FEATURE ARTICLE

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From solid-phase synthesis of π-conjugated oligomers to combinatorial library construction and screening†

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Received (in Cambridge, UK) 28th September 2001, Accepted 8th March 2002
First published as an Advance Article on the web 22nd March 2002

A feature article describing concepts for the solid-phase synthesis of π-conjugated oligomers as material-related structures and the translation of the synthetic routes into combinatorial protocols.

Introduction

Significant developments in combinatorial chemistry, namely high-speed synthesis in conjunction with high-throughput screening, have realized new ways to investigate novel bioactive compounds that could not have been envisioned just a few years ago.[1] Subsequently, these promising discoveries in medicinal chemistry pointed the way for material chemists to solve their multi-parameter problems by varying the reaction parameters, structural and functional variables in a combinatorial format.[2,3,4] In general, combinatorial chemistry strategies are going from strength to strength where the understanding of structure–property relationships is important but correlations are not readily predictable by the current theories. This is especially true for the discovery of solid-state materials where the behavior is mainly determined by bulk properties. To date, diverse inorganic solid-state material libraries, *e.g.* for superconducting, magnetoresistant, dielectric, ferroelectric and luminescent materials were successfully designed, optimized and screened for desired properties.[2a] In addition, combinatorial chemistry strategies were extensively used to design novel catalytic systems and powerful screening techniques were developed to monitor catalytic activities.[5,6] More recently, the concepts were used to accelerate material discovery in polymer science.[7] These investigations illustrate clearly that materials science can benefit immensely from combinatorial experiment performance.

A further research field where empirical exploration and serendipity are the most common routes to discovery rather than rational design based on structure–property relationships is the field of organic materials. Although the development of potential materials in the conventional one-at-a-time manner is well-established they are laborious and time-consuming, methodologies for the combinatorial design and screening of organic material-related structures have scarcely been addressed.[2a] In particular, π-conjugated oligomers appear ideally suited for a combinatorial approach. Their construction generally involves an iterative two-step sequence for oligomer growth and their screening for optical and electronic properties should be amenable to parallel processing.

π-Conjugated oligomers have attracted much attention recently as structurally-defined (monodisperse) model compounds for the corresponding (polydisperse) bulk polymers.[8,9] These model compounds of precise length and constitution provide specific information concerning correlations between structural parameters and physical behavior that are necessary to design polymers with improved material performance. In addition to serving as model systems for the parent polymers, these oligomers were recognized as materials in their own right as they show, in some respects, properties superior to those found for polymers. In order to tailor these materials, developmental efforts have been devoted to control not only structural parameters but also to achieve control over the material organization.[10] Today, structurally-defined oligomers are at the core of several emerging technologies. They are promising active materials for electronic and photonic applications, such as organic light-emitting devices,[11] organic field-effect transistors[12,13,14] and photovoltaic cells.[15] Even more, certain high-purity single crystalline π-conjugated oligomers have been found to become superconducting at low temperatures[16] and show amplified light emission in a field-effect transistor device.[17]

Stimulated by advances in macromolecular chemistry, the scientific development of modern electronics tends towards nanotechnology where electronic devices are built on the scale

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Peter Bäuerle (born 1956) studied chemistry at the University of Stuttgart, Germany, where he obtained his Ph.D. degree under the supervision of Professor Franz Effenberger in 1985. From 1985–1986, he worked with Professor Mark S. Wrigthon at the MIT, Boston, USA, where he developed novel conducting polymers and microelectrochemical devices. In 1987, he returned to the Institute of Organic Chemistry at the University of Stuttgart, Germany, and started independent research in the field of conjugated polymers and oligomers. After habilitation, he has been full Professor of Organic Chemistry at the University of Würzburg, Germany, from 1994 to 1996. Since 1996, he holds a chair for Organic Chemistry and is head of the Department of Organic Chemistry II and the Section Mass Spectrometry at the University of Ulm, Germany. His current research activities are centered around organic materials and combinatorial chemistry, including conjugated polymers and oligomers, their functionalization, structure–property relationships, supramolecular chemistry and self-assembling properties and applications in organic devices and molecular electronics. Combinatorial techniques are developed and applied to the accelerated synthesis and characterization of novel conjugated materials, e.g. conjugated oligomers, fluorescent dyes, liquid crystalline materials and pharmaceutically active heterocyclic lead structures. In November 2000, he was awarded with the René Descartes prize of the European Union for his research on π-conjugated systems.

† Dedicated to Professor Manfred Christl on the occasion of his 60th birthday.

DOI: 10.1039/b108846g

of single molecules.[18] As one of the building blocks required for these proposed future molecular electronics, linear π-conjugated oligomers were recently discussed. These compounds could function as molecular wires for information storage and transfer.[9,19]

As will be shown in the following article, the paradigm of combinatorial chemistry provides sophisticated strategies for manipulating the molecular behavior of π-conjugated oligomers as a result of combining the limited scientific understanding with the data collections gained by combinatorial strategies. We illustrate the efforts *en route* to the combinatorial discovery of organic π-conjugated materials. A brief overview of the synthetic strategies to π-conjugated oligomers is provided dealing in detail with the solid-phase synthesis of these material-related structures. Aspects of material design, purification and screening are addressed by discussing the example of the recently published combinatorial approaches to phenylene ethynylene and oligothiophene libraries. It is shown that combinatorial methodologies in materials science can pave the way for a purely rational design of organic π-conjugated materials.

Synthesis of π-conjugated oligomers on solid support

Since Merrifield investigated the use of substituted resins as matrices for the synthesis of peptides in 1963,[20] the synthetic repertoire of solid-phase reactions has rapidly increased. Transition metal-catalyzed cross-coupling reactions of Heck, Stille and Suzuki type have attracted much attention and were successfully adapted to polymer-supported chemistry.[21] These cross-coupling reactions on solid support have been used primarily for the synthesis of one-step coupling products including bisarene, vinylarene and phenylacetylene moieties. Recent examples of solid-phase synthesis demonstrated the possible incorporation of transition metal-catalyzed cross-coupling reactions also for the synthesis of π-conjugated oligomers as will be shown in the following paragraphs.

