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Combinatorial parallel synthesis and automated screening of a novel class of liquid crystalline materials†

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Combinatorial parallel synthesis has led to the rapid generation of a single-compound library of novel fluorinated quaterphenyls. Subsequent automated screening revealed liquid crystalline (LC) behaviour and gave qualitative relationships of molecular structures and solid state properties.

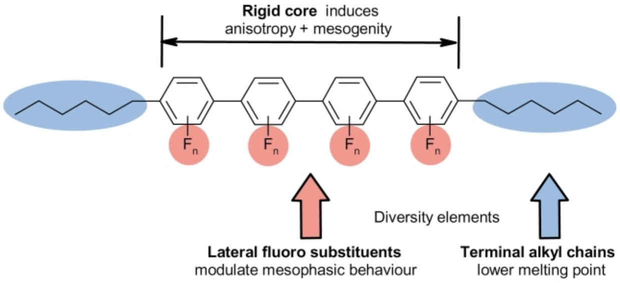
Combinatorial materials research (CMR) which was launched in 1995 by Schultz *et al.*, in the meanwhile has led to a change of paradigm in the search and development of inorganic solid state materials and was quickly extended to catalysts and polymer science.[1] In the area of organic materials there is a strong urge to continuously provide new and better materials for rapidly advancing technological applications in shorter time scales. Combinatorial methods that were developed for high-speed synthesis and high-throughput screening of pharmaceuticals[2] could be the key to accelerate organic materials development and to overcome the bottlenecks in materials science.

First examples of combinatorial organic material research (COMR) in which libraries of fluorescent dyes[3] and organic electronic materials[4] were created by combinatorial strategies have only been published very recently. Automated screening of molecular properties in solution successfully led to rapid generation of large data sets and their subsequent translation into improved structure–property relationships which may enable the rational design of novel functional materials.

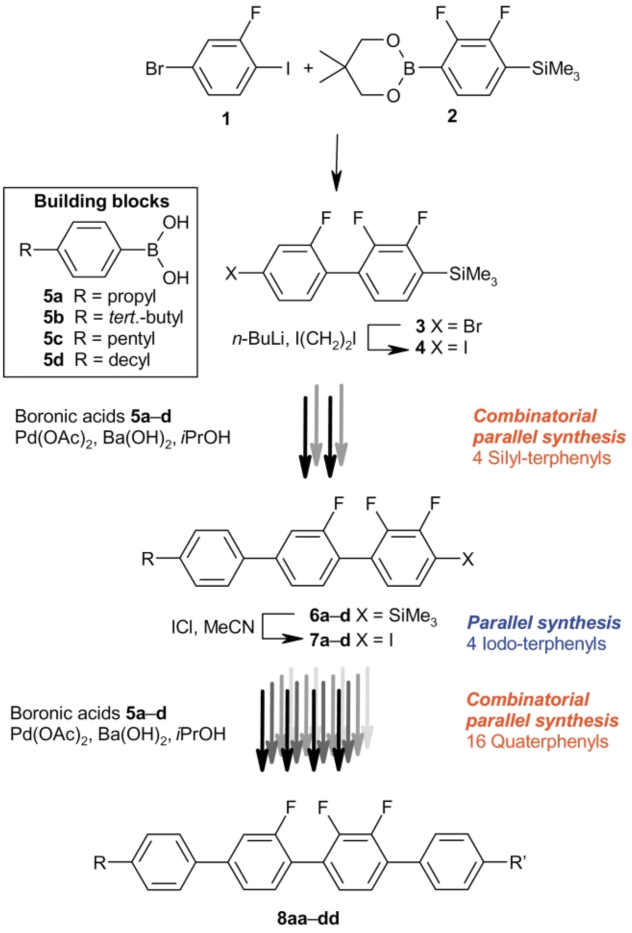
The correlation of molecular structures with bulk properties in the solid state represents a general problem in materials research, because these properties typically relate on numerous interdependent parameters.[1] In this context, the development of a library of liquid crystals (LCs) for LC display applications by a combinatorial discovery process seems to be particularly challenging. To date, bulk properties of LCs cannot be predicted by any current theory, but have to be evaluated empirically. Herein, we wish to report the generation and screening of a first single-compound library of novel LCs optimised by a complete combinatorial discovery process: *1.* Design of the lead structure; *2.* elaboration of the synthetic route; *3.* generation of the library and purification; *4.* screening, and *5.* data analysis.

p-Quaterphenyl was chosen as lead structure, because the rigid rod structure of the molecule anticipates the occurrence of LC phases. Diversity was introduced into the core structure by attaching terminal alkyl residues and lateral fluoro substituents. By variation of these substituents, the subtle intermolecular interactions in the solid state should be controlled and allow the systematic investigation of substituent effects on the phase transition temperatures and mesophase morphology as well as the specific tailoring of material properties.

