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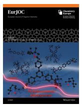

Rigid Multidimensional Alkoxyamines: A Versatile Building Block Library

Yannick Matt,[a, b] Isabelle Wessely,[a] Lisa Gramespacher,[a] Manuel Tsotsalas,[c] and Stefan Bräse*[a, b, d]

Since the discovery of the "living" free-radical polymerization, alkoxyamines were widely used in nitroxide-mediated polymerization (NMP). Most of the known alkoxyamines bear just one functionality with only a few exceptions bearing two or more alkoxyamine units. Herein, we present a library of novel multidimensional alkoxyamines based on commercially available, rigid, aromatic core structures. A versatile approach allows the introduction of different sidechains which have an impact on the steric hindrance and dissociation behavior of the alkoxyamines. The reaction to the alkoxyamines was optimized by implementing a mild and reliable procedure to give all target compounds in high yields. Utilization of biphenyl, *p*-terphenyl, 1,3,5-triphenylbenzene, tetraphenylethylene, and tetraphenyl-methane results in linear, trigonal, square planar, and tetrahedral shaped alkoxyamines. These building blocks are useful initiators for multifold NMP leading to star-shaped polymers or as a linker for the nitroxide exchange reaction (NER), to obtain dynamic frameworks with a tunable cross-linking degree and self-healing abilities.

Introduction

The nitroxide-mediated polymerization (NMP), as one of the first "living" free-radical polymerization techniques, was discovered in the early 1980s at the Commonwealth Scientific and Industrial Research Organization (CSIRO).[1] Since its patenting in 1985, NMP has gained high attention as it exhibits a living character allowing to generate well-controlled polymers with low polydispersity at low costs while tolerating functional groups.[1–5] The crucial step in radical polymerization is the suppression of an irreversible termination of the propagating radical, such as a combination of active chain ends, the abstraction of a hydrogen atom (disproportionation), or interaction with impurities. This suppression is achieved through a dynamic equilibrium between the reactive radical species and a non-reactive dormant species. In the case of NMP, alkoxyamines with their weak C–O bond function as dormant species, which can be activated thermally to give a free nitroxide and the carbon-centered radical species that can react further. The transition between active and dormant species accounts for high control during polymerization. Considering that the alkoxyamine also serves as an end group after the polymerization, the subsequent addition of a second monomer allows to achieve defined block-copolymers.[3,5]

Several procedures to synthesize functional alkoxyamines have been developed over the years. Among others, these include trapping of C-radicals created with radical starters like di-*tert*-butyl peroxide, generation from *N*-oxoammonium salts, the addition of radicals to nitrones, and the addition of nitroxides to alkenes.[6–15] However, the most popular route, which was used in the herein described work, was developed by Matyjaszewski et al. and was improved by Nicolas et al. In their approach, elemental copper was used to generating alkyl radicals by homolytic cleavage of alkyl halides and subsequent trapping with a suitable nitroxide.[16,17]

Despite the innumerable procedures and known alkoxyamines, very few examples of multifunctional alkoxyamines have been reported.[18–21] This is remarkable since such multifunctional alkoxyamines allow the generation of star-shaped polymers with a defined center and thereby a fixed number of arms, which find application as viscosity improvers, organic nanoparticles, and drug delivery systems.[22–25] Alkoxyamines can also be used as building blocks in the nitroxide exchange reaction (NER). Nitroxides with (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) being the most prominent derivative, are stable free radicals that have unique magnetic and catalytic properties and serve as a counterpart to the labile alkoxyamines in the NER.[26–29] During the NER, the alkoxyamine is heated under inert

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[a] *Y. Matt, I. Wessely, L. Gramespacher, Prof. Dr. S. Bräse*
Institute of Organic Chemistry – IOC
Karlsruhe Institute of Technology (KIT)
Fritz-Haber-Weg 6, 76131 Karlsruhe, Germany
E-mail: braese@kit.edu
https://www.ioc.kit.edu/braese
[b] *Y. Matt, Prof. Dr. S. Bräse*
3DMM2O – Cluster of Excellence (EXC-2082/1-390761711)
Karlsruhe Institute of Technology (KIT)
Kaiserstraße 12, 76131 Karlsruhe, Germany
[c] *Dr. M. Tsotsalas*
Institute of Functional Interfaces – IFG
Karlsruhe Institute of Technology (KIT)
Hermann-von-Helmholtz-Platz 1, 76344 Eggenstein-Leopoldshafen, Germany
[d] *Prof. Dr. S. Bräse*
Institute of Biological and Chemical Systems – IBCS-FMS
Karlsruhe Institute of Technology (KIT)
Hermann-von-Helmholtz-Platz 1, 76344 Eggenstein-Leopoldshafen, Germany

