JOC*Note*
pubs.acs.org/joc

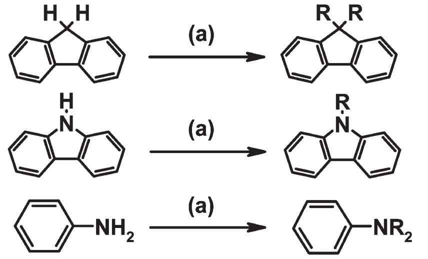
Facile C−H Alkylation in Water: Enabling Defect-Free Materials for Optoelectronic Devices

Gunin Saikia and Parameswar K. Iyer*

Department of Chemistry, Indian Institute of Technology, Guwahati 781039, Assam, India

pki@iitg.ernet.in

Received January 13, 2010



(a) = R-X, aq. NaOH, PTC, 70 °C. R = C_6H_{13}

A facile method for the alkylation of fluorene achieved via direct C−H alkylation under aqueous conditions is reported, wherein the formation of fluorenone is inhibited, resulting in the exclusive formation of the desired dialkyl-substituted fluorene monomer. As a proof of concept, this method has also been successfully extended to perform N-alkylation of carbazole, diphenylamine, and N,N-dialkylation of aniline in high yields.

Polydialkylfluorenes possess excellent photophysical, thermal, and processing properties, which have made them one of the most promising materials presently being used to fabricate blue-light emitting diodes (LEDs) and biosensor applications.[1,2] The presence of a rigidly planar biphenyl unit with a methylene bridge allows functionalization at the 9-position resulting in high solubility and processability in the resulting polymers. However, several studies have demonstrated that poly(9,9-dialkylfluorene) degrades to give a longer wavelength emission band in the presence of oxygen over time which is more intense in electroluminescence (EL) than in photoluminescence (PL).[3] Numerous papers attribute this band to the formation of emissive fluorenone units in the polymer backbone[4] that intensifies with increasing fluorenone concentration. Thus, under all circumstances, the 9-position hydrogens in fluorene are the sole culprits that undergo oxidation to form fluorenone units when subjected to high thermal conditions during device fabrication or photo-degradation when exposed to light. Hence, finding an appropriate and facile method for the preparation of "defect free" alkyl-substituted fluorene monomers not only remains a challenge but would also be a striking achievement to produce stabilized blue light emitting devices.

A common practice associated with C9 alkylation reactions of fluorene reported so far utilizes high-boiling solvents such as DMSO, DMF, HMPA, etc. as the reaction medium.[5−10] Yields obtained by these methods were in the range of 63−80%. DMSO, a solvent used very often, has several drawbacks, most prominently its environmentally adverse impact and second the tedious reaction workup for the separation of DMSO from the final product. Few other alkylation methods reported in the literature have utilized a combination of different solvents with metal catalysts, phase-transfer catalysts (PTCs), very strong bases, multiple synthetic steps, and extreme reaction conditions,[7−10] yet the art of making defect-free dialkylated fluorene has not been achieved. Employing the above routes affects the overall economy of the reaction and needs extraordinary precautions and specialized conditions for obtaining defect-free dialkylated product. This encouraged us to investigate a simpler route for the dialkylation of fluorene that would be economical, environmental friendly, and high yielding in contrast to the existing methods. The reactivity of the C−H bond present at the 9-position of "unsubstituted fluorene" is extremely poor compared to the fluorene molecule having electron-withdrawing halogen substituents at the 2,7-positions or only at the 2-position. Hence, activation of the C−H bond in "unsubstituted fluorene" is predominantly challenging owing to which this compound has been avoided or overlooked for alkylation reactions. In this paper, we demonstrate that alkylation of "unsubstituted fluorene" can be performed by means of an uncomplicated and facile route, allowing insertion of a wide variety of alkyl chains on the 9-position of fluorene in exceptional yields. Importantly, we establish that this alkylation route could be extended to

---

(1) Grell, M.; Knoll, W.; Lupo, D.; Meisel, A.; Miteva, T.; Neher, D.; Nothofer, H.-G.; Scherf, U.; Yasuda, A. *Adv. Mater.* **1999**, *11*, 671–675.