For the preparation of the π-conjugated systems the general advantages of solid-phase synthesis can be exploited. All of the reported solid-phase approaches to π-conjugated oligomers were initially developed in solution.[22] However, the efforts to transfer the syntheses in solution to solid-supported strategies reflect the major drawbacks of a solution-phase approach to π-conjugated oligomers: (a) transition metal-catalyzed cross-couplings as oligomer growth reactions are often accompanied by undesirable side-reactions such as homocoupling and loss of functionalization; (b) in order to drive the usually moderate yielding cross-coupling reactions to completion and to maximize the conversion of the valuable oligomers, high excesses of monomer building blocks are used; (c) laborious chromatographic purification is necessary at every growth step to separate the desired oligomer from undesired by-products. The adaptation of the optimized solution-phase approaches to the solid support demonstrated clearly the advantages of a polymer-supported strategy to π-conjugated oligomers: (a) cross-coupling and oligomer activation reactions can be driven to completion by using reagents in excess which can be easily removed by filtration; (b) purification of the growing oligomers is simplified by washing the polymer support with appropriate solvents; (c) an optimized solid-phase protocol can be easily translated into a combinatorial synthesis protocol and is amenable to automation; (d) site–site isolation of functionalized monomers within the polymer support allows (to a certain extent) the synthesis of oligomers without the appearance of undesired oligomerizations or polymerizations (pseudo high-dilution conditions).

To profit from the aforementioned advantages of solid-phase synthesis several synthetic approaches to π-conjugated oligomers have been realized.[23–28] These approaches can be categorized into four different synthetic strategies **A**–**D** which are exemplified in Fig. 1.

Stepwise addition approach in one direction: in a stepwise addition approach (**A**) monofunctional monomer building blocks are coupled successively to the resin-bound oligomer. As one terminus of the oligomer is blocked by the polymer support the oligomer grows in one direction. This stepwise approach was shown to be especially suitable for the preparation of small homo- and co-oligomers.

Iterative divergent–convergent approach in one direction: following the iterative divergent–convergent strategy (**B**)

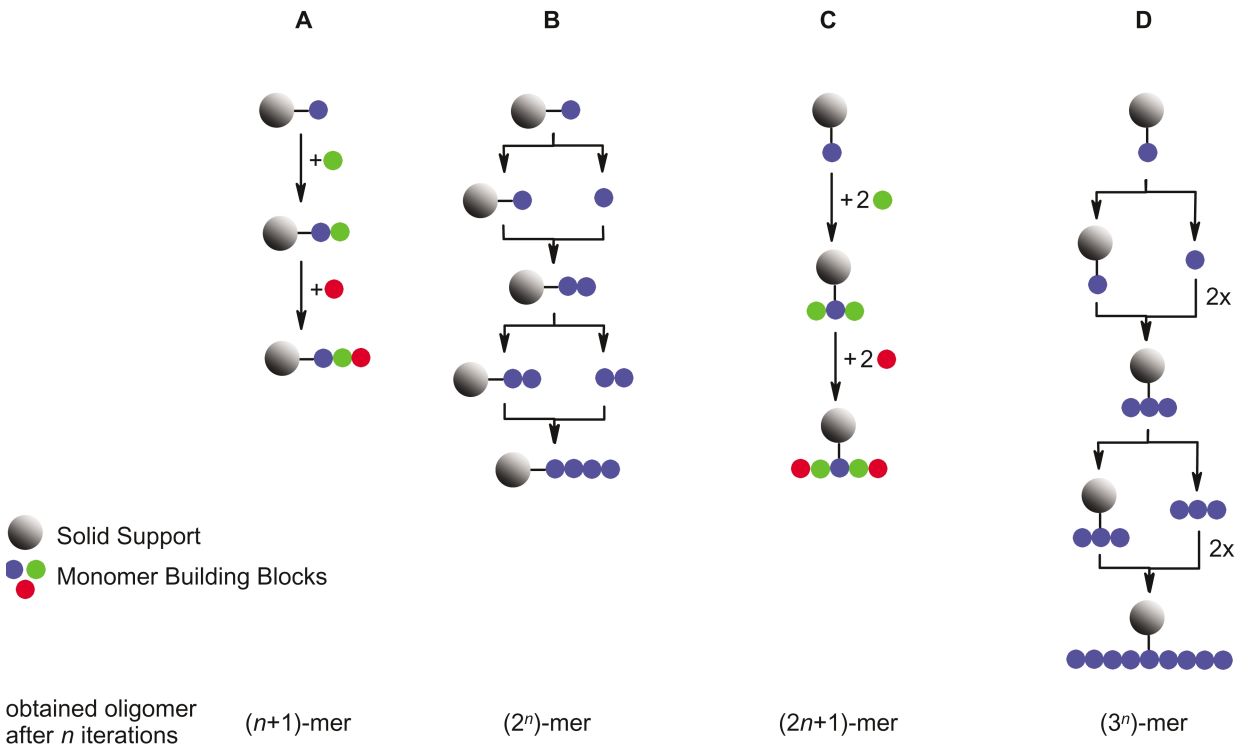


Fig. 1 Synthetic strategies for the solid-phase synthesis of π-conjugated oligomers: (**A**) stepwise addition approach in one direction; (**B**) iterative divergent–convergent approach in one direction; (**C**) bi-directional stepwise addition approach; (**D**) bi-directional iterative divergent–convergent approach.

(which is also termed "fragment condensation approach") the molecular length of the resin-bound oligomer is doubled with each iteration of the reaction sequence. One portion of the growing oligomer is cleaved from the resin and functionalized to be coupled with the remaining portion of the resin-bound oligomer. Relative to the stepwise addition approach, overall yields and purities of the final oligomers are enhanced as the number of the synthetic steps on solid support is reduced for a given oligomer. Since the molecular length is doubled with each iteration isolating the product oligomer from the non-reacted starting materials is simplified because of the difference in molecular size (*e.g.* 4-mer *vs*. 8-mer). This approach proved to be useful for the synthesis of large homooligomers.

