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# 9-(Guanidinomethyl)-10-vinylanthracene: a suitable fluorescent monomer for MIPs

Huiqi Zhang, Willem Verboom* and David N. Reinhoudt

*Laboratory of Supramolecular Chemistry and Technology, Mesa⁺ Research Institute, University of Twente, PO Box 217, 7500 AE Enschede, The Netherlands*

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**Abstract**—9-(Guanidinomethyl)anthracene derivatives with a bromo (**6**) or a vinyl group (**10**) at the 10-position have been prepared starting from 9-bromoanthracene (**1**). They show 1:1 complexation with carboxylic acids or carboxylates with *K*-values of 1.2–1.4×$10^5$ $M^{-1}$ in deuteriomethanol. Copolymerization of 9-vinylanthracene, 9-(guanidinomethyl)-10-vinylanthracene hydrochloride (**10**), and the 1:1 complex of **10** and ammonium benzoate with ethyleneglycol dimethacrylate (EDMA) gave the polymers in 77–92% yield. © 2001 Elsevier Science Ltd. All rights reserved.

Molecular imprinting is an increasingly important methodology for the introduction of recognition or catalytic sites into highly cross-linked polymeric matrices. A template-directed assembly of specifically functionalized monomers enables the formation of discrete cavities, complementary in both shape and functionality to the original template. Meanwhile molecular imprinting has been successfully applied in a wide variety of disciplines ranging from separation science, catalysis to biomimetic sensors.[1–5]

*Fluorescent* molecularly imprinted polymers (MIPs) are very interesting, since a binding-dependent change of the fluorescence allows the detection of an analyte at very low concentrations.[6] Recently, Wang et al.[7] reported the preparation of a MIP-based fluorescent sensor for D-fructose based on the covalent interaction of a boronic acid-containing anthracene derivative with a *cis*-diol.

In this communication we report our preliminary results on the development of MIPs containing anthracene as a fluorescent tag to which a guanidinium moiety as a recognition element is attached. This allows the detection of suitable carboxylic acids.

Our first approach is outlined in Scheme 1. 9-Bromoanthracene (**1**) was reacted with *N*-(hydroxymethyl)phthalimide (**2**) in a 9:1 mixture of acetic acid and sulfuric acid at 80°C for 24 h to give 9-bromo-10-(phthalimidomethyl)anthracene (**3**) in 52% yield. Subsequent deprotection with hydrazine monohydrate afforded the aminomethyl derivative **4** in 75% yield. Reaction of **4** with *N*,*N*′-(bis-*tert*-butoxycarbonyl)thiourea[8] in the presence of Mukaiyama's reagent gave the BOC-protected guanidinomethylanthracene **5** in 81% yield. Deprotection with trifluoroacetic acid in dichloromethane (1:4 v/v) followed by base treatment of the resulting trifluoroacetate salt afforded 9-bromo-10-(guanidinomethyl)anthracene (**6**)[9] in 87% yield. Unfortunately, in our hands the bromo atom in either compounds **5** or **6** could not be converted into a vinyl group using Stille cross-coupling reaction conditions. However, compound **6** could be used as a model compound to investigate the complexation properties. From a $^1$H NMR dilution experiment a *K*-value of 1.2×$10^5$ $M^{-1}$ was calculated for the 1:1 complex of compound **6** and toluic acid in deuteriomethanol, demonstrating the strong non-covalent interaction between the two components in this polar solvent. Comparison of the fluorescence spectra of ethanol solutions (5×$10^{-5}$ M) of compound **6** and of its 1:1 complex with toluic acid showed a fluorescence enhancement of about 1.5 for the complex. This large increase is very promising for the potential use of this fluorescent recognition element in MIPs.

The desired 9-(guanidinomethyl)-10-vinylanthracene hydrochloride salt (**10**) was obtained as summarized in

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* Corresponding author. Tel.: +31 (0)53 4892977; fax: +31 (0)53 4894645; e-mail: w.verboom@ct.utwente.nl