(2) (a) Gaylord, B. S.; Heeger, A. J.; Bazan, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 896–900. (b) Wang, S.; Gaylord, B. S.; Bazan, G. C. *Adv. Mater.* **2004**, *16*, 2127–2132.

(3) (a) Weinfurtner, K.-H.; Fujikawa, H.; Tokito, S.; Taga, Y. *Appl. Phys. Lett.* **2000**, *76*, 2502–2504. (b) Uckert, F.; Tak, Y. H.; Müllen, K.; Bässler, H. *Adv. Mater.* **2000**, *12*, 905–908.

(4) (a) Lee, J.-I.; Klaerner, G.; Miller, R. D. *Chem. Mater.* **1999**, *11*, 1083–1088. (b) List, E. J. W.; Guentner, R.; Scanducci de Freitas, P.; Scherf, U. *Adv. Mater.* **2002**, *14*, 374–378. (c) Scherf, U.; List, E. J. W. *Adv. Mater.* **2002**, *14*, 477–487. (d) Zojer, E.; Pogantsch, A.; Hennebicq, E.; Beljonne, D.; Brédas, J. L.; Scandiucci de Freitas, P.; Scherf, U.; List, E. J. W. *J. Chem. Phys.* **2002**, *117*, 6794–6802.

(5) (a) Murphy, W. S.; Hauser, C. R. *J. Org. Chem.* **1966**, *31*, 85–88. (b) González, J. J.; García, N.; Gómez-Lor, B.; Echavarren, A. M. *J. Org. Chem.* **1997**, *62*, 1286–1291.

(6) (a) Pie, Q.; Yang, Y. *J. Am. Chem. Soc.* **1996**, *118*, 7416–7417. (b) Belfield, D. K.; Schafer, K. J.; Mourad, W.; Reinhardt, B. A. *J. Org. Chem.* **2000**, *65*, 4475–4481. (c) Fujiwara, S.-I.; Maeda, H.; Matsuya, T.; Shin-I., T.; Kambe, N.; Sonoda, N. *J. Org. Chem.* **2000**, *65*, 5022–5025.

(7) Fedorynski, M.; Wojciechowski, K.; Matacz, Z.; Makosza, M. *J. Org. Chem.* **1978**, *43*, 4682–4684.

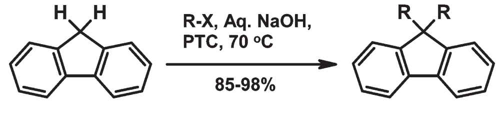
(8) Xia, C.; Advincula, R. C. *Macromolecules* **2001**, *34*, 6922–6928.

(9) Leonetti, F.; Favia, A.; Rao, A.; Aliano, R.; Paluszcak, A.; Hartmann, R. W.; Carotti, A. *J. Med. Chem.* **2004**, *47*, 6792–6803.

(10) (a) Ranger, M.; Rondeau, D.; Leclerc, M. *Macromolecules* **1997**, *30*, 7686–7691. (b) Hagaman, E. W.; Lee, S. K. *Energy Fuels* **1999**, *13*, 1006–1014. (c) Stigers, K. D.; Koutroulis, M. R.; Chung, D. M.; Nowick, J. S. *J. Org. Chem.* **2000**, *65*, 3858–3860. (d) Cho, S. Y.; Grimsdale, A. C.; Jones, D. J.; Watkins, S. E.; Holmes, A. B. *J. Am. Chem. Soc.* **2007**, *129*, 11910–11911.