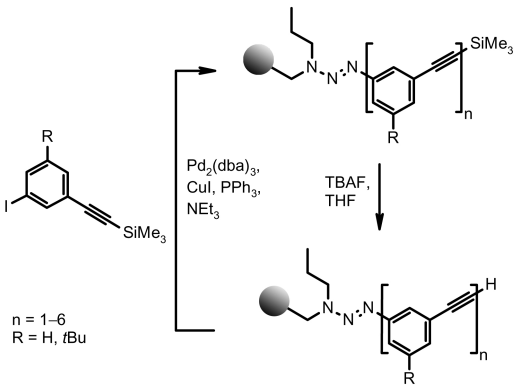
Bi-directional stepwise addition approach: the bi-directional approach **C** allows the rapid oligomer growth in two directions as two monomer building blocks are coupled to the bifunctional polymer-bound substrate. Large symmetrical homo- and co-oligomers become readily available by this stepwise addition approach.

Bi-directional iterative divergent–convergent approach: when the aforementioned iterative divergent–convergent strategy **B** is performed in two directions, as depicted in strategy **D**, the efficiency of the solid-phase synthesis can be increased even more. Starting from a bifunctional resin-bound monomer a repeating nonamer becomes available after only two elongation steps.

Whereas the one-directional approaches **A** and **B** allow the synthesis of odd- and even-numbered oligomers, strategies **C** and **D** can only provide odd-numbered species.

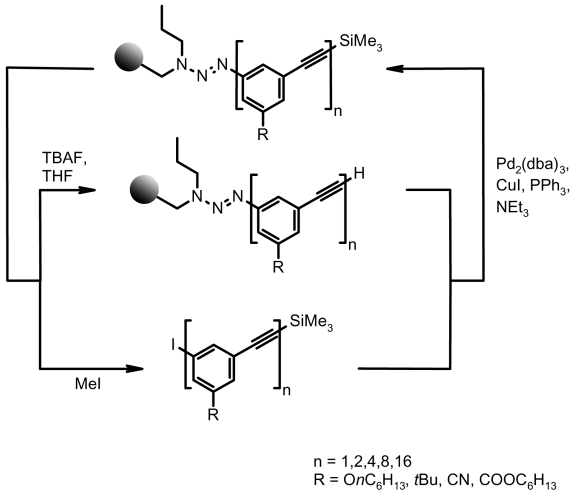
To demonstrate the scope and feasibility of the four synthetic strategies **A**–**D** for the solid-phase synthesis of π-conjugated oligomers some literature examples are highlighted in the following paragraphs.

In 1994, Young and Moore demonstrated the first synthesis of π-conjugated oligomers on solid support by preparing a series of oligo(1,3-phenylene ethynylene)s.[23] Schemes 1 and 2



Scheme 1 Stepwise addition approach to oligo(1,3-phenylene ethynylene)s.

illustrate the elegant synthetic protocols that were developed to synthesize the oligomers in a stepwise addition (strategy **A**) and an iterative divergent–convergent approach (strategy **B**), respectively. In both syntheses, terminal acetylenes and aryl halides were orthogonally masked as trimethylsilylated (TMS) acetylene and 1-aryl-3,3-dialkyltriazene groups, respectively. Following the stepwise addition approach (Scheme 1), silyl protected resin-bound phenylacetylene was deprotected by protiodesilylation with tetrabutylammonium fluoride (TBAF) in THF. The oligomer growth sequence was completed by performing a Sonogashira cross-coupling of the resulting deprotected acetylene with a silyl protected iodinated phenylacetylene using a palladium–copper catalytic system. Iteration of the synthetic sequence afforded (after cleavage with iodomethane) phenylacetylene hexamers in 48–58% overall yield. Furthermore, this polymer-supported synthesis was slightly modified to generate phenylacetylene oligomers in an iterative divergent–convergent fashion (Scheme 2). In a typical



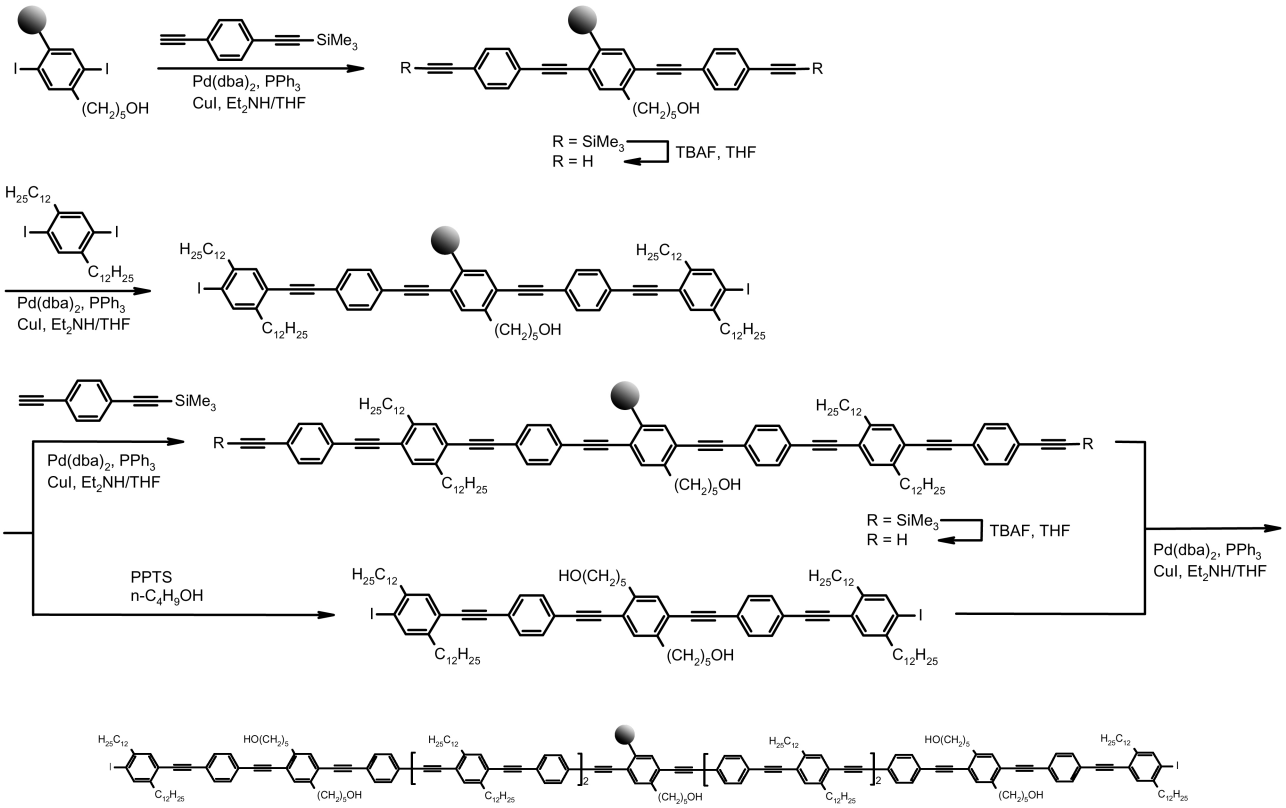
Scheme 2 Iterative divergent–convergent approach to oligo(1,3-phenylene ethynylene)s.