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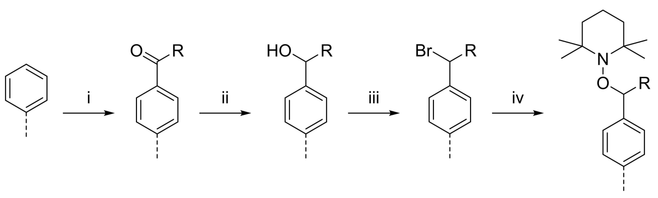
conditions, to obtain the C-centered radical and a free nitroxide. Upon addition of a second nitroxide, both nitroxide species compete for the recombination with the C-radical. Since the NER is reversible, the thermodynamically favored product is formed.[30,31] The progress of the NER can be monitored via electron paramagnetic resonance (EPR) spectroscopy due to the involved nitroxides with different hyperfine coupling constants.[32] The NER has been employed for cross-over reactions, to generate crosslinked polymers as well as self-assembled microcrystals and to shift reactions out of their equilibrium using light as an activator.[30,33–39] Recently, we were able to facilitate the NER with multifunctional alkoxyamines and nitroxides to give fully reversible frameworks with an adjustable crosslinking degree and self-healing abilities. Furthermore, we combined the multifold NER technique with classical NMP to produce frameworks where the strands could be elongated, as proven by size exclusion chromatography.[40,41] Simultaneously, a first route from unsubstituted aromatic core structures to multifold alkoxyamines was established utilizing triphenylbenzene as a scaffold. Scheme 1 gives an overview of the necessary reaction steps consisting of a Friedel-Crafts Acylation, followed by reduction, substitution with HBr, and conversion to the alkoxyamine with the help of elemental copper and TEMPO.[40]



Scheme 1. Synthetic route to multidimensional alkoxyamines as established in our group: i) Friedel-Crafts acylation, ii) Reduction with $LiAlH_4$, iii) HBr in acetic acid, iv) Cu, Cu(II) salt, ligand, TEMPO.

Herein, we optimized the above-mentioned synthetic route and describe the synthesis of a library of novel multidimensional alkoxyamines based on rigid, aromatic core structures. Overall, ten alkoxyamine building blocks with different geometries based on their core have been synthesized (Figure 1).

Results and Discussion

Biphenyl (**1 a**) and terphenyl (**2 a**) were used as ditopic linear cores, triphenylbenzene (**3 a**) as a tritopic trigonal core, tetraphenylmethane (**4 a**) and -ethylene (**5 a**) as tetratopic square planar and tetrahedral cores, respectively. The variable sidechains of the alkoxyamines demonstrate the versatility of the approach and provide alkoxyamines with different sterical hindrance/dissociation behavior.

We started our investigation by optimization and upscaling of the synthetic route described in Scheme 1 towards model alkoxyamine **3 j**. We intended to identify reaction conditions that can be readily transferred to other core structures. The following paragraphs contain a description of each synthetic step with the conditions applied to the model system and a discussion of the other scaffolds.

Friedel-Crafts acylation

Initially, the Friedel-Crafts acylation to the model system precursor **3 d** was carried out in methylene chloride by mixing $AlCl_3$ and triphenylbenzene, followed by slow addition of

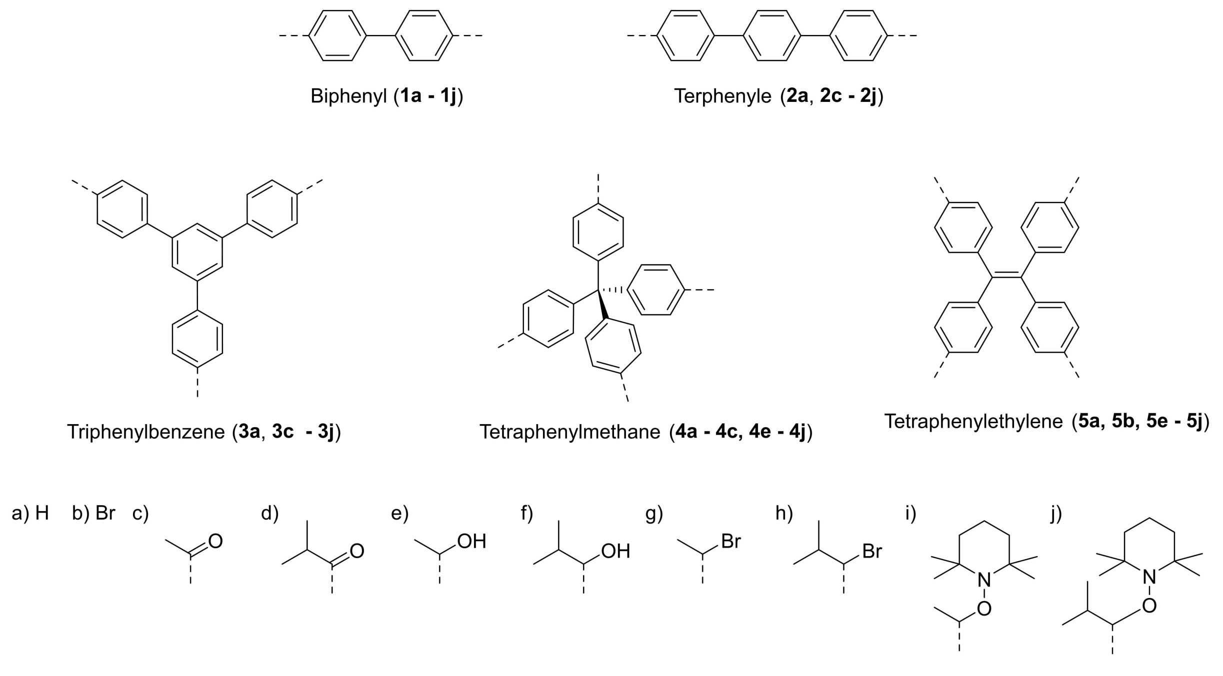


Figure 1. Overview of the synthesized alkoxyamines and intermediate building blocks.

isobutyryl chloride at 0 °C. The desired ketone **3d** was isolated in a yield of 72 % after recrystallization from acetone. However, the yield was not robust to small changes of the reaction conditions, and purification was hindered by the formation of a polymeric byproduct. Several changes to the procedure, including solvent and an "inverse addition" of the aromatic core to the reaction mixture, made it more robust and allowed synthesis in up to 20 g scale (details see SI). The reaction of triphenylbenzene with acetyl chloride under the same conditions gave the methyl-substituted ketone **3c** with excellent yield (96 % after recrystallization).

