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Fluoride-Catalyzed Deblocking as a New Route to Polymeric Urethanes

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Abstract: We report a fluoride-catalyzed deblocking of urethanes as "blocked" isocyanates. Organic and inorganic sources of fluoride ion proved effective for deblocking urethanes and for converting polyurethanes to small molecules. Distinct from conventional deblocking chemistry involving organometallic compounds and high temperatures, the method we describe is metal-free and operates at or slightly above room temperature. The use of fluorescent blocking agents enabled visual and spectroscopic monitoring of blocking/deblocking reactions, and the selected conditions proved applicable to urethanes containing a variety of blocking groups. The method additionally enabled a one pot deblocking and polymerization with α,ω -diols. Overall, this deblocking/polymerization strategy offers a convenient and efficient solution to problems that have limited the breadth of applications of polyurethane chemistry.

Since their discovery by Bayer and co-workers, polyurethane-based materials have elevated to a position of major societal importance.¹⁻² The polyurethane market continues rapid growth, owing to the superior properties of these polymers in numerous applications,³⁻⁵ including as sealants,⁶⁻⁷ adhesives,⁸⁻ ⁹ foams,¹⁰⁻¹¹ and coatings.¹²⁻¹³ Polyurethane properties are tailored by monomer selection,¹⁴⁻¹⁶ involving diisocyanates, diols, and/or polyols.¹⁷ However, even conventional polyurethane chemistry carries significant challenges, including moisture sensitivity and toxicity of the isocyanate monomers.¹⁸⁻¹⁹ "Blocked" isocyanates, obtained by reacting isocyanates with alcohols, are more stable and less toxic, and serve as isocyanate surrogates in polyurethane synthesis.²⁰⁻²² At elevated temperature and in the presence of a catalyst, losing the blocking group regenerates the isocyanate, which polymerizes with diols or polyols. This chemistry presents its own complexities by requiring high deblocking temperatures and variable success depending on the selected isocyanate, solvent, catalyst, and blocking moiety.¹⁷⁻¹⁹ Solvents and co-reactants induce disparities in deblocking temperatures, with higher temperatures promoting isocyanurate formation and degradation.^{17,23} As such, efficient new methods for isocyanate deblocking are needed on both a small and large scale.

Here we report a mild and effective route to isocyanate deblocking involving halide ions, and especially fluoride salts. This methodology was tested successfully on a variety of urethanes, including 1) fluorescent versions that enabled facile spectroscopic characterization of blocking group exchange and 2) precursors to polyurethanes and cross-linked polyurethanes using sequential deblocking and polymerization. Our selection of fluoride ion for these reactions exploits its strong hydrogen bonding interactions with N-H groups of organic compounds.²⁴ As

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shown in **Figure 1**, blocked isocyanates **2a-e** were prepared by reacting toluene diisocyanate (TDI) with selected alcohols in anhydrous dimethylformamide (DMF). The reactions were monitored by infrared spectroscopy, showing the loss of NCO signals (2265 cm⁻¹) and emergence of bands for the carbonyl (1710-1716 cm⁻¹) and N-H (3326 cm⁻¹) groups of urethanes. For the pyrene-blocked sample, ¹H NMR spectroscopy revealed aromatic resonances from 8.05 to 8.35 ppm (from pyrene) and 7.05-7.25 ppm (from TDI), as well as broad N-H resonances at 9.05 and 9.75 ppm (**Figures S1-S23**). The fluorescence spectrum of pyrene-blocked TDI exhibited characteristic vibronic bands at 395 nm (0-0 transition) and 415 nm (0-2 transition), as well as excimer emission at 480 nm.²⁵⁻²⁶

With respect to the deblocking mechanism, we note that anion coordination depends on ionic and dipolar interactions.24-28 The literature describes fluoride ion as a versatile reagent for ureas, involving N-H deprotonation, formation of bifluoride anion (HF2), and subsequent structural transformations.²⁹⁻³¹ For example, the combination of fluoride ion with aromatic ureas produced colorimetric chemosensors, with color changes induced by N-H deprotonation.³²⁻³⁴ Unlike ureas, N-H deprotonation of urethanes can trigger elimination to generate isocyanates by Hofmann-type rearrangement.³⁵⁻³⁶ We investigated urethane deblocking using fluoride, chloride, bromide, and iodide salts. As illustrated in Figure 2, addition of 5 mole percent of tetra-nbutylammonium fluoride (*n*-Bu₄NF) to pyrene-blocked TDI in DMF led to an immediate loss of pyrene fluorescence, due to elimination and precipitation of pyrene. Similar experiments performed with *n*-Bu₄NCl produced only a small fluorescence reduction, while *n*-Bu₄NBr and *n*-Bu₄NI afforded no visual change to the solution. DMF solutions of CsF performed similarly to n-Bu₄NF, prompting our focus on the effect of fluoride ion on urethane deblocking and catalysis of polyurethane formation from blocked isocyanate monomers.