reaction cycle, a portion of the support-bound oligomer was treated with TBAF to remove the trimethylsilyl protecting group of the terminal acetylene. The iodinated phenylacetylene oligomers that were used for the subsequent Pd-catalyzed cross-coupling reaction with the resin-bound acetylene were generated by cleaving another portion of the derivatized polymer support with iodomethane. Following this reaction sequence the synthesis of phenylacetylene hexadecamers was achieved in 50% overall yield after 11 synthetic steps (including the cleavage from solid support with iodomethane).

In a similar fashion, Jones and Tour reported the polymer-supported synthesis of linear oligo(2-alkyl-1,4-phenylene ethynylene)s.[24] Following the iterative divergent–convergent approach (strategy **B**) 2-dodecyl substituted hexadecamers were available.

In contrast to the aforementioned oligo(1,4-phenylene ethynylene) syntheses where a dialkyltriazenyl masking of the aromatic iodides was needed, Huang and Tour reported an efficient synthetic strategy for the preparation of oligo(1,4-phenylene ethynylene)s on solid support that avoids the required masking and unmasking steps for aryl iodides.[25] The synthesis which combines the bi-directional stepwise addition approach (strategy **C**) and a variant of the bi-directional divergent–convergent approach (strategy **D**) is outlined in Scheme 3. 1,4-Diiodo-2,5-di(5'-hydroxypentyl)benzene was utilized as a starting monomer and was affixed to dihydropyran-modified Merrifield resin using pyridinium *p*-toluenesulfonate (PPTS) in dichloromethane. The resin-bound bifunctional monomer was then subjected to a palladium–copper catalyzed Sonogashira cross-coupling with a mono-protected phenyl-1,4-diacetylene monomer to afford the polymer-supported trimer that was (after deprotection with TBAF) cross-coupled with substituted 1,4-diiodobenzene to afford the polymer-supported pentamer. Following the general iterative divergent–convergent approach, a portion of the oligomer was reacted with the monoprotected bisacetylene whereas another portion of the pentamer was liberated from support and reacted with the deprotected, resin-bound heptamer. Due to site–site isolation within the polymer support undesired oligomerizations and polymerizations could almost completely be suppressed. Finally, cleavage from solid support using PPTS afforded a 17-mer in 20% overall yield. Similarly, a pentablock 23-mer incorporating two quater(2,5-thiophene ethynylene) and three quinque(1,4-phenylene ethynylene) homooligomer blocks was available in 21% yield over a total of nine reaction steps.

Malenfant and Fréchet more recently reported the polymer-supported synthesis of asymmetric oligothiophenes following the stepwise addition approach (strategy **A**).[26] Starting from an unsubstituted resin-bound bithiophene, alternating sequences of bromination and Stille cross-coupling reactions afforded α-

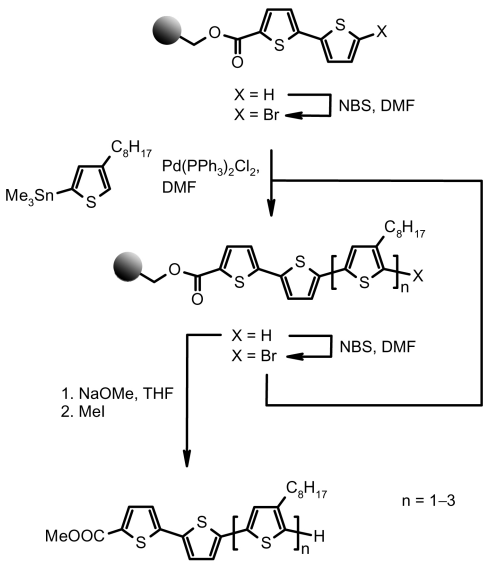


Scheme 3 Bi-directional approach to oligo(1,4-phenylene ethynylene)s.

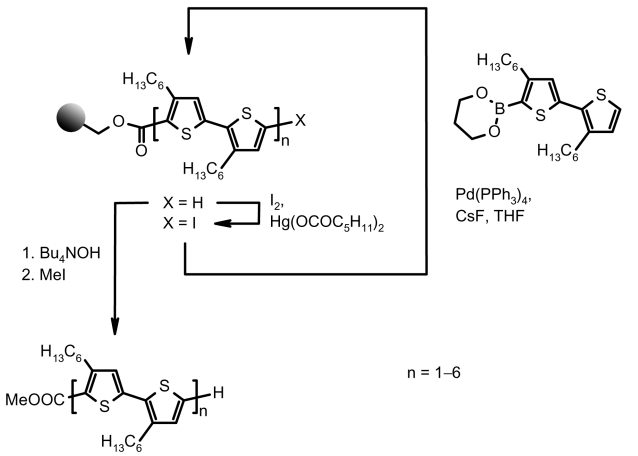
carboxy-substituted oligomers up to the pentamer after cleavage from the polymer matrix (Scheme 4). A highly crosslinked macroporous Merrifield-type resin was employed for the synthesis as it was expected to lessen the susceptibility of homocoupling of resin-bound oligomers during oligomer growth. Bromination at the terminal α-position of the ester-linked oligothiophenes was accomplished using *N*-bromosuccinimide (NBS) in DMF. The brominating reagent could be used in excess to halogenate resin-bound bithiophene. Excessive NBS, however, resulted in over-bromination when the trimer and tetramer were reacted and consequently, only a stoichiometric amount of NBS was used. Cross-coupling of the brominated oligomers with trimethylstannyl thiophene afforded (in a Stille-type cross-coupling reaction) the polymer-supported trimer, tetramer and pentamer. The oligomers were cleaved from the resin by transesterification using NaOMe in THF. Additional treatment with iodomethane (in order to increase the yield of the methyl ester) afforded α-carboxy substituted oligomers in excellent yield and purity.