Transferring this protocol to the biphenyl core yielded the ketone with methyl sidechain **1c** in a yield of 64 % (additional 26 % of mono-acylated product **S2**), while the ketone with isopropyl sidechain **1d** was achieved in only 9 % yield (additional 91 % yield for the mono-acetylated product **S3**).

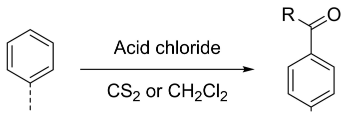
For the terphenyl core, both ketones **2c** and **2d** could be synthesized in excellent yield (95 % yield for **2c**, 92 % yield for **2d**) and multigram scale (4–5 g). For tetraphenylmethane, only the methyl sidechains could be introduced to the molecule (76 % yield for the tetra-ketone **4c**). We suspect that the lower reactivity of isobutyryl chloride and a polymeric byproduct that hindered the purification, as already discovered for triphenylbenzene, are responsible. Cross-linking of tetraphenylmethane under Lewis acid catalysis is literature known, explaining the polymeric byproduct.[42,43]

As expected, acetyl chloride exhibits a higher reactivity than isobutyryl chloride resulting in higher yields for the acylation reactions introducing methyl sidechains (Table 1).

Introduction of the hydroxy groups

The reductions of the ketones to the alcohols were conducted with $LiAlH_4$ in dry tetrahydrofuran. In this procedure, the order of reagents added ($LiAlH_4$, THF, ketone in portions) is crucial to achieving a high conversion. This procedure allowed the reduction of the ketones into the respective alcohols in good to excellent yields and quantities up to 24 g. One attempt to reduce diketone **1d** failed due to a side reaction during workup (see SI for details).

Table 1. Overview of acylation reactions.



Entry	Pre-cursor	Acyl Chloride	Product	R=	Yield
1	**1a**	Acetyl chloride	**1c**	Methyl	64 %
2	**1a**	Isobutyryl chloride	**1d**	Isopropyl	9 %
3	**2a**	Acetyl chloride	**2c**	Methyl	93 %
4	**2a**	Isobutyryl chloride	**2d**	Isopropyl	92 %
5	**3a**	Acetyl chloride	**3c**	Methyl	96 %
6	**3a**	Isobutyryl chloride	**3d**	Isopropyl	72 %
7	**4a**	Acetyl chloride	**4c**	Methyl	76 %

Considering the scaffolds of which the ketones were not obtained or their purification was difficult (**1d**, **4c**/**4d**, and **5c**/**5d**), a direct synthetic route to the alcohols was developed starting from lithiation of the respective bromo precursors and further conversion with either acetaldehyde or isobutyraldehyde (Table 2). This procedure allowed the synthesis of diol **1f** from commercial 4,4′-dibromo-1,1′-biphenyl in 83 % yield.

Both tetraphenylmethane derivatives **4e** and **4f** were synthesized from tetrakis(4-bromophenyl)methane (**4b**) according to this procedure and gave yields of 42 % and 39 %, respectively. Transferring this procedure to 1,1,2,2-tetrakis(4-bromophenyl)ethylene (**5b**) leads to the generation of the desired alcohols **5e** (70 % yield) and **5f** (58 % yield) after a necessary reduction step was performed in the purification (see SI for details). The yields for all reactions are summarized in Table 2.

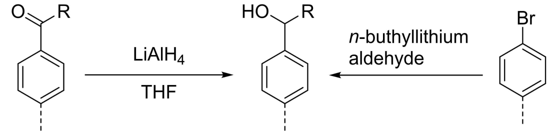
Nucleophilic substitution of alcohols to bromides

The conversion of the alcohols to their respective bromides proved to be straightforward and occurred without any problems for all synthesized derivatives. The slow addition of HBr in acetic acid to a premixed and cooled suspension of the alcohol in methylene chloride gave the bromides in good to excellent yields (Table 3) and quantities of up to 35 g. However, it is striking that the methyl sidechain derivatives generally give a lower yield than the isopropyl chain derivatives.

Formation of multidimensional-alkoxyamines

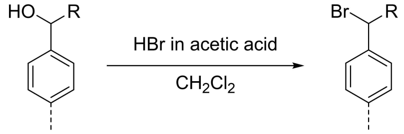
Previously, we reported the synthesis of the model alkoxyamine **3j** based on the Matyjaszewski method, using a Cu/Cu(II) system with excess of elemental copper, small amounts of the ligand 4,4′-di-*tert*-butyl-2,2′-dipyridyl, and an excess of TEMPO (Table S1) at 75 °C.[16,40] The original process suffered from problems during the purification, which was often hindered by a sticky, polymeric byproduct. Alkoxyamine **3i** was already

Table 2. Overview of the alcohol formation via $LiAlH_4$ or direct route via *n*-butyllithium.