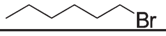
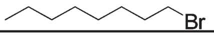
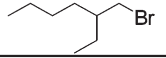
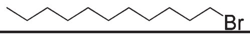
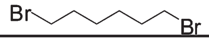
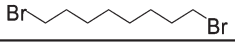
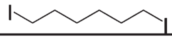
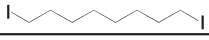
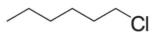
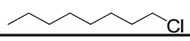
DOI: 10.1021/jo100028d

SCHEME 1. General Synthetic Scheme for Synthesis of Unsubstituted 9,9-Dialkylfluorene[a]



[a] R-X = alkyl halide.

TABLE 1. Yields Obtained for Alkylation of Fluorene with Ten Different Alkyl Halides in Aqueous NaOH, TBAI as PTC at 70 °C

entry no.	RX (alkyl halide)	time (h)	isolated yield (%)
1a		4	96
1b		4	98
1c		4	88
1d		6	88
1e		6	95
1f		6	90
1g		5	90
1h		5	88
1i		7	85
1j		7	87

several other important intermediates and precursors for, e.g., dialkylation of substituted and partially substituted fluorene, N-alkylation of carbazole and diphenylamine, and N,N-dialkylation of aniline, all of which are vital as charge-transporting and luminescent materials for optoelectronic devices and sensors. While working on this challenge, we emphasized on the use of reagents and reaction conditions that are economical, safe, and lead to high-yielding products.

Initial attempts to perform dialkylation on “unsubstituted fluorene” in the presence of excess haloalkane (up to 20 times), aq NaOH, and tetrabutylammonium iodide (TBAI) in DMSO and/or water at elevated temperatures yielded fluorenone as the sole product, which made us realize that the art of making dialkylated fluorene is not so straightforward as perceived and one of the prime reasons for “unsubstituted fluorene” to be overlooked. Several repetitions of the reaction under varying conditions confirmed that the foremost problem in these reactions is trace amounts of oxygen, which was found to be so reactive that in the presence of base, fluorenone was formed as the exclusive product even at temperatures of 35−50 °C. Fluorenone formation can be easily visualized by the distinct yellow color of the isolated product and from the 1720 cm^{-1} ketone peak in the IR data. This trace oxygen has either been ignored or considered to be very trivial while performing the fluorene dialkylation reactions; nonetheless, it is the most perilous condition in obtaining defect-free dialkylated fluorene to be used as intermediates and precursors for numerous applications in foreseeable future. After several failed attempts, modifications were made in the reaction (Scheme-1) so as to obtain the desired dialkylated product in 85−98% yields. (Table-1) To the best of our knowledge, there are no literature reports wherein difunctionalization of alkanes, more specifically “unsubstituted fluorene”, has been successfully performed with a series of haloalkanes in the absence of metal catalysts, organic solvents, inert gases, and high pressure/temperature to obtain desired dialkylation products in high yields as reported here.

Fluorene was reacted with a range of alkyl halides that include chloro-, bromo-, and iodo-terminated hydrocarbons (Scheme-1) at moderate temperature of 70 °C in the presence of 50% aq NaOH and TBAI to obtain the desired dialkylated products in high yields (Table-1). Before the addition of alkyl halide into the reaction mixture, the complete removal of oxygen via repeated freeze−thaw degassing cycles of 15 min each (alternatively warming to room temperature) was performed to remove undesired oxygen gas. Bromoalkanes, due to their economy and better reactivity, have been extensively used for alkylation of fluorene. We have chosen six different types of bromoalkanes that include long-chain, branched-chain, and dibromo-substituted-chain derivatives. Exceptionally high yields of up to 98% (entry 1b) have been obtained on reacting fluorene with 1-bromooctane. Similarly, highly dialkylated fluorene yields were also obtained by the reaction of fluorene with 1-bromohexane (96%), 1-bromoundecane (88%), 2-ethylhexyl bromide (88%), 1,6-dibromohexane (95%), and 1,8-dibromooctane (90%) (entries 1a, 1c−f). Reaction of fluorene with 1,6-diiodohexane (90%) and 1,8-iodooctane (88%) (entries 1g,h) also gave highly dialkylated product yields, whereas less reactive chloroalkanes, i.e., 1-chlorohexane and 1-chlorooctane, when treated with fluorene gave decent yields of 85% and 87% (entries 1i,j) within 7 h under the same conditions, proving the versatility of this reaction for a wide variety of substrates having diverse structure and less reactivity. Since the reaction is performed in aqueous medium the separation of the desired dialkylated product was also very straightforward. All the dialkylated products obtained were well characterized by FT-IR, ^{1}H NMR, ^{13}C NMR, and mass spectroscopy and confirmed to be free from fluorenone (Supporting Information).