In a first library, the influence of alkyl side chains on the mesomorphic behaviour was investigated. In a rapid convergent combinatorial parallel synthesis a library of 16 novel quaterphenyls was created (Scheme 1).[5] The core, 4-iodo-2,2′,3′-trifluoro-4′-(trimethylsilyl)biphenyl **4** at first was synthesized by palladium-catalysed Suzuki coupling of 4-bromo-2-fluoro-iodobenzene **1** with silylated difluorophenyl boronic ester **2** and subsequent transformation of the bromo function of the resulting biphenyl **3** into an iodo group by treatment with n-butyllithium and 1,2-diiodoethane (74% overall yield).



By combinatorial parallel synthesis, Suzuki coupling of four different *p*-alkylbenzeneboronic acids **5a–d** with biphenyl **4** resulted in the corresponding terphenyls **6a–d**. Quantitative yields of trimethylsilyl-substituted terphenyls **6** were obtained by the use of palladium acetate as catalyst precursor without the addition of additional ligands. Moreover, the typical contamina-



8aa–dd

Scheme 1 Combinatorial quaterphenyl synthesis.

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† Electronic supplementary information (ESI) available: experimental section. See http://www.rsc.org/suppdata/cc/b2/b207630f/

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tion of the crude product by Pd-black, that was observed when [Pd(PPh$_3$)$_4$] was used, could be completely avoided. In four parallel reactions, the silylated terphenyls **6a–d** were reacted with iodo chloride in acetonitrile and interconverted to the corresponding iodoterphenyls **7a–d**. The products **7** turned out to be poorly soluble in MeCN and therefore could be isolated by simple filtration in yields of typically 90% and purities of > 98%. Each iodoterphenyl **7a–d** was split into four aliquots and subsequently coupled with boronic acids **5a–d** in the second combinatorial parallel synthesis generating a library comprising 16 quaterphenyls **8aa–dd**.

In contrast to libraries of drug-like molecules, where for biological screenings in general purities of about 70–80% are satisfactory, in material libraries purities of 99% and higher are required for the reliable screening of their physical properties.[3,4] Therefore, special emphasis has been put on the purification of the individual library members. Since quaterphenyls **8aa–dd** could not be purified by chromatography, a most efficient and rapid parallel recrystallisation technique was developed. By using the custom-made recrystallisation flasks shown in Fig. 1, that allow low-loss handling of the crystals and their convenient separation from the mother liquor by centrifugation, in very short time the complete library was twice recrystallised in parallel from nonane. All library members **8aa–dd** could be isolated as HPLC-pure products in amounts of 30–40 mg corresponding to yields of 30–76% which are sufficient for the screening of the solid state properties.

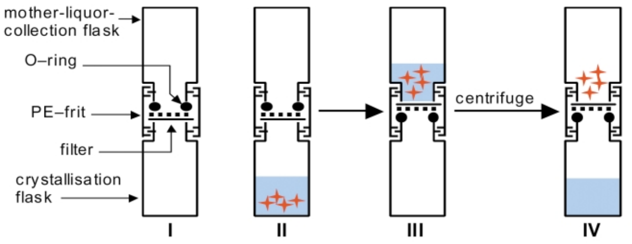
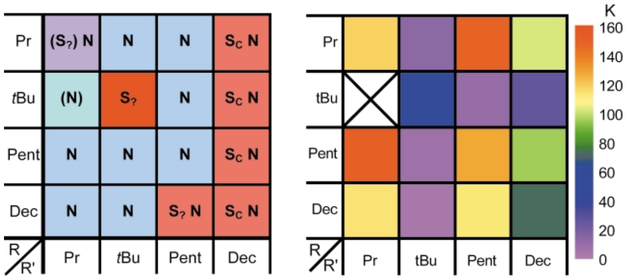


Fig. 1 Device used for parallel recrystallisation of products **8**.

