**-impregnated μPAD expressed by changes in the ratio of blue and green channel levels (Blue/Green). Inset: picture of μPAD under illumination by a UV lamp. $[BH_4^-] = 0–5.0 \times 10^{-5}$ M, $[NaOH] = 2.5 \times 10^{-3}$ M in a phosphate buffer solution (pH 11.0, 10 mM) containing 1% (*v*/*v*) DMSO.

(Supplementary data), ratiometric plot revealed that the signaling of the **1-PA**-borohydride system varied by less than 10% in the presence of the relevant metal ions, including Fe^{2+} and Fe^{3+}, as the background. Signaling of borohydride by **1-PA** was fast, and a stable response could be observed within 15 min (Fig. S12, Supplementary data).

Fluorescence titration of **1-PA** with borohydride afforded a useful calibration plot for up to 150 μM borohydride (Fig. S13, Supplementary data). With increasing borohydride concentration, the emission intensity at 473 nm decreased while the strong vibronic emissions at 370–395 nm increased. The concentration-dependent responses of **1-PA** toward borohydride were analyzed by ratiometry using the fluorescence intensity ratio I_{377}/I_{473}. The detection limit was estimated to be 15.7 μM (0.23 ppm) from the plot of I_{377}/I_{473} vs. $\log[BH_4^-]$ (Fig. S14, Supplementary data).[22] Borohydride signaling by probe **1-PA** was realized by the reduction of **1-PA** to 1-pyrenemethanol **2** (Scheme 2), as confirmed by ^{1}H NMR (Fig. S15, Supplementary data) and mass spectral data (obsd. $m/z = 231.8$, calcd. for $C_{17}H_{12}O = 232.1$) (Fig. S16, Supplementary data).

The application of the investigated borohydride signaling system was tested using μPAD, which is advantageous for the convenient on-field or out-of-laboratory analysis of various compounds. [24] μPAD prepared by wax printing was impregnated with an acetonitrile solution of **9-AA** (1.0×10^{-2} M) and dried in air. Treatment of the μPAD with solutions of various concentrations of borohydride resulted in a color change from green to blue. The developed image was captured with a smartphone (iPhone 7, Apple Inc.) under illumination by a hand-held UV-lamp (VILBER, VL-4LC). Because the color change was mostly in the green and blue region, we plotted the changes in the ratio of blue and green levels (Blue/Green = (value of blue channel)/(value of green channel)) as a function of $[BH_4^-]$ (Fig. 7). The plot showed a linear relationship for up to 5.0×10^{-5} M borohydride concentration ($R^2 = 0.9946$), which could be exploited for the determination of borohydride concentrations in practically relevant chemical and industrial analytes.

In summary, a new reaction-based chemosignaling system for chemically and industrially important borohydride was devised based on the aldehyde-to-alcohol transformation of simple arylaldehydes. Two representative aldehydes based on anthracene (**9-AA**) and pyrene (**1-PA**) backbone were tested, and their signaling behavior was determined. The tested aldehydes exhibited pronounced borohydride-selective fluorescent signaling behavior over other industrially and environmentally important metal ions and anions. The detection limit was found to be 7.40 μM for **9-AA** and 15.7 μM for **1-PA**. The practical application of the proposed method was demonstrated by using an easy-to-use and handy μPAD.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tetlet.2018.11.056. These data include MOL files and InChiKeys of the most important compounds described in this article.