Aqueous NaOH was used as a base in the above-described alkylation reaction that facilitated the synthesis of desired dialkylated fluorene in high yields. To ensure that dialkylation of fluorene proceeds smoothly, excess alkyl halide is used in these reactions. It is important that all the fluorene monomers get dialkylated before being exposed to oxygen, since any monoalkylated fluorene remaining in the reaction can still form fluorenone in the presence of oxygen during device fabrication.[11] As discussed earlier, besides the role of base and PTC in the alkylation of fluorene, it is important to ensure that no oxygen is present in these reactions because the fluorene would react with this oxygen to generate undesired fluorenone. Since the conditions reported in Scheme 1 are easy and strikingly efficient, we expect this simple alkylation reaction to be of prime interest to the synthetic community and materials scientists to develop defect-free polyfluorene derivatives.

Furthermore, we observed that the PTC has a prominent role in facilitating the dialkylation reaction, in addition to other favorable conditions required to achieve the dialkylated

---

[11] Gong, X.; Iyer, P. K.; Moses, D.; Xiao, S. S.; Bazan, G. C.; Heeger, A. J. *Adv. Funct. Mater.* **2003**, *4*, 325–330.

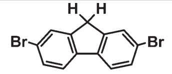
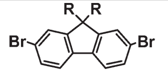
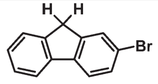
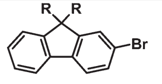
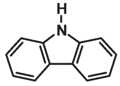
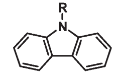
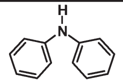
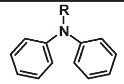
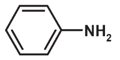
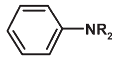
TABLE 2. Comparative Reactivity Study of Fluorene Dialkylation by 1-Bromohexane in the Presence of Various PTCs in Water at 70 °C

entry no.	phase-transfer catalyst (PTC)	time (h)	isolated yield (%)
2a	tetrabutylammonium iodide(TBAI)	4	96
2b	tetrabutylammonium bromide(TBAB)	8	90
2c	tetrabutylammonium chloride(TBAC)	8	60
2d	tetrabutylammonium fluoride (TBAF)	12	50
2e	tetraethylammonium iodide (TEAI)	8	90
2f	tetraethylammonium bromide (TEAB)	10	85
2g	tetraethylammonium chloride (TEAC)	12	50
2h	15-crown-5	12	30
2i	sodium dodecyl sulfate (SDS)	12	15
2j	without PTC	24	12

TABLE 3. Optimizing the Accurate Quantity of PTC Required for Obtaining Maximum Dialkylated Fluorene

entry no.	TBAI quantity	time (h)	isolated yield (%)
3a	0.01 g (2.5 mol %)	10	50
3b	0.02 g (5 mol %)	10	75
3c	0.03 g (7.5 mol %)	10	82
3d	0.046 g (10 mol %)	6	98
3e	0.1 g (25 mol %)	6	98
3f	0.5 g (> 100 mol %)	6	98

TABLE 4. Alkylation of Different Substrates in Water at 70 °C with 1-Bromohexane[a]

entry no.	substrate	product	time (h)	isolated yield (%)
4a			1	99
4b			2	98
4c			8	91
4d			8	75
4e			8	72

[a] $R = C_6H_{13}$.