After addition of *n*-Bu₄NF to a DMF solution of pyreneblocked TDI, FTIR analysis of an aliquot taken from the reaction mixture showed the return of a characteristic NCO stretching band at 2265 cm⁻¹ (Figure 3a); additionally, ¹H NMR spectroscopy confirmed the disappearance of N-H signals from 9.1-9.8 ppm, while signals typical of TDI re-emerged (Figures S47-S58). Upon addition of the phenolic TokyoGreen (TG),37-38 a rapid color change, from blue to yellow, was observed as the generated isocyanate was consumed. The TG-blocked TDI products were obtained in 75-80% yield, with structural confirmation by FTIR, ¹H NMR, ESI-MS, and UV-Vis spectroscopy (Figure 3). FTIR spectroscopy showed characteristic bands at 1712 cm⁻¹ and 3326 cm⁻¹ for the carbonyl and N-H groups, respectively and ¹H NMR showed signals corresponding to TG (6.45-7.80 ppm), characteristic TDI resonances from 7.20-7.30 ppm, and broad NH resonances at 9.10 and 9.62 ppm (Figure S51); these data confirmed the desired deblocking and nucleophile exchange. The TG-blocked compound had a bright yellow fluorescence under UV-light, with absorption and photoluminescence (PL) emission at 520 nm and 540 nm, respectively (Figure 3b).

Fluoride-catalyzed deblocking was then tested on polyurethane **2f** (**Figure 1**) that had been prepared from TDI and triethylene glycol ($M_n \sim 30$ kDa, **Figure 4**). This was performed in anhydrous DMF with 5 mole percent *n*-Bu₄NF or CsF, followed by addition of 2 molar equivalents TG (based on TDI) to afford a product which was confirmed spectroscopically (by ¹H NMR,

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Figure 1. Synthetic strategy for isocyanate blocking (urethane formation) and halide-catalyzed deblocking.



Figure 2. Fluoride-catalyzed urethane exchange, from pyrene-to-TG, with photographs of the corresponding solutions.

FTIR, UV-Vis) to have undergone deblocking, and which by GPC showed a reduction in molecular weight from the original polyurethane to the low molecular weight bis-substituted TDI (Figure 4b) in 76% yield. Similar experiments were conducted on conventional blocked isocyanates prepared from TDI or methylene diphenyl diisocyanate (MDI) with propargyl alcohol, isopropanol, and tert-butanol (Figures S1-S46). The relatively low boiling points of these alcohols allowed their removal under vacuum after deblocking, driving the reactions towards product. In a typical reaction, after 30 minutes stirring under vacuum (500 mbar), the mixture was returned to ambient pressure, water was added, and the product was recovered as an orange solid in 75-80% yield. ¹H NMR spectroscopy showed a loss of signals corresponding to the original blocking groups as well as the ΤG resonances S51-S58). appearance of (Figures Approximately 5 mol% F⁻ proved optimal – using lower amounts (2-3 mol %) required longer reaction times (>5 hours) or led to only partial deblocking

The stability of blocked isocyanates makes them attractive for long-term storage and reducing exposure/toxicity concerns. Coupling those advantages with convenient, catalytic polymerization methodology is attractive for the preparation of polyurethanes. As shown in **Figure 5**, blocked isocyanates **2a-e** were used to prepare polyurethanes starting from a slight molar







Figure 4. (a) Fluoride-catalyzed deblocking of polyurethane 2f with TG; (b) GPC traces of 2f (red) and TG-blocked TDI (blue).

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excess of the blocked structure relative to diol. Attempted polymerizations at room temperature led to little increase in molecular weight, but at 50 °C the polymerizations proceeded to to afford **4a-e** with M_n values of 8-10 kDa. When the polymerizations were conducted at 50 °C for 6 hours under vacuum (500 mbar), molecular weight values were higher (M_n reaching 27 kDa) (**Figure 5b**) and PDIs ranged from 2.3-3.1. Precipitation was observed during the polymerizations, and polymers **4a-e** were obtained as white solids in 60-75% yield; notably, in the case of **4e**, residual 1-pyrenemethanol was removed by extraction into CH₂Cl₂ and the polyurethane obtained had no fluorescent signature, confirming the absence of the original blocking group in the structure. Similar experiments were conducted on blocked isocyanates prepared from MDI (**Figures S63-S70**). These polymerizations proceeded



Figure 5. (a) Preparation of polyurethanes **4a-e** by deblocking and polymerization; (b) representative GPC trace of polyurethane **4a** (DMF as mobile phase); (c) temporal evolution of molecular weight of polymer **4a** (estimated by GPC).