Entry	Pre-cursor	Reagent	Product	R=	Yield
1	**1c**	$LiAlH_4$	**1e**	Methyl	98 %
2	**1b**	Isobutyraldehyde	**1f**	Isopropyl	83 %
3	**2c**	$LiAlH_4$	**2e**	Methyl	99 %
4	**2d**	$LiAlH_4$	**2f**	Isopropyl	97 %
5	**3c**	$LiAlH_4$	**3e**	Methyl	90 %
6	**3d**	$LiAlH_4$	**3f**	Isopropyl	99 %
7	**4c**	$LiAlH_4$	**4e**	Methyl	67 %
8	**4b**	Acetaldehyde	**4e**	Methyl	42 %
9	**4b**	Isobutyraldehyde	**4f**	Isopropyl	39 %
10	**5b**	Acetaldehyde	**5e**	Methyl	70 %
11	**5b**	Isobutyraldehyde	**5f**	Isopropyl	58 %

Table 3. Overview of the yields for nucleophilic substitution to the bromides.

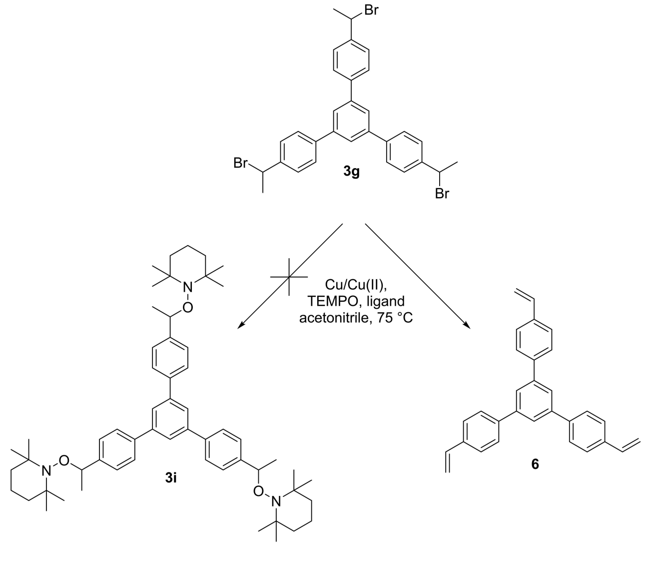


Entry	Pre-cursor	Product	R=	Yield
1	**1e**	**1g**	Methyl	72%
2	**1f**	**1h**	Isopropyl	84%
3	**2e**	**2g**	Methyl	90%
4	**2f**	**2h**	Isopropyl	91%
5	**3e**	**3g**	Methyl	80%
6	**3f**	**3h**	Isopropyl	81%
7	**4e**	**4g**	Methyl	72%
8	**4f**	**4h**	Isopropyl	94%
9	**5e**	**5g**	Methyl	71%
10	**5f**	**5h**	Isopropyl	89%

known to literature and synthesized from Suzuki cross-coupling of a previously prepared alkoxyamine boronic ester and 1,3,5-tribromobenzene.[21] However, attempts to synthesize alkoxyamine **3i** following our method failed. Nevertheless, we were able to isolate and fully characterize the threefold elimination product **6** in 18% yield (Scheme 2).

We assume that the excess of copper and the comparably high temperature are responsible for the elimination. Polymerization of the alkene then could have led to the polymeric byproduct, explaining the difficulties with both syntheses. Thus, we changed the reaction conditions according to a procedure reported by Nicolas et al. in 2011.[17] The main changes implied a) stoichiometric amounts of elemental copper and ligand without Cu(II) salt, b) only a slight excess of TEMPO, and c) reaction at room temperature (see Table S1).

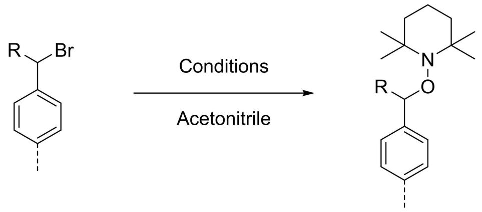
These mild conditions allowed the synthesis of all multi-alkoxyamines in good to excellent yield without complicated purification (Table 4). A highly useful side effect of the new procedure is that all conversions can be easily determined visually (Figure 2). A freshly prepared reaction mixture has a slightly reddish color due to the dissolved TEMPO, and elemental copper can be seen at the bottom of the vial. During the reaction, the color changes to dark red first and then to dark green. At this point in the reaction, the copper was no longer visible at the bottom of the vial. Upon further stirring, the green color became brighter and finally turned into turquoise indicating the end of the reaction.



Scheme 2. Attempt to synthesize alkoxyamine **3i** from **3g** resulting in alkene **6** due to threefold elimination.

Reaction times depend on the substrate as was already reported by Nicolas et al.[17] Derivatives of biphenyl and terphenyl showed a fast conversion, while derivatives of triphenylbenzenes and tetraphenylmethanes required several days and of tetraphenylethylenes one (**5i**) or two weeks (**5j**) to achieve complete conversion. Heating the reaction could have accelerated the conversion, but at the loss of the favorable mild conditions, risking elimination. Triphenylbenzene was especially outstanding in that term. Alkoxyamine **3j** formed extremely

Table 4. Overview of the yields for alkoxyamine formation.