Recently, we reported two stepwise addition approaches (strategy **A**) for the construction of regioregular head-to-tail coupled oligothiophenes. A series of regioregular head-to-tail coupled oligo(3-alkylthiophene)s up to a dodecamer were available following the synthetic route outlined in Scheme 5.[27] Similar to the strategy of Malenfant and Fréchet[26] bithiophene carboxylic acid was anchored to chloromethylated polystyrene in the first step. To accelerate the synthesis to the final dodecamer, bithiophene building blocks (instead of monomeric units) were employed for the oligomer elongation sequence. Suzuki-type reaction with $Pd(PPh_3)_4$ as the catalyst and caesium fluoride as the base was found to be efficient at cross-coupling resin-bound iodothiophenes with bithiophene boronic esters. Iodinated oligomers were available in nearly quantitative yield by reacting the bead-bound oligothiophenes with iodine and mercuric hexanoate in CH_2Cl_2. In contrast to the NBS bromination used by Malenfant and Fréchet, these halogenation reagents could be used in excess, regardless of the oligomer length. Iterative sequence of iodination and Suzuki cross-coupling afforded the series of regioregular head-to-tail coupled oligo(3-alkylthiophene)s in excellent yield and purity. Treatment of the resin-bound oligomers with tetrabutylammonium hydroxide and iodomethane led to the corresponding oligothiophene methyl esters. The 12 step reaction sequence to the dodecamer furnished the oligomer in 15% overall yield after purification by HPLC.

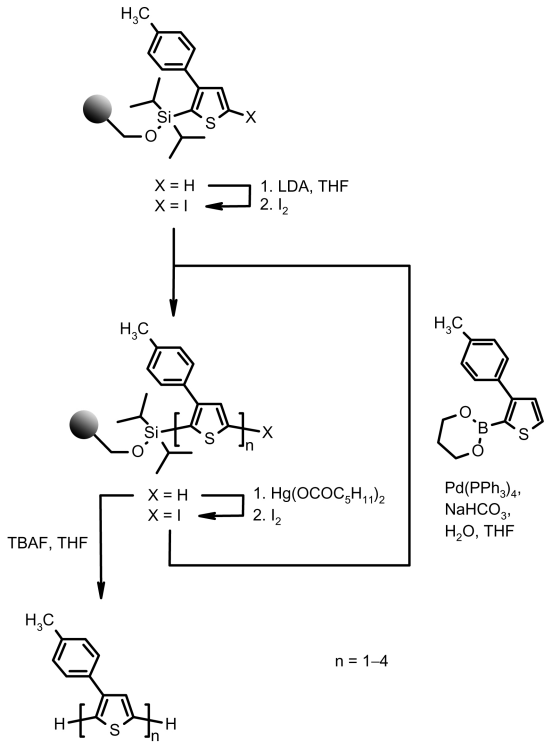
Utilizing a traceless silyl ether linkage for the anchoring of the growing π-conjugated oligomer facilitated the polymer-supported synthesis of non-functionalized regioregular head-to-tail coupled oligo(3-arylthiophene)s.[28] Chlorosilyl functionalized 3-(*p*-tolyl)thiophene was employed as a building block to attach the first thiophene unit to the hydroxymethylated polystyrene. As shown in Scheme 6, the resulting resin-bound 3-*p*-tolylthiophene was iodinated after metalation with LDA before being reacted with a thiophene boronic ester under



Scheme 4 Stepwise addition approach to asymmetric oligothiophenes.



Scheme 5 Stepwise addition approach to regioregular head-to-tail coupled oligo(3-alkylthiophene)s.



Scheme 6 Stepwise addition approach to regioregular head-to-tail coupled oligo(3-arylthiophene)s.

Suzuki cross-coupling conditions. The following iterative two-step sequence of electrophilic iodinations and C–C cross-coupling reactions granted access to the regioregular head-to-tail coupled quater(3-*p*-tolylthiophene). Removal of the conjugated oligomers from the solid support could be effectively achieved at any stage of the synthesis by treatment with tetrabutylammonium fluoride. After purification by HPLC the π-conjugated tetramer was available in 48% overall yield.

En route to π-conjugated oligomer libraries and screening

Based on the aforementioned synthetic protocols the combinatorial creation of π-conjugated oligomer libraries should be possible. In general, similar to the efforts in the drug discovery process a combinatorial loop towards organic materials is comprised of five development stages that are shown in the flowchart of Fig. 2. (1) Selection and design of the lead structure; (2) developmental studies including the optimization of the synthetic route and the analytical quality control; (3) library generation and purification; (4) screening and device construction and (5) data analysis.

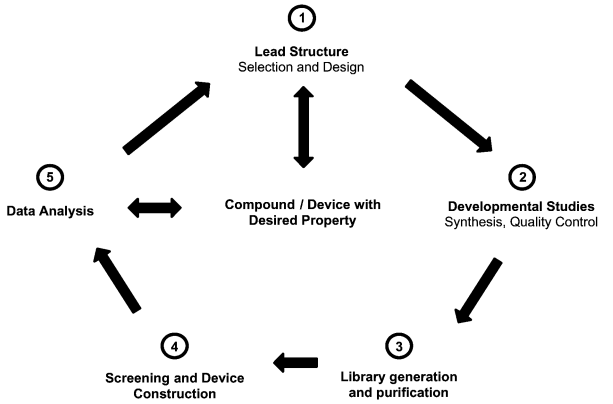


Fig. 2 Flowchart for the development process of combinatorial lead structure generation and optimization.