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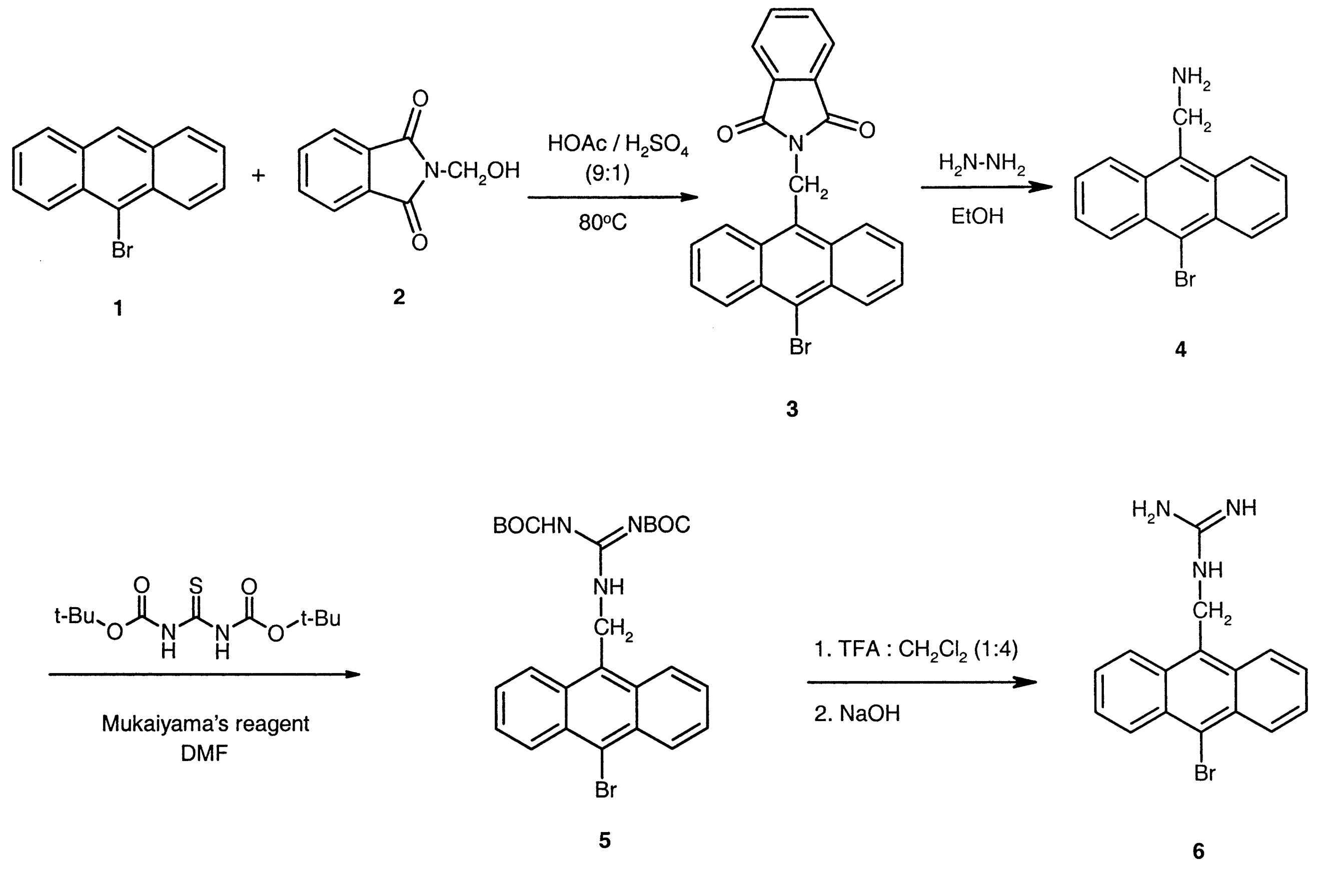
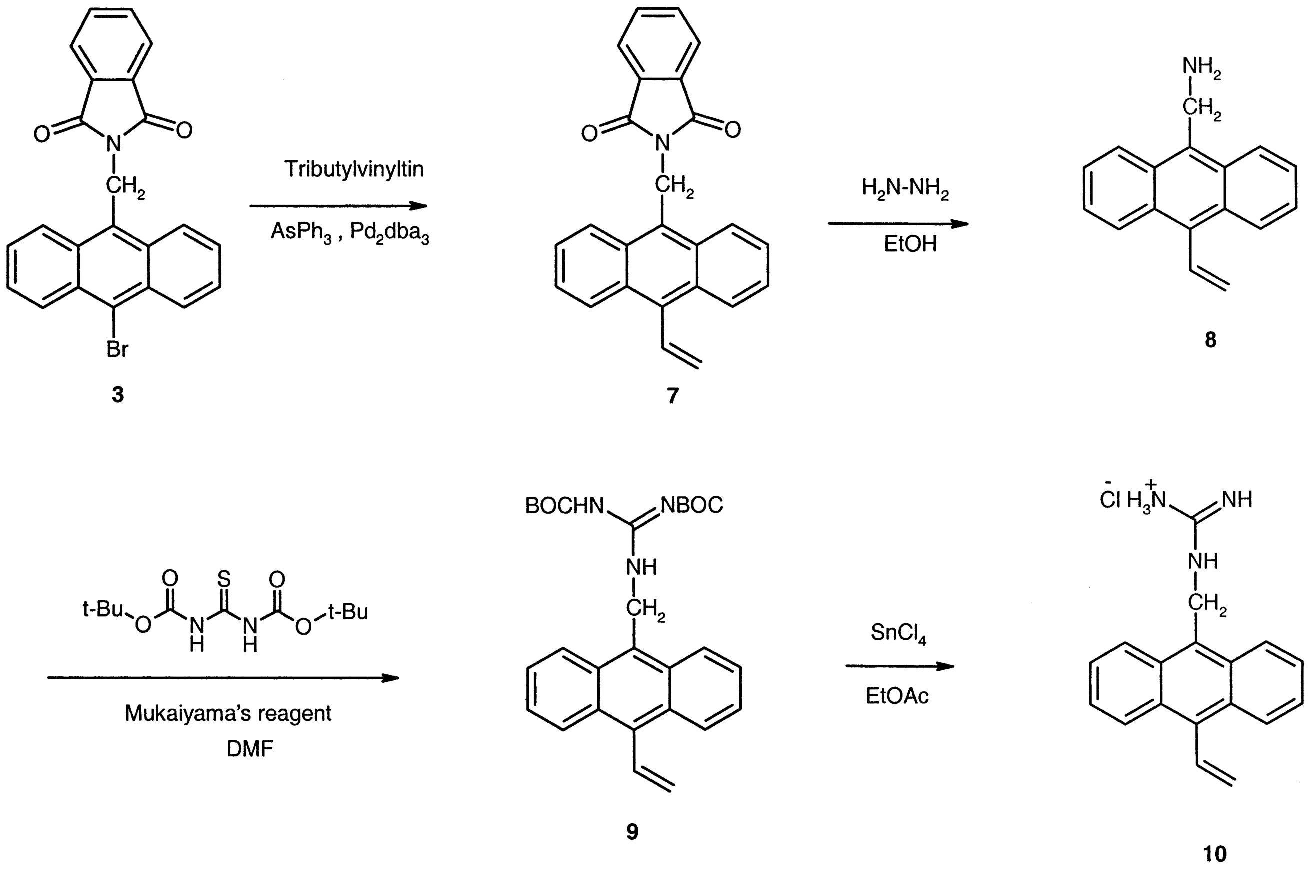