The phase transition temperatures and enthalpies of the individual quaterphenyls **8aa–dd** were measured by automated sequential differential scanning calorimetry (DSC). The corresponding mesophases were determined by polarization microscopy. All 16 compounds exhibited liquid crystalline behaviour, from which 15 had a nematic phase and 8 were nematogens, *i.e.*, the nematic phase is the only mesophase (Fig. 2, left). Melting points in the range of 85–177 °C and mesophasic ranges up to 150 K clearly demonstrate that the chosen lead structure results in potential candidates for LC display mixtures. The latter parameter, ΔT_{meso}, which is the difference between the clearing and the melting temperature is very important for applications and is shown in Fig. 2 (right) as a colour-coded matrix diagram. From this qualitative structure–property relationship it becomes immediately evident, that in contrast to compounds that have linear alkyl chains, quaterphenyls **8** bearing one *tert*-butyl group exhibit a very small mesophasic range of below 30 K. Moreover, di-*tert*-butyl-substituted derivative **8bb** is the only library member showing an unfavourable smectic phase as the only mesophase.



R \ R'	Pr	tBu	Pent	Dec
Pr	($S_?$) N	N	N	S_C N
*t*Bu	(N)	$S_?$	N	S_C N
Pent	N	N	N	S_C N
Dec	N	N	$S_?$ N	S_C N

Fig. 2 Mesophases (N = nematic, S = smectic, (X) = monotropic) (left) and mesophasic ranges of quaterphenyls **8** (right).

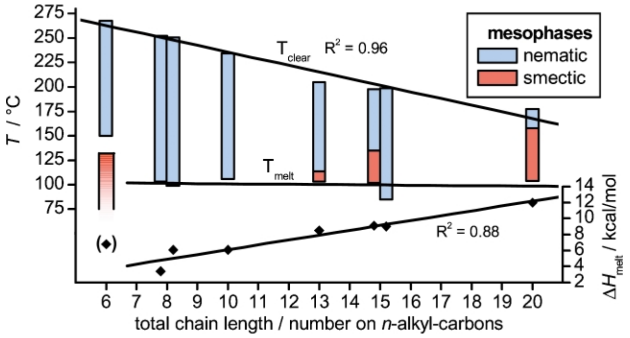


Fig. 3 Least squares fit correlation of the solid state properties of the quaterphenyls **8** with the total number of alkyl carbons in the linear *n*-alkyl chains (*tert*-butyl derivatives are not included in the figure).

A more detailed data analysis, that takes into account the dependence of mesophases, phase transition temperatures and melting enthalpies on the total length of the *n*-alkyl chains of the molecules, reveals that *1.* there is barely a correlation between T_{melt} and the alkyl chain length, as the compounds uniformly melt around 100°C; *2.* the clearing temperature (T_{clear}) decreases with increasing number of alkyl carbons and consequently leads to a decreasing mesophasic range; *3.* the melting enthalpy (ΔH_{melt}) linearly correlates with the chain length of the molecules (Fig. 3). In a least square fit correlation, correlation coefficients of $R^2 = 0.96$ (T_{clear}) and 0.88 (ΔH_{melt}) should be considered as appreciable fits, since the molecular structure is not correlated with the molecular, but the solid state properties of the materials.

In summary, the use of a full combinatorial development process has led to the accelerated generation and screening of a novel class of liquid crystalline materials as potential candidates for LC displays: quaterphenyls **8aa–dd**. Effective parallel Pd-catalysed cross-coupling reactions in conjunction with automated screening of the solid state properties led to first qualitative structure–property correlations. As a next step, the combinatorial preparation of a confined 200+ membered library of quaterphenyls encompassing optimised alkyl side chains and a systematical variation of the fluoro substitution pattern is under progress and could enable the rational design of LCs in the future.

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Notes and references

1 For review, see: B. Jandeleit, D. J. Schaefer, T. S. Powers, H. W. Turner and W. H. Weinberg, *Angew. Chem., Int. Ed.*, 1999, **38**, 2494.

2 *Combinatorial Chemistry—Synthesis, Analysis, Screening*, ed. G. Jung, Wiley-VCH, Weinheim, 1999.

3 M.-S. Schiedel, C. A. Briehn and P. Bäuerle, *Angew. Chem., Int. Ed.*, 2001, **40**, 4677.

4 (*a*) C. A. Briehn, M.-S. Schiedel, E. M. Bonsen, W. Schumann and P. Bäuerle, *Angew. Chem., Int. Ed.*, 2001, **40**, 4860; (*b*) S. Anderson, *Chem. Eur. J.*, 2001, **7**, 4706; (*c*) C. A. Briehn and P. Bäuerle, *Chem. Commun.*, 2002, 1015; (*d*) M.-S. Schiedel, C. A. Briehn and P. Bäuerle, *J. Organomet. Chem.*, 2002, **653**, 200.

5 P. Bäuerle, O. Deeg, D. Pauluth and P. Kirsch, *Ger. Pat. Appl.*, 10211597.4 (15.3. 2002).