Entry	Precursor	Product	R=	Yield
1	**1g**	**1i**	Methyl	73%
2	**1h**	**1j**	Isopropyl	77%
3	**2g**	**2i**	Methyl	79%
4	**2h**	**2j**	Isopropyl	88%
5	**3g**	**3i**	Methyl	78%
6	**3h**	**3j**	Isopropyl	77%
7	**4g**	**4i**	Methyl	82%
8	**4h**	**4j**	Isopropyl	81%
9	**5g**	**5i**	Methyl	74%
10	**5h**	**5j**	Isopropyl	81%

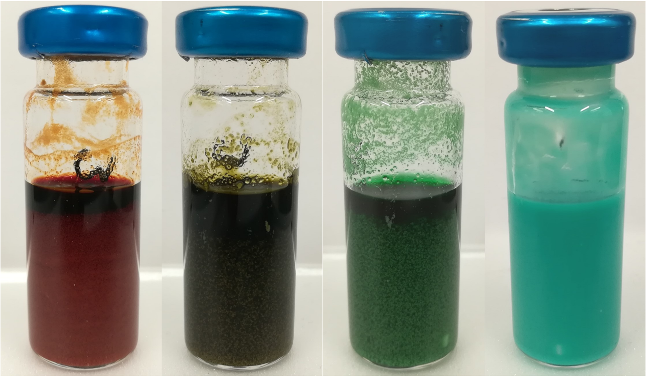


Figure 2. The reaction from the bromides to the alkoxyamines has a general color change from dark red (shortly after start) via dark and light green to turquoise indicating the end of the reaction. The presented pictures are exemplary for the formation of alkoxyamine **3j** and were recorded on the day of the start and then every 24 h of the three-day reaction.

slow at room temperature (21 °C) so that the reaction was conducted at slightly elevated temperature (35 °C), while alkoxyamine **3 i** could not be synthesized at room temperature at all. Several attempts ended with the formation of a sticky liquid, most likely the polymerized poly-alkene **6**, in the reaction vessel. Starting and stirring the reaction at −20 °C for three days before warming to room temperature gave the desired alkoxyamine **3 i** in good yield (78 %) at last.

Conclusion

In this report, we present an efficient and scalable synthetic route to complex multifunctional alkoxyamines starting from various commercial aromatic building blocks. The versatile synthetic approach allows us to introduce different side chains that have an impact on the steric hindrance and dissociation behavior of the alkoxyamines. The multistep procedure gave access to linear, trigonal planar, square planar, and tetrahedral multialkoxyamines. The conditions for the conversion of the bromides to the alkoxyamines were optimized by implementing a reliable and mild procedure to give all target structures in high yield. Furthermore, this synthetic procedure allows a quick and easy visual estimation of the conversion due to a color change during the reaction.

Overall, we developed a synthetic path towards ten rigid, multidimensional alkoxyamines on five core structures, which have enormous potential as building blocks in the nitroxide exchange reaction and/or nitroxide mediated polymerization.

Experimental Section

Following, the synthetic procedures towards the model alkoxyamine **3 j** are given, while full experimental details, analytical data (^{1}H, ^{13}C, MS, HRMS, IR), and additional comments are given in the supporting information (SI). The description of reactions and the original analytical data files can be accessed, examined, and downloaded from the repository Chemotion (https://www.chemotion-repository.net/) via the DOIs given in the SI.

1,3,5-Tris(4′-isobutyronylphenyl)benzene (3 d)

Under an argon atmosphere, aluminum trichloride (34.8 g, 261 mmol, 4.00 equiv.) was suspended in 150 mL of methanedithione. 2-methylpropanoyl chloride (28.4 g, 28.1 mL, 266 mmol, 4.08 equiv.) was added dropwise under ice bath cooling, followed by 1,3,5-triphenylbenzene (20.0 g, 65.3 mmol, 1.00 equiv.) dissolved in 250 mL of methanedithione over 1 h, also under ice-bath cooling. The mixture was stirred under cooling until the end of gas evolution and then slowly warmed to 21 °C. Stirring was repeated until no significant gas evolution was observed anymore. The mixture was then heated to 30 °C until no further gas evolution was observed (~2 hours) either. After cooling to 21 °C, the supernatant was decanted from the formed solid and the solid was mixed with 500 g of ice water, 100 mL of conc. HCl and 400 mL of CH_2Cl_2. This mixture was stirred until the solid was completely dissolved. The organic phase was separated, washed with NaOH (10 %), water, saturated NaCl solution, dried over Na_2SO_4, and the solvent was removed under reduced pressure. The residue was refluxed in a mixture of ethanol/ethyl acetate (200 mL/30 mL) and filtered after cooling to give 24.3 g (46.9 mmol, 72 % yield) of 1,3,5-tris(4′-isobutyronylphenyl)benzene of a colorless solid in 72 % yield.

$R_f = 0.53$ (CH_2Cl_2).