Scheme 1.

Scheme 2. In compound **3** the vinyl group was introduced via a Stille cross-coupling reaction under the conditions developed by Farina and Krishnan.[10] Reaction of 9-bromo-10-(phthalimidomethyl)anthracene (**3**) with 3 equiv. of tributylvinyltin in the presence of tris(dibenzylideneacetone)dipalladium ($Pd_2dba_3$) as a catalyst and $AsPh_3$ as additional ligand (ratio 1:4) for 9 days at 55°C gave, after chromatography, an inseparable mixture of starting compound **3** (25%) and the corresponding vinylanthracene **7** (61%). Prolonged reaction times did not give rise to higher product yields. Deprotection of the mixture of **3** and **7** with hydrazine monohydrate in refluxing ethanol gave a mixture of compound **4** and 9-(aminomethyl)-10-vinylanthracene (**8**) that crystallized from the reaction mixture upon cooling. Column chromatography drastically lowered the yield of compound **8** because of decomposition on the column. Both of the reactions described above were carried out in the presence of a trace of 2,6-di-*tert*-butyl-4-methylphenol as a radical scavenger. Reaction of the mixture of **4** and **8** with *N*,*N'*-(bis-*tert*-butoxycarbonyl)thiourea, as described for the formation of compound **5**, afforded, after chromatography, the BOC-protected guanidinomethylanthracene **9** as a yellow–green solid in 66% yield. Subsequent deprotection of compound **9** with $SnCl_4$[11] in ethyl acetate gave the target compound **10** in quantitative yield. $^1H$ NMR dilution experiments gave *K*-values of $1.2\times10^5$ and $1.4\times 10^5$ $M^{-1}$ for the 1:1 complex of compound **10** with ammonium acetate and tetrabutylammonium acetate, respectively, in deuteriomethanol. Also in the case of compound **10** ($5\times10^{-5}$ M) complexation with different carboxylates, ammonium acetate and -benzoate and tetrabutylammonium acetate, in ethanol induced significant changes in the fluorescence.