Table 1. Number-average molecular weight (M_n) and PDI values of **4a-e** estimated by GPC with DMF as mobile phase (calibrated against polystyrene standards). ^aYields after precipitation.

Blocked Isocyanate	Polyurethane	Mn (g/mol)	PDI	Yield ^a [%]
2a	4a	21000	3.1	73
2b	4b	27000	2.8	70
2c	4c	25000	3.1	72
2d	4d	28000	2.4	75
2e	4e	19000	2.3	58

generated polyurethanes **4f-j** with M_n values of 12-18 kDa (**Table S1**) and with PDI 1.2-1.9. These fluoride-catalyzed polyurethane syntheses, monitored by GPC (**Figure 5c**), exhibited classic stepgrowth polymerization kinetics, with little molecular weight increase early in the reaction timeframe, and rapid molecular weight growth in the later stages. These polymerizations predict easy scalability, as they were conducted easily at the two-gram scale.

We also examined a blocking agent which, following deblocking, undergoes chemistry to render it unreactive with the

generated isocyanate. Oxime blocking agents undergo intramolecular cyclization to yield 3-methylisoxazol-5-one.³⁹⁻⁴⁰ We synthesized oxime-blocked isocyanate **2d**, derived from ethyl acetoacetate oxime (EAO), for fluoride-catalyzed deblocking (**Figure 6**). Addition of F⁻ caused deblocking and release of EAO, and the generated isocyanate was subsequently treated with 4-methylumbelliferone to form the bright blue fluorescent coumarinblocked isocyanate. The product was isolated in 86% yield and characterized by NMR, FTIR, UV-Vis, and fluorescence spectroscopy (**Figures S71-S74**). Notably, polymerizations conducted with **2d** at 50 °C without vacuum afforded polyurethane with M_n value of 28 kDa in good yield 65-75% since removal of deblocked structure from solution is unnecessary (Table 1).



Figure 6. Fluoride-catalyzed urethane exchange, from oxime-tocoumarin, and photographs of the corresponding solutions.

This fluoride-catalyzed methodology is anticipated to be applicable to many types of polyurethane structures and preparative methods. As outlined in **Figure 7**, when a solution of blocked isocyanate **2d** (3 mmol) in DMF was treated with 5 mol% n-Bu₄NF or CsF, followed by addition of 1,1,1-trishydroxymethyl ethane (2 mmol), an insoluble white gel formed as a result of this $A_2 + B_3$ polymerization (**Figure S75**). Going forward, polyurethane-based thin films, coatings, foams, and printed objects from blocked urethanes are anticipated to be similarly amenable to this halide-catalyzed process.



Figure 7. Preparation of cross-linked polyurethane by fluoridecatalyzed deblocking of oxime-blocked TDI (**2d**) and polymerization with 1,1,1-trishydroxymethylethane.

In summary, we described a new method of urethane deblocking and polyurethane formation by exploiting fluoride ion as an efficient and mild catalyst. The reactions are enabled by the propensity of fluoride anion to engage in urethane deblocking and generate reactive isocyanates for polymerization. Our selection of fluorescent blocking agents enabled easy visual and spectroscopic monitoring of these reactions, and we anticipate the methods described to be amenable to numerous polyurethane preparations and formulations.

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REFERENCES

- O. Bayer, W. Siefhen, H. Rinke, L. Orther, H. Schild, *DE Pat*, 728981C, 1937.
 O. Bayer, *Angew. Chem.* 1947, 59, 257.
- [3] D. A. Wicks, Z. W. Wicks, Prog. Org. Coat. 2000, 41, 1.
- [4] A. Lavrenova, D. W. R. Balkenende, Y. Sagara, S. Schrett, Y. C. Simon, C. Weder, J. Am. Chem. Soc. 2017, 139, 4302.
- [5] R. P. Sijbesma, F. H. Beijer, L. Brunsveld, B. J. B. Folmer, J. H. K. K. Hirschberg, R. F. M. Lange, J. K. L. Lowe, E. W. Meijer, *Science*, **1997**, *278*, 1601.
- [6] K. Dusek, M. Duskova-Smrckova, Prog. Polym. Sci. 2000, 25, 1215.
- [7] T. A. Potter, H.G. Schmelzer, R. D. Baker, *Prog. Org. Coat.***1984**, *12*, 321.
 [8] K. P. Somani, S. S. Kansara, N. K. Patel, A. K. Rakshit, *Int. J. Adhes. Adhes.*
- 2003, 23, 269.
 [9] H. Du, Y. Zhao, Q. Li, J. Wang, M. Kang, X. Wang, H. Xiang, J. Appl. Polym. Sci. 2008. 110, 1396.