^{1}H NMR (400 MHz, Chloroform-d [7.27 ppm], ppm) $\delta = 8.12$–8.09 (m, 6H, $C_{ar}H$), 7.89 (s, 3H, $C_{ar}H$), 7.83–7.79 (m, 6H, $C_{ar}H$), 3.63 (sept, $J = 6.9$ Hz, 3H, $CH(CH_3)_2$), 1.28 (d, $J = 6.9$ Hz, 18H, CH_3); ^{13}C NMR (100 MHz, Chloroform-d [77.0 ppm], ppm) $\delta = 204.0$ (3 C, CO), 144.8 (3 C, C_q), 141.6 (3 C, C_q), 135.4 (3 C, C_q), 129.1 (6 C, $C_{ar}H$), 127.5 (6 C, $C_{ar}H$), 126.0 (3 C, $C_{ar}H$), 35.5 (3 C, $CH(CH_3)_2$), 19.2 (6 C, CH_3); EI (m/z, 70 eV, 200 °C): 516 (20) [M^+], 474 (38) [$M^+ - C_3H_7 + H$], 473 (100) [$M^+ - C_3H_7$], 446 (20) [$M^+ - C_4H_7O + H$], 404 (30), 403 (95) [$M^+ - C_3H_7 - C_4H_7O + H$], 332 (20) [$M^+ - C_3H_7 - 2C_4H_7O + H$]. HRMS-EI *(m/z)*: $[M]^+$ calcd for $C_{36}H_{36}O_3$, 516.2664; found, 516.2665; IR (ATR, $\tilde{v}$) = 2968 (w), 2931 (w), 2871 (w), 1676 (vs), 1596 (vs), 1561 (w), 1465 (w), 1443 (w), 1408 (w), 1381 (m), 1368 (w), 1350 (w), 1286 (w), 1248 (w), 1220 (vs), 1159 (s), 1119 (w), 1084 (w), 979 (vs), 931 (w), 905 (w), 892 (w), 871 (w), 849 (s), 827 (s), 761 (vs), 721 (w), 697 (s), 669 (w), 663 (w), 640 (w), 620 (w), 608 (w), 572 (w), 521 (w), 490 (m), 455 (w), 446 (w), 435 (w), 418 (w), 407 (w), 395 (w), 377 (w) cm^{-1}.

The experimental data are consistent with the literature.[40]

1,3,5-Tris(4′-(1′′-hydroxy-2-methylpropyl)phenyl)benzene (3 f)

Under an argon atmosphere, lithium;alumanuide (3.53 g, 93.0 mmol, 1.98 equiv.) was suspended in 700 mL of dry THF and 1,3,5-tris(isopropyl 4′-phenyl ketone)benzene (24.3 g, 47.0 mmol, 1.00 equiv.) was added in portions. The reaction mixture was stirred for 19 h at 21 °C. Subsequently, the reaction was quenched with water and 10 % NaOH solution was added until everything was dissolved. The phases were separated and the aqueous phase was extracted with ethyl acetate. The combined organic phases were washed with a saturated NaCl solution, dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was absorbed in a few mL of an ethyl acetate/cyclohexane mixture (1 : 1) and treated in an ultrasonic bath, filtered off, and dried to give 24.3 g (46.5 mmol, 99 % yield) of 1,3,5-tris(4′-(1′′-hydroxy-2-methylpropyl)phenyl)benzene as a colorless solid.

$R_f = 0.88$ (ethyl acetate).

^{1}H NMR (400 MHz, DMSO-d6 [2.50 ppm], ppm) $\delta = 7.86$ (s, 3H, $C_{ar}H$), 7.82–7.79 (m, 6H, $C_{ar}H$), 7.42–7.40 (m, 6H, $C_{ar}H$), 5.14 (d, $J = 4.4$ Hz, 3H, OH), 4.33–4.31 (m, 3H, CHOH), 1.92–1.80 (m, 3H, $CH(CH_3)_2$), 0.90 (d, $J = 6.6$ Hz, 9H, CH_3), 0.80 (d, $J = 6.8$ Hz, 9H, CH_3). ^{13}C NMR (100 MHz, DMSO-d6 [39.5 ppm], ppm) $\delta = 144.6$ (3 C, C_q), 141.5 (3 C, C_q), 138.4 (3 C, C_q), 127.1 (6 C, $C_{ar}H$), 126.4 (6 C, $C_{ar}H$), 123.8 (3 C, $C_{ar}H$), 77.2 (3 C, CHOH), 35.0 (3 C, $CH(CH_3)_2$), 19.1 (3 C, CH_3), 17.9 (3 C, CH_3). FAB (3-NAB, m/z): 523 [$M^+ + H$], 522 [M^+], 506 [$M^+ - O$], 505 [$M^+ - OH$], 480 [$M^+ - C_3H_7 + H$], 479 [$M^+ - C_3H_7$], 433 [$M^+ - C_4H_9O - CH_3 - H$], 407 [$M^+ - C_4H_9O - C_3H_7$]. HRMS-FAB *(m/z)*: [M^+] calcd for $C_{36}H_{42}O_3$, 522.3134; found, 522.3133; IR (ATR, $\tilde{v}$) = 3292 (w), 3247 (w), 3241 (w), 2961 (w), 2925 (m), 2907 (w), 2898 (w), 2868 (w), 2850 (w), 1595 (w), 1513 (w), 1468 (w), 1449 (w), 1384 (m), 1366 (w), 1324 (w), 1275 (w), 1239 (w), 1205 (w), 1033 (s), 1020 (vs), 935 (w), 864 (w), 841 (w), 824 (vs), 792 (s), 761 (w), 727 (w), 722 (w), 705 (m), 662 (w), 646 (w), 636 (w), 612 (m), 579 (s), 555 (w), 538 (w), 504 (m), 401 (w) cm^{-1}.

The experimental data are consistent with the literature.[40]

1,3,5-Tris(4′-(1′′-bromo-2-methylpropyl)phenyl)benzene (3 h)

To a suspension of 1,3,5-tris(4′-(1′′-hydroxy-2-methylpropyl)phenyl) benzene (35.2 g, 67.3 mmol, 1.00 equiv.) in 600 mL of methylene chloride, hydron;bromide in acetic acid (98.1 g, 69.1 mL, 400 mmol, 5.94 equiv.) was slowly added via a dropping funnel at 0 °C. The reaction mixture was stirred for 3.5 h at 21 °C. Afterward, water was added, the phases were separated and the organic phase was washed with saturated $NaHCO_3$ solution, water, saturated NaCl solution, and dried over Na_2SO_4. The solvent was removed under reduced pressure. The residue was recrystallized from acetone and washed with cyclohexane to give 38.9 g (54.7 mmol, 81 % yield) of 1,3,5-tris(4′-(1′′-bromo-2-methylpropyl)phenyl)benzene as a colorless solid.