The homo- and copolymerization of 9-vinylanthracene (9-VA) have been investigated by different groups because of the potential use of the polymers as semiconductors, photoresist materials, fluorescent probes, etc.[12] The radical polymerization of 9-vinylanthracene is rather slow which is attributed to steric hindrance and the formation of stabilized unreactive dibenzylic radicals inhibiting the addition of the next monomer. Katz[13] obtained the homopolymer of 9-VA in only 16.5% yield after a reaction time of eight days, while even the copolymer with styrene was only isolated in 7–11% yield. Takeuchi et al.[12] found that in the presence of ethylaluminium sesquichloride, 9-VA copolymerizes with methyl methacrylate (MMA) in yields up to 28%, dependent on the conditions. Both Krakovyak et al.[14] and Tiera et al.[15] reported the copolymerization of 9-VA with MMA in yields up to 43% containing 0.5 and 0.12 mol percent anthracene. There is some confusion about the way 9-VA is incorporated in the polymer chain. In principle, there are two possibilities, viz. 1,2-addition and 1,6-addition. For the radical copolymerization of 9-VA and MMA, Tiera et al.[15] concluded that only 1,2-addition of 9-VA took place, while both Takeuchi et al.[12] and Krakovyak et al.[14] found that



Scheme 2.

mainly 1,6-addition and only a small amount of 1,2-addition occurred.

For the ultimate application in MIPs crosslinking of our monomer was performed with ethyleneglycol dimethacrylate (EDMA). As a model reaction first 9-VA was copolymerized with 15 equiv. of EDMA in the presence of AIBN as initiator in THF at 60°C for 60 h to give the polymer in a surprisingly high yield of 92%. Elemental analysis showed the presence of 5.33 mol percent of 9-VA (theoretical value 6.25%). Thermogravimetric analysis revealed that the polymer had good thermal stability (decomposition >250°C). IR spectroscopy pointed to 1,6-addition since the signal at 733 $cm^{-1}$, assigned to the anthracene, disappeared and a new signal at 780 $cm^{-1}$ appeared, which is characteristic for the formed exocyclic double bond.[12] In the same way 9-(guanidinomethyl)-10-vinylanthracene (**10**) was copolymerized in refluxing methanol for 48 h to give the polymer in 83% yield. Copolymerization in the presence of ammonium benzoate using identical reaction conditions gave the pure MIP in 77% yield.

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9. All new compounds show satisfactory spectral data. Compound **6**: mp 168–170°C; $^1H$ NMR ($CD_3OD$): $\delta$ 8.68–8.64 (m, 2 H, ArH), 8.36–8.32 (m, 2 H, ArH), 7.72–7.68 (m, 4 H, ArH), 5.35 (s, 2 H, $CH_2$); MS–FAB (3-nitrobenzyl alcohol) $m/z$ 328.1 ($[M+H]^+$; calcd for $C_{16}H_{15}BrN_3$: 328.2). Compound **10**: mp 232–234°C; $^1H$ NMR ($CD_3OD$): $\delta$ 8.45–8.42 (m, 2 H, ArH), 8.29–8.26 (m, 2 H, ArH), 7.68–7.50 (m, 5 H, ArH+1 vinyl H), 6.09 (dd, 1 H, $J=2.0$ and 11.4 Hz, vinyl H), 5.55 (dd, 1 H, $J=2.0$ and 17.7 Hz, vinyl H), 5.37 (s, 2 H, $CH_2$); $^{13}C$ NMR ($CD_3OD$): $\delta$ 156.6, 135.45, 132.95, 129.50, 128.4, 126.1, 126.0, 125.75, 124.4, 122.65, 122.15, 37.4; MS–FAB (3-nitrobenzyl alcohol) $m/z$ 276.1 ($[M-Cl]^+$, calcd for $C_{18}H_{18}N_3$: 276.1).
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