[10] M. J. Elwell, A. J. Ryan, H. J. M. Gruenbauer, H. C. Van Lieshout, Macromolecules, 1996, 29, 2960.

[11] L. Zhang, H. K. Jeon, J. Malsam, R. Herrington, C. W. Macosko, *Polymer*, **2007**, *48*, 6656.

[12] D. K. Chattopadhyay, K. V. S. N. Raju, Prog. Polym. Sci. 2007, 32, 352.

[13] M. Melchiors, M. Sonntag, C. Kobusch, E. Jürgens, *Prog. Org. Coat.* 2000, 40, 99.

[14] D. A. Wicks, Z. W. Wicks, Prog. Org. Coat. 1999, 36, 148.

[15] B. J. B. Folmer, R. P. Sijbesma, R. M. Versteegen, J. A. J. van der Rijit, E. W. Meijer, *Adv. Mater.* 2000, *12*, 874.

[16] D. W. R. Balkenende, C. A. Monnier, G. L. Fiore, C. Weder, *Nat. Commun.* 2016, 7, 10995.

[17] E. Delebecq, J. – P. Pascault, B. Boutevin, F. Ganachaud, *Chem. Rev.* 2013, 113, 80.

[18] P. Krol, Prog. Mater. Sci. 2007, 52, 915.

[19] M. S. Rolph, A. L. J. Markowska, C. N. Warriner, R. K. O'Reilly, *Polm. Chem.* 2016, 7, 7351.

[20] L. Maisonneuve, O. Lamarzelle, E. Rix, E. Grau, H. Cramail, *Chem. Rev.* 2015, 115, 12407.

[21] D. A. Wicks, Z. W. Wicks, Prog. Org. Coat. 2001, 43, 131.

[22] (5) H. Sardon, A. C. Engler, J. M. W. Chan, J. M. Garcia, D. J. Coady, A. Pascul, D. Mecerreyes, G. O. Jones, J. E. Rice, H. W. Horn, J. L. Hedrick, *J. Am. Chem. Soc.* **2013**, *135*, 16235.

[23] M. A. Semsarzadeh, A. H. Navarchian, J. Appl. Polym. Sci. 2003, 90, 963.
[24] C. Jia, W. Zuo, D. Zhang, X. –J. Yang, B. Wu, Chem. Commun. 2016, 52, 9614.

[25] L. Gai, H. Chen, B. Zou, H. Lu, G. Lai, Z. Li, Z. Shen, *Chem. Commun.*, **2012**. *48*, 10721.

- [26] K. Kalyanasundaram, J. K. Thomas, J. Am. Chem. Soc. 1977, 99, 2039.
- [27] P. A. Gale, Coord. Chem. Rev. 2003, 240, 1.
- [28] Y. Zhou, J. F. Zhang, J. Yoon, Chem. Rev. 2014, 114, 5511.
- [29] M. Boiocchi, L. D. Boca, D. E. Gómez, L. Fabbrizzi, M. Licchelli, E. Monzani, J. Am. Chem. Soc. 2004, 126, 16507.
- [30] Y. Qu, J. Hua, H. Tian, Org. Lett. 2010, 12, 3320.
- [31] A. Roy, D. Kand, T. Saha, P. Talukdar, Chem. Commun. 2014, 50, 5510.

[32] D. E. Gómez, L. Fabbrizzi, M. Licchelli, J. Org. Chem. 2005, 70, 5717.

[33] V. Amendola, G. Bergamaschi, M. Boiocchi, L. Fabbrizzi, L. Mosca, J. Am.

Chem. Soc. 2013, 135, 6345.

[34] J. H. Clark, Chem. Rev. 1980, 80, 429.

[35] L. Rand, M. J. Albinak, J. Org. Chem. 1960, 16, 1837

[36] L. Rand, R. Dolinski, J. Org. Chem. 1965, 30, 48.

[37] L. F. Mottram, S. Boonyarattanakalin, R. E. Kovel, B. R. Peterson, Org. Lett. 2006, 8, 581.

[38] Y. Urano, M. Kamiya, K. Kanda, T. Ueno, K. Hirose, T. Nagano, J. Am. Chem. Soc. 2005, 127, 4888.

[39] J. W. Carter, S. P. Pappas, J. Coat. Technol. 1992, 64, 29.

[40] M. Cocivera, A. Effio, H. E. Chen, S. Vaish, J. Am. Chem. Soc. 1976, 23, 7362.



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We report a new method of urethane deblocking and polyurethane formation using fluoride ion as an efficient catalyst. Fluorescent blocking groups enabled easy visual and spectroscopic monitoring of blocking/deblocking reactions, and we anticipate that this method will offer a convenient and efficient solution to problems that have limited the breadth of applications of polyurethane chemistry.