With the target structure defined and the library designed one has to decide which synthetic strategy provides the desired compound ensemble in the most efficient manner. In principle, all of the aforementioned four synthetic approaches **A**–**D** can be translated into a combinatorial format. As indicated by the different colors of the building blocks in Fig. 1, the coupling of structurally different monomer units to the growing oligomer (adopting the stepwise addition approaches **A** and **C**) results in an ensemble of asymmetric and symmetric co-oligomers, respectively, when the synthesis is performed in a combinatorial manner. In contrast, homooligomers are obtained when the divergent–convergent strategies **B** and **D** are applied. However, these approaches can also be used for the combinatorial generation of co-oligomers when differently loaded resins instead of different monomers are used as 'building blocks'. Then, the portions of liberated functionalized monomers are exchanged among each other and subsequently reacted with another portion of resin.

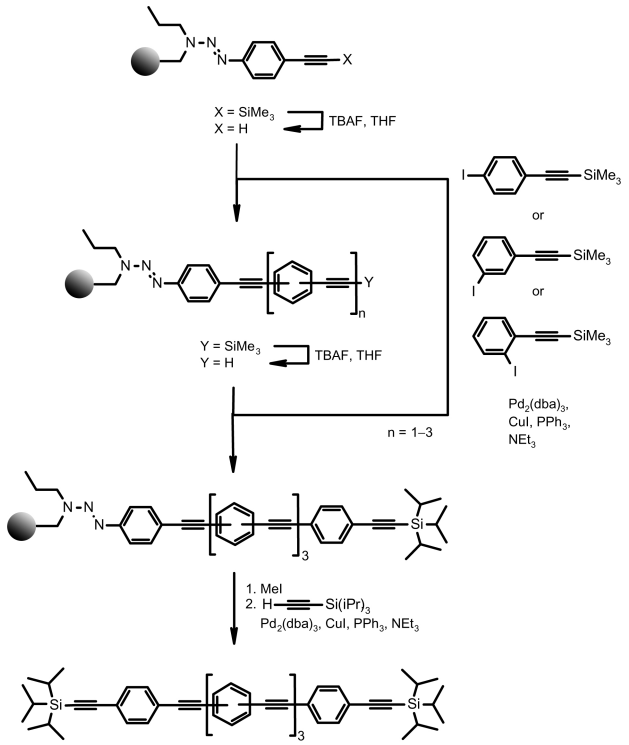
Generally, for all materials where the microscopic molecular behavior and macroscopic bulk properties are of interest, prerequisites of a reliable screening are high purities and the necessity to have the compounds or compositions as individuals. Both well-established combinatorial methodologies, the multiple parallel synthesis of spatially addressable compound arrays and the directed sorting variant of the mix-and-split synthesis, can be utilized for the generation of individual compound libraries. In the multiple parallel synthesis an array of individual compounds is simultaneously prepared and the physical position of a reaction vessel serves as a code for each library member. Following the directed sorting strategy several portions of resins are enclosed in solvent-permeable microreactors that are individually labeled for identification.[29] The following mix-and-split process includes (1) the sorting of the encapsulated resin portions into several pools, (2) the coupling of different diversity reagents to each of the pools and (3) the recombination of all resin portions. This three-step process is repeated until the desired library is constructed. The selection of the most appropriate combinatorial method depends largely on the nature of the target compound, on the size of the proposed library and on the quantities needed to perform the screening experiments.

In contrast to combinatorial approaches in pharmaceutical research or solid state material research,[2] the development of efficient screening methodologies for organic material libraries is even less advanced than the methodologies utilized for the library construction. In order to accelerate the whole combinatorial discovery loop (and not to shift the bottleneck within the loop) it is essential to perform the screening in a time-efficient manner. Ideally, an efficient screening procedure should allow for the parallel and automated probe analysis and have a high sample throughput. Additionally, miniaturization of the screening device is necessary since library members are usually prepared on a small scale to keep the library construction economical. Efficient screening methods have been developed

to investigate the properties of inorganic solid-state materials as 'integrated materials chips'[30] and to simultaneous evaluate catalysts libraries.[5] By contrast, an efficient high-throughput evaluation methodology for organic materials is less advanced. An elegant example recently reported by Lewandowski and Fréchet is the screening of a library of enantioselective selectors for chiral HPLC by observing the enantioselectivity for resolution on a chiral stationary phase.[31]

To illustrate the combinatorial process towards synthesis and screening of π-conjugated oligomers developmental steps are consecutively discussed for an oligo(phenylene ethynylene) library and an oligo(3-arylthiophene) library. These are, to the best of our knowledge, the only combinatorial approaches to this class of organic materials published to date.

Anderson reported a combinatorial approach towards phenylene ethynylenes whose organic electroluminescent (OEL) features are of interest for low voltage multicolor displays.[32] In addition to the library generation, the author reported on the screening of photoluminescence in solution and solid-state as well as the incorporation of selected oligomers for device construction. Utilizing *ortho*-, *meta*- and *para*-substituted phenylacetylene linkages different molecular geometries were available covering different conjugation lengths and molecular shapes that should translate into the optoelectronic behavior of these π-conjugated oligomers. A library of 18 isomeric triisopropylsilyl capped phenylene ethynylene pentamers was constructed by parallel synthesis adopting the well-established 'tea bag' methodology.[33] Oligomers were grown on propylaminomethylated polystyrene as polymer support in a stepwise addition approach (Scheme 7).



Scheme 7 Synthetic sequence for the construction of the 18-membered phenylene ethynylene pentamer library.