^{1}H NMR (400 MHz, Chloroform-d [7.27 ppm], ppm) $\delta = 7.78$ (s, 3H, $C_{ar.}H$), 7.66 (d, $J = 8.3$ Hz, 6H, $C_{ar}H$), 7.49 (d, $J = 8.3$ Hz, 6H, $C_{ar}H$), 4.80 (d, $J = 8.5$ Hz, 3H, $CHBr$), 2.46–2.34 (m, 3H, $CH(CH_3)_2$), 1.25 (d, $J = 6.5$ Hz, 9H, CH_3), 0.94 (d, $J = 6.6$ Hz, 9H, CH_3); ^{1}H NMR (400 MHz, Dichloromethane-d2 [5.32 ppm], ppm) $\delta = 7.82$ (s, 3H, $C_{ar}H$), 7.69 (d, $J = 8.3$ Hz, 6H, $C_{ar.}H$), 7.50 (d, $J = 8.3$ Hz, 6H, $C_{ar.}H$), 4.82 (d, $J = 8.6$ Hz, 3H, $CHBr$), 2.46–2.34 (m, 3H, $CH(CH_3)_2$), 1.24 (d, $J = 6.5$ Hz, 9H, CH_3), 0.92 (d, $J = 6.8$ Hz, 9H, CH_3); ^{13}C NMR (100 MHz, ppm) $\delta = 141.7$ (3 C, C_q), 141.1 (3 C, C_q), 140.6 (3 C, C_q), 128.4 (6 C, $C_{ar.}$H), 127.3 (6 C, C_{ar}H), 125.1 (3 C, C_{ar}H), 63.9 (3 C, CHBr), 36.6 (3 C, $CH(CH_3)_2$), 21.6 (3 C, CH_3), 20.6 (3 C, CH_3); FAB (3-NBA, m/z): 709/711/713/715 [$M^+ + H$] 633/631/629 [$M^+ - Br$], 552/550 [$M^+ - 2Br$]. HRMS-FAB *(m/z)*: $[M+H]^+$ calcd for $C_{36}H_{40}{}^{79}Br_2{}^{81}Br$, 711.0660; found, 711.0660; IR (ATR, $\tilde{v}$) = 2959 (m), 2931 (w), 2907 (w), 2867 (w), 1595 (w), 1565 (vw), 1510 (m), 1465 (w), 1445 (w), 1414 (w), 1397 (w), 1384 (m), 1366 (w), 1317 (vw), 1307 (vw), 1244 (w), 1211 (w), 1170 (m), 1120 (w), 1068 (vw), 1018 (w), 942 (w), 928 (w), 887 (vw), 839 (m), 822 (vs), 803 (m), 786 (vs), 771 (m), 744 (m), 707 (m), 669 (vs), 653 (s), 635 (s), 613 (m), 575 (m), 534 (w), 507 (w), 476 (w), 452 (vw), 405 (vw) cm^{-1}.

The experimental data are consistent with the literature.[40]

1,1′-(((5′-(4-(2-Methyl-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propyl)phenyl)-[1,1′:3′,1′′-terphenyl]-4,4′′-diyl)bis(2-methylpropane-1,1-diyl))bis(oxy))bis(2,2,6,6-tetramethyl-piperidine) (3 j)

Under an argon atmosphere, 1,3,5-tris(4′-(1′′-bromo-2-methylpropyl)phenyl)benzene (1.00 g, 1.41 mmol, 1.00 equiv.), 1-oxidanyl-2,2,6,6-tetramethylpiperidine (696 mg, 4.46 mmol, 3. 17 equiv.), copper (134 mg, 2.11 mmol, 1.50 equiv.) and 4-*tert*-butyl-2-(4-*tert*-butylpyridin-2-yl)pyridine (1.13 g, 4.22 mmol, 3.00 equiv.) were suspended in 30 mL of dry acetonitrile. The reaction mixture was degassed for 10 minutes by bubbling with argon, before being stirred at 35 °C for 3 days. Afterward, methylene chloride was added, and the mixture was washed with semi-concentrated ammonia, water, saturated NaCl solution and dried over Na_2SO_4. The solvent was removed under reduced pressure. The crude product was passed through a short column (methylene chloride/ethyl acetate 4/1) to remove 4-*tert*-butyl-2-(4-*tert*-butylpyridin-2-yl)pyridine. The residue was recrystallized from ethanol to give 1.02 g (1.09 mmol, 77 % yield) of 1,1′-(((5′-(4-(2-methyl-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propyl)phenyl)-[1,1′:3′,1′′-terphenyl]-4,4′′-diyl)bis(2-methylpropane-1,1-diyl))bis(oxy))bis(2,2,6,6-tetramethylpiperidine) as a colorless solid. $R_f = 0.40$ (CH_2Cl_2/cyclohexane 1 : 1).