products. Table 2 represents a comparative reactivity study of the dialkylation of fluorene by 1-bromohexane in the presence of several PTCs at 70 °C. TBAI showed the best performance (entry 2a) both in terms of facilitating higher dialkylated product yields and lesser reaction time compared to all other PTCs examined here. These include tetrabutylammonium bromide (TBAB), tetrabutylammonium chloride (TBAC), tetrabutylammonium fluoride (TBAF), tetraethylammonium iodide (TEAI), tetraethylammonium bromide (TEAB), tetraethylammonium chloride (TEAC), 15-crown-5, sodium dodecyl sulfate (SDS), etc. As observed in Table 2, the product yield is best when performed in the presence of TBAI, followed by TBAB and TEAI (entries 2b and 2e) closely followed by TEAB (entry 2f). A general trend observed in these reactions indicated that the iodide-containing PTC were most efficient (entries 2a and 2e) compared to bromide (entries 2b and 2f), chloride (entries 2c and 2g), and fluoride (entry 2d) both in terms of shorter time durations and higher yields. 15-crown-5 and SDS showed little or no effect on the product yields (entries 2h and 2i). Alkylation performed in the absence of PTC gave very poor product yield in 24 h (entry 2j), validating the use of appropriate PTC in these reactions. Since TBAI is one of the cheapest and most easily available PTCs, its application benefits the overall economy of the alkylation reactions.

After establishing that TBAI is the best PTC, we investigated its accurate quantity required for the best product yields. Table 3 depicts that 10 mol % of TBAI was sufficient for successful conversion of fluorene to dialkylated fluorene (entry 3d). Adding greater than 10 mol % of TBAI did not enhance the yields of dialkylated products (entries 3e and 3f). However, decreasing the amount of TBAI below 10 mol % reduced the yield as well as prolonged the reaction time (entries 3a−c). As part of our objective to bring simpler synthetic routes into the realm of "materials", the above-developed alkylation method was extended to other important substrates and reactions to authenticate this synthetic route for broader applications. Using the same conditions as above (Supporting Information), 2,7-dibromofluorene (entry 4a) and 2-bromofluorene (entry 4b) were dialkylated in outstanding yields of 99% and 98% with 1-bromohexane in a shorter time duration than existing methods. Most notably, there was no fluorenone formation along with any of the final products, confirmed by TLC as well as the absence of ~1720 cm^{-1} ketone peak in IR data.

Furthermore, this alkylation method has been successfully extended to perform N-alkylation of carbazole, diphenylamine, and N,N-dialkylation of aniline. The high yields of 91%, 75%, and 72% obtained for carbazole, diphenylamine, and aniline (Table 4, entries 4c−e) confirm that this facile and economical method is very efficient for the N-alkylation of primary and secondary amines (in addition to C-alkylation) that have been extensively applied in optoelectronic devices as emitting/transporting materials, sensors, and dopants.[12−14] This method represents the first example of aqueous N-alkylation reaction performed with such high efficiency in the absence of metal catalyst, organic solvent, and moderate reaction conditions on this important class of materials with a scope of extension to other challenging N-substitution reaction.

In summary, we have established a simple and economical methodology for the alkylation of fluorene (unsubstituted and substituted) and N-alkylation reactions in aqueous medium whose efficiency is much higher than that of currently applied methods. In view of the fact that these reactions are fundamental in organic synthesis and very critical for the

---

(12) (a) Peng, Z.; Bao, Z.; Yu, L. *J. Am. Chem. Soc.* **1994**, *116*, 6003–6004. (b) Kuo, W.−J.; Hsiue, G.-H.; Jeng, R.-J. *Macromolecules* **2001**, *34*, 2373–2384. (c) Liu, S.; Jiang, X.; Ma, H.; Liu, M. S.; Jen, A. K. Y. *Macromolecules* **2000**, *33*, 3514–3517. (d) Huang, Q.; Evmenenko, G.; Dutta, P.; Marks, T. J. *J. Am. Chem. Soc.* **2003**, *125*, 14704–14705.