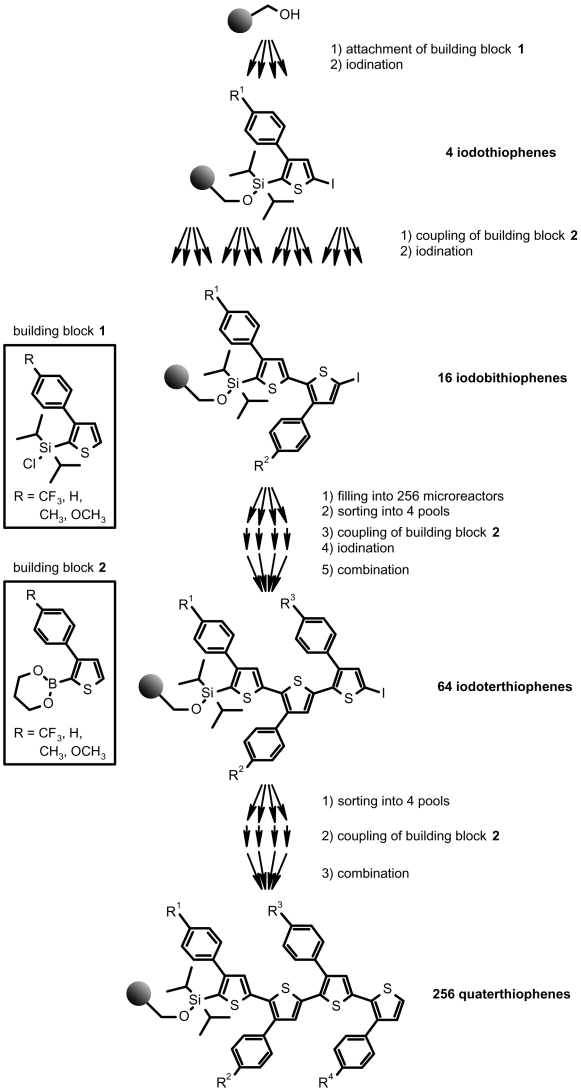
Based on the iterative synthetic sequence developed by Nelson and Moore (*cf*. Scheme 1),[23b] pentamers were generated by using Pd catalyzed cross-couplings and acetylene deprotections as oligomer elongation reactions. Starting from a resin-bound phenylacetylene the aforementioned mix-and-split synthesis was initiated. Portions of the derivatized resin were filled into 18 permeable 'tea bags' and labeled for identification. These polyester microreactors were now distributed to three reaction flasks and reacted with one of the three *ortho*-, *meta*-, or *para*-iodinated phenylacetylene building blocks. With the coupling reaction complete, the 'tea bags' were processed together, washed and treated with TBAF to remove the TMS protecting group. After redistribution of the 18 'tea bags' into three reaction flasks, the process of cross-coupling (with the three building blocks), recombination (for washing and deprotection) and splitting were repeated twice furnishing 18 isomeric resin-bound phenylene ethynylene tetramers. The fifth phenylacetylene unit substituted with a triisopropylsilyl group was then attached to the oligomers. Subsequent individual treatment of the 18 bead-bound oligomers with MeI (to liberate the compounds from solid support) and triisopropylacetylene yielded the 18 desired phenylene ethynylene pentamers. The crude library members were then purified by flash chromatography and recrystallization. The overall yields of the pure oligomers ranged from 16–47%.

To assess the influence of structural factors on photoluminescence characteristics, the optical emission and absorption behavior of the purified library members was studied. For π-conjugated oligomers microscopic molecular properties are important but the device performance is additionally determined by macroscopic bulk properties, such as the film forming ability and the self-assembly. Moreover, device configuration can be crucial for a successful application. Consequently, the next conceptual steps towards the material application is the detailed evaluation of bulk properties in solid state and the device optimization. Towards this end, the oligomers were characterized in solution and in solid-state. Since the pentamer with an *ortho*-substitution at the central phenyl unit (other phenyl groups are *para*-substituted) was found to exhibit the highest fluorescence quantum yield in solution, this oligomer was incorporated as active layer into a simple OEL device showing blue electroluminescence. As an obvious drawback of the study the author mentioned the time-consuming one-at-a-time generation and evaluation of the OEL devices. To overcome this bottleneck of the screening process the manufacturing of arrays of devices with varied device architectures would be necessary.

Large combinatorial libraries of inorganic solid state lumophores produced on a substrate could efficiently be screened simultaneously by the use of a CCD-camera.[2] Recently, a combinatorial approach for the screening and optimization of organic electron transport materials and device configurations was reported that addresses the problem of parallel device preparation and evaluation. Schmitz and Schmidt reported the construction of spatially addressable organic light-emitting devices (OLED).[34] A matrix of 49 two-layer devices was generated by employing vapor deposition of the components in combination with elaborate masking techniques to ascertain the ideal layer thickness of ITO/TPD/Alq_3/Al two-layer devices. By correlating current density with luminescence, photometric efficiency and power efficiency an optimum Alq_3 layer thickness could be determined. Moreover, an improvement in photometric efficiency was obtained for certain layer thicknesses of different combinations of Alq_3/spiro-quinoxaline. Obviously, this approach provided a fast and efficient method to evaluate ideal device parameters even in complex multiparameter systems. The technique to create arrays of conjugated oligomers or polymers has recently been applied by others to accelerate screening and optimization processes of organic light emitting devices.[35]

Based on the unidirectional stepwise addition approach to regioregular head-to-tail coupled oligo(3-arylthiophene)s discussed above (*cf*. Scheme 6) we developed a combinatorial protocol for the construction of a 256-membered oligothiophene library as outlined in Scheme 8.[36]

In order to systematically investigate the electronic influence of the backbone substituents on the optical and electrochemical properties, we selected thiophene boronic esters and silyl chlorides as diversity building blocks each bearing *p*-trifluormethylphenyl, phenyl, *p*-tolyl or *p*-anisyl groups in the 3-position. The combinatorial strategy (parallel synthesis and radio-frequency encoded mix-and-split synthesis) facilitated the



Scheme 8 Synthetic protocol for the construction of the 256-membered quater(3-arylthiophene) library.

synthesis of quaterthiophenes in which these building blocks are permutated along the four positions of the oligomer target structure. To anchor the first thiophene building block the polymer support was equally distributed into four portions and these were reacted in parallel with the four chlorosilylthiophenes (building blocks **1**). The resulting resin-bound silylthiophenes were iodinated in parallel and each of the four iodothiophenes was again split into four portions. These were cross-coupled in parallel with the four boronic esters (building blocks **2**) providing 16 polymer-supported bithiophenes. After iodination, the resulting iodobithiophenes were filled into 256 microreactors (each labeled by a radiofrequency tag) and the mix-and-split synthesis was employed for the following synthetic steps. The microreactors were sorted into four identical sets (each containing the 16 iodobithiophenes) before being reacted with the four boronic esters. The resulting four sets of terthiophenes were iodinated and again sorted into four identical pools (each containing the 64 iodoterthiophenes). These were then cross-coupled with the boronic ester building blocks to yield a total of 256 resin-bound quaterthiophenes. Finally, the resin-bound quaterthiophenes were individually treated with TFA in parallel to cleave the desired oligomers from the resin. At this stage, all library components were purified and analyzed by an automated HPLC coupled to a mass spectrometer. The purification furnished 243 of 256 oligomers in purities of greater than 98% and 13 compounds of greater than 90%. The isolated yields of these compounds over 8 steps ranged from 2–51%.