References

[1] L. Banfi, E. Narisano, R. Riva, N. Stiasni, M. Hiersemann, T. Yamada, T. Tsubo, Encyclopedia of Reagents for Organic Synthesis, John Wiley & Sons, Weinheim, 2014, ch. Sodium borohydride.
[2] M.B. Smith, March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, 6th ed., John Wiley & Sons Inc:, New Jersey, 2007, pp. 1197–1203.
[3] M. Periasamy, M. Thirumalaikumar, J. Organomet. Chem. 609 (2000) 137–151.
[4] (a) K.-S. Lee, H.-J. Kim, G.-H. Kim, I. Shin, J.-I. Hong, Org. Lett. 10 (2008) 49–51; (b) R.M. El-Shishtawy, F.A.M. Al-Zahrania, Z.M. Al-amshany, A.M. Asiri, Sens. Actuator B-Chem. 240 (2017) 288–296.
[5] J. Lv, F. Wang, J. Qiang, X. Ren, Y. Chen, Z. Zhang, Y. Wang, W. Zhang, X. Chen, Biosens. Bioelectron. 87 (2017) 96–100.
[6] (a) X.-F. Yang, M. Zhao, G. Wang, Sens. Actuator B-Chem. 152 (2011) 8–13; (b) X. Cheng, P. He, Z. Zhong, G. Liang, Luminescence 31 (2016) 1372–1378; (c) S. Yu, X. Yang, Z. Shao, Y. Feng, X. Xi, R. Shao, Q. Guo, X. Meng, Sens. Actuator B-Chem. 235 (2016) 362–369; (d) H. Agarwalla, S. Pal, A. Paul, Y.W. Jun, J. Bae, K.H. Ahn, D.N. Srivastava, A.J. Das, Mater. Chem. B 4 (2016) 7888–7894.
[7] C. Xu, H. Li, B. Yin, Biosens. Bioelectron. 72 (2015) 275–281.
[8] P. Wei, W. Yuan, F. Xue, W. Zhou, R. Li, D. Zhang, T. Yi, Chem. Sci. 9 (2018) 495–501.
[9] (a) O. Rusin, N.N.S. Luce, R.A. Agbaria, J.O. Escobedo, S. Jiang, I.M. Warner, F.B. Dawan, K. Lian, R.M. Strongin, J. Am. Chem. Soc. 126 (2004) 438–439; (b) W. Lin, L. Long, L. Yuan, Z. Cao, B. Chen, W. Tan, Org. Lett. 10 (2008) 5577–5580; (c) K.-S. Lee, T.-K. Kim, J.H. Lee, H.-J. Kim, J.-I. Hong, Chem. Commun. (2008) 6173–6175.
[10] (a) F. Tanaka, N. Mase, C.F. Barbas III, J. Am. Chem. Soc. 126 (2004) 3692–3693; (b) H.-M. Guo, F. Tanaka, J. Org. Chem. 74 (2009) 2417–2424; (c) N. Mase, K. Takabe, F. Tanaka, Tetrahedron Lett. 54 (2013) 4306–4308, In this paper, the authors reported novel fluorogenic probe based on 9-anthracenecarboxaldehyde for the monitoring of chemical transformations such as aldol reaction and acetal formation.
[11] J. Mao, D.H. Gregory, Energies 8 (2015) 430–453.
[12] T. Vilarinho-Franco, R. Tenu, J. Delmas, M. Heitzmann, P. Capron, C. Goutaudier, Energy Procedia 36 (2013) 1192–1201.
[13] M. Huang, H. Zhong, L. Ouyang, C. Peng, X. Zhu, W. Zhu, F. Fang, M.J. Zhu, Alloy. Compd. 729 (2017) 1079–1085.
[14] C.N. Rudie, P.R. Demko, J. Am. Oil Chem. Soc. 56 (1979) 520–521.
[15] H.C. Brown, A.C. Boyd Jr., Anal. Chem. 27 (1955) 156–157.
[16] D.D. Perrin, B. Dempsey, Buffers for pH and Metal Ion Control, Chapman and Hall Ltd: London, 1974, p. 151. Phosphate buffer (Na_2HPO_4-NaOH buffer, pH 11.0) was prepared using 0.2 M Na_2HPO_4 and 0.4 M NaOH solution.
[17] Rohm and Haas Sodium Borohydride Digest, The Dow Chemical Company, 2003.
[18] E.P. Crowell, C. Varsel, J. Anal. Chem. 35 (1963) 189–192.
[19] K. Kubo, R. Ishige, T. Sakurai, Talanta 49 (1999) 339–344.
[20] F.P. Mehr, M. Khanjani, P. Vatani, Orient. J. Chem. 31 (2015) 1831–1833.
[21] M.M. Cook, J.A. Lander, J. Appl. Photogr. Eng. 5 (1979) 144–147.
[22] M. Shortreed, R. Kopelman, M. Kuhn, B. Hoyland, Anal. Chem. 68 (1996) 1414–1418.
[23] D.A. Werner, C.C. Huang, D. Aminoff, Anal. Biochem. 54 (1973) 554–560.
[24] A.W. Martinez, S.T. Phillips, G.M. Whitesides, E. Carrilho, Anal. Chem. 82 (2010) 3–10.