(13) (a) Cho, J.-S.; Kimoto, A.; Higuchi, M.; Yamamoto, K. *Macromol. Chem. Phys.* **2005**, *206*, 635–641. (b) Chi, C.-C.; Chiang, C.-L.; Liu, S.-W.; Yueh, H.; Chen, C.-T.; Chen, C.-T. *J. Mater. Chem.* **2009**, *19*, 5561–5571.

(14) (a) Brunner, K.; Dijken, A. V.; Boerner, H.; Bastiaansen, J. J. A. M.; Kiggen, N. M. M.; Langeveld, B. M. W. *J. Am. Chem. Soc.* **2004**, *126*, 6035–6042. (b) Thomas, K. R. J.; Velusamy, M.; Lin, J. T.; Chuen, C.-H.; Tao, Y.-T. *Chem. Mater.* **2005**, *17*, 1860–1866. (c) You, Y.; Kim, S. H.; Jung, H. K.; Park, S. Y. *Macromolecules* **2006**, *39*, 349–356. (d) Tao, Y.; Wang, Q.; Yang, C.; Wang, Q.; Zhang, Z.; Zou, T.; Qin, J.; Ma, D. *Angew. Chem., Int. Ed.* **2008**, *47*, 8104–8107.

development of defect free polymeric materials, this methodology offers advantages not just for fluorene alkylation reactions but also to a variety of N-alkylations. As a proof of concept, we utilized this reaction for the alkylation of primary and secondary aromatic amines, offering a wide variety of potential applications in peptide synthesis. We are presently making efforts to extend this reaction procedure for various other classes of substrates and chemoselective synthesis. Since our protocol proceeds under purely aqueous conditions, utilizes readily available, inexpensive, stable, and nontoxic chemicals and avoids use of metal catalyst, this method is very facile, economical, and environmentally benign and could be applied to wide-ranging alkylation reactions.

Experimental Section

Materials. Alkyl halides, fluorene, and tetrabutylammonium halides were used as received. Freshly distilled solvent was always used for workup and purification processes. Milli-Q grade water was used in all the experiments.

General Procedure Followed for the Dialkylation of Fluorene (1c). Fluorene (0.21 g, 1.26 mmol), 50% aq NaOH, and a catalytic amount of tetrabutylammonium iodide (0.046 g, 10 mol %) were added to a flask. The flask was degassed three times by applying freeze−thaw cycles. 2-Ethylhexyl bromide (1.70 g, 8.82 mmol) was added via syringe (degassed) and the mixture heated at 70 °C continuously for 4 h. The reaction mixture was cooled to room temperature and extracted with chloroform. The organic layer was washed with water and dried over anhydrous sodium sulfate. The solvent was removed under vacuum, and the crude was purified via column chromatography over a small pad of silica gel with 10% chloroform in hexane as the eluent to give the desired dialkylated product. The same procedure was adopted for all substrates (**1a**−**4b**) (Supporting Information).

9,9-Bis(2-ethylhexyl)-9*H*-fluorene (1c): $C_{29}H_{42}$ (0.43 g, 88%); ^{1}H NMR (400 MHz, $CDCl_3$) 7.68 (d, 2H), 7.30 (m, 6H), 1.97 (m, 4H), 0.75 (m, 26H), 0.50 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) 150.5, 141.5, 126.8, 126.5, 124.2, 119.7, 55.0, 44.7, 34.7, 34.7, 33.8, 28.2, 27.0, 22.8, 14.2, 10.4; exact mass 390.3287; HR MS 390.3253.

Acknowledgment. We thank DST, India, and CSIR, India, for financial assistance. G.S. thanks CSIR for a Senior Research Fellowship.

Supporting Information Available: Experimental details and copies of spectral data for the compounds mentioned in the tables. This material is available free of charge via the Internet at http://pubs.acs.org.