With the purified oligomer library in hand, the process of screening and subsequent data analysis was started. In addition to optical investigations, the systematical analysis of the electrochemical behavior should allow the deduction of valuable structure–property relationships between redox potentials and the molecular structure of the oligothiophenes which are necessary to tailor these and similar materials for electrooptical applications. For the electrochemical screening of the oligo(3-arylthiophene) library we constructed an apparatus for the sequential recording of cyclic voltammograms.[37] The fully automated screening device (Fig. 3) is comprised of a 96-well

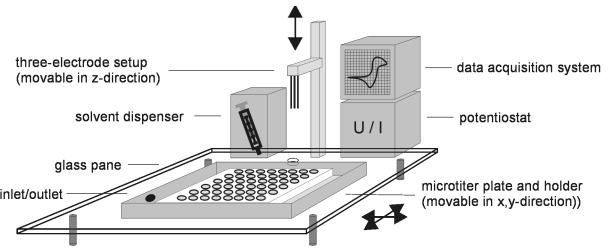


Fig. 3 Schematic representation of the screening apparatus constructed for the automated sequential acquisition of cyclic voltammetric data.

plate (which was used as an array of electrochemical cells), a three-electrode setup (Pt working, Pt counter electrode, Ag/AgCl reference electrode), a solvent dispenser, a potentiostat and a computer for data acquisition. The tailored software allowed precise positioning of the electrode-setup into the wells of the microtiter plate, the dosing of the electrolyte and the acquisition of the cyclovoltammetric data. In a typical experiment, the electrochemical response of 48 compounds can be investigated in less than two hours, indicating the enormous acceleration of this screening process with respect to conventional cyclic voltammetric experiments.

Some of the screening results obtained with the apparatus are summarized in Fig. 4 in which the first oxidation potentials for

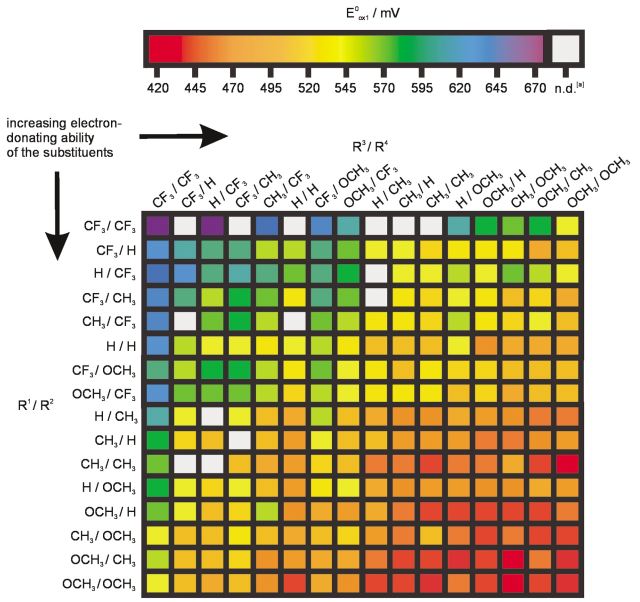


Fig. 4 First oxidation potentials of the 256-membered quater(3-arylthiophene) library. Potentials are color-coded according to the scale at the top. The arylthiophene units are given along the axis. [a] not determined.

the 256-membered oligomer library are indicated as ranges according to a color scale coded legend. The first oxidation potentials of the quaterthiophene library members span the range of E^0_{ox} = 0.42–0.68 V. This range clearly indicates the electronic influence of the substituents on the core structure. The four substituents substantially alter the redox potentials in correlation to their respective electron-donating or electron-accepting ability. On first inspection, the electronic nature of the

four substituents appears to be additive. However, the comparison of the oxidation potentials of isomeric oligomers reveals that the substitution pattern (the sequence of the four substituents) is a second determinant of the oxidation potential. These electrochemical studies (together with further optical investigations) clearly revealed that substitution of the oligothiophene core with electronically different groups allows an efficient control and fine tuning of the optical and electrochemical properties.

Conclusion and outlook

To fashion organic materials with the requirements for successful applications and to deepen the understanding of physical processes and material behavior exhibited by these compounds, the development of facile and reliable synthetic routes and effective screening procedures is still essential. In the case of π-conjugated oligomers as model compounds for the parent polymers and as materials in their own right, synthetic access to structurally-defined oligomers and the corresponding monomer building blocks is of considerable interest. Although impressive material breakthroughs have been made, more efficient strategies towards synthesis and screening must be implemented to aid the pursuit of new materials. Thereby, combinatorial chemistry appears as the most promising approach to address the challenge of material design. The aforementioned discussion demonstrated the possibility to generate and evaluate organic material libraries by means of combinatorial strategies. Both the parallel synthesis and the mix-and-split strategy enabled the rapid library generation of individual π-conjugated oligomers. However, catch-up demand exists for the development of efficient screening methods. The manufacturing and screening of OLED device arrays with varied device architectures and the automated sequential electrochemical screening are the first steps towards a complete combinatorial discovery loop to organic materials. Similarly, screening devices for the investigation of bulk and aggregation properties such as electrical conductivity and charge carrier mobility (for organic field effect transistors, OFETs) are necessary to shorten the overall development period for organic materials from design to application. Regarding the recent discussion about molecular electronics, the quest for suitable π-conjugated oligomers as molecular wires for information storage and transfer could be accelerated by developing high-throughput screening devices (*e.g.* for single molecule conductance).[38] Such future efforts using combinatorial methods in materials science could provide more sophisticated strategies for manipulating the properties of π-conjugated organic materials and pave the way for a purely rational design of materials properties.

Acknowledgements

We are grateful to the Fonds der Chemischen Industrie and the BMBF for a Kekulé grant to C.A.B.

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