^{1}H NMR (400 MHz, CD_2Cl_2 [5.32 ppm], ppm) $\delta = 7.84$ (s, 3H, $C_{ar}H$), 7.67 (d, $J = 8.3$ Hz, 6H, $C_{ar.}H$), 7.35 (d, $J = 8.3$ Hz, 6H, $C_{ar.}H$), 4.60 (d, $J = 5.5$ Hz, 3H, CHO), 2.65–2.53 (m, 3H, $CH(CH_3)_2$), 1.70–0.97 (m, 45H, CH_2 CH_3 TEMPO), 0.85 (m, 18H, CH_3 Sidechain), 0.67 (s, 9H, CH_3 TEMPO); ^{13}C NMR (100 MHz, CD_2Cl_2 [54.0 ppm], ppm) $\delta = 142.6$ (3 C, C_q), 140.5 (3 C, C_q), 139.9 (3 C, C_q), 130.0 (6 C, $C_{ar}H$), 126.4 (6 C, $C_{ar}H$), 125.1 (3 C, $C_{ar}H$), 91.5 (3 C, CHO), 60.3 (6 C, C_q TEMPO), 41.2 (6 C, CH_2 TEMPO), 35.2 (3 C, CH_3 TEMPO), 34.4 (3 C, CH_3 TEMPO), 31.8 (3 C, $CH(CH_3)_2$), 20.9 (3 C, CH_3 TEMPO), 20.7 (3 C, CH_3 TEMPO), 20.6 (3 C, CH_3 Sidechain), 17.8 (3 C, CH_2 TEMPO), 16.7 (3 C, CH_3 Sidechain); FAB (3-NBA, m/z): 941 [$M^+ + H$], 784 [$M^+ -$TEMPO], 628 [$M^+ - 2$ TEMPO], 488, 472 [$M^+ - 3$ TEMPO + H], 471 [$M^+ - 3$ TEMPO], 456 [$M^+ - 3$ TEMPO-CH_3], 441 [$M^+ - 3$ TEMPO-2CH_3], 158, 157, 156 [$TEMPO^+$], 140 [$TEMPO^+$-O]. HRMS-FAB *(m/z)*: $[M+H]^+$ calcd for $C_{63}H_{94}N_3O_3$, 940.7295; found, 940.7293; IR (ATR, $\tilde{v}$) = 3002 (w), 2963 (s), 2929 (vs), 2870 (m), 2847 (w), 1596 (w), 1568 (vw), 1510 (w), 1468 (m), 1460 (m), 1375 (m), 1360 (s), 1350 (m), 1313 (w), 1258 (w), 1241 (m), 1208 (w), 1180 (w), 1133 (s), 1079 (w), 1011 (s), 987 (s), 976 (s), 953 (s), 912 (w), 878 (w), 841 (m), 817 (vs), 744 (w), 707 (m), 616 (w), 584 (w), 557 (w), 507 (w), 452 (w), 424 (w), 375 (w) cm^{-1}.

The experimental data are consistent with the literature.[40]

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Conflict of Interest

The authors declare no conflict of interest.

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[1] G. Moad, E. Rizzardo, *Nitroxide Mediat. Polym. from Fundam. to Appl. Mater. Sci.*, Royal Society of Chemistry**1993**, pp. 1–44.
[2] P. Cacioli, E. Rizzardo, D. H. Solomon, *EP 0135280A2 New Polymerization Process and Polymers Produced Thereby*, European Patent Office**1985**.
[3] J. Nicolas, Y. Guillaneuf, C. Lefay, D. Bertin, D. Gigmes, B. Charleux, *Prog. Polym. Sci.* **2013**, *38*, 63–235.
[4] M. K. Georges, R. P. N. Veregin, P. M. Kazmaier, G. K. Hamer, *Macromolecules* **1993**, *26*, 2987–2988.
[5] D. Benoit, V. Chaplinski, R. Braslau, C. J. Hawker, *J. Am. Chem. Soc.* **1999**, *121*, 3904–3920.
[6] Y. Miura, K. Hirota, H. Moto, B. Yamada, *Macromolecules* **1998**, *31*, 4659–4661.
[7] B. A. Howell, D. B. Priddy, I. Q. Li, P. B. Smith, P. E. Kastl, *Polym. Bull.* **1996**, *37*, 451–456.
[8] C. J. Hawker, G. G. Barclay, A. Orellana, J. Dao, W. Devonport, *Macromolecules* **1996**, *29*, 5245–5254.
[9] T. J. Connolly, M. V. Baldoví, N. Mohtat, J. C. Scaiano, *Tetrahedron Lett.* **1996**, *37*, 4919–4922.
[10] R. Braslau, L. C. Burrill, M. Siano, N. Naik, R. K. Howden, L. K. Mahal, *Macromolecules* **1997**, *30*, 6445–6450.
[11] B. Moon, M. Kang, *Macromol. Res.* **2005**, *13*, 229–235.
[12] T. Krause, W. D. Habicher, M. Messerschmidt, B. I. Voit, *Des. Monomers Polym.* **2004**, *7*, 391–397.
[13] J. Dao, D. Benoit, C. J. Hawker, *J. Polym. Sci. Part A* **1998**, *36*, 2161–2167.
[14] E. Harth, B. Van Horn, C. J. Hawker, *Chem. Commun.* **2001**, 823–824.
[15] P. Nesvadba, *Chimia (Aarau).* **2006**, *60*, 832–840.
[16] K. Matyjaszewski, B. E. Woodworth, X. Zhang, S. G. Gaynor, Z. Metzner, *Macromolecules* **1998**, *31*, 5955–5957.
[17] S. Harrisson, P. Couvreur, J. Nicolas, *Polym. Chem.* **2011**, *2*, 1859–1865.
[18] D. Glé, T. N. T. Phan, V. Monier, L. Charles, D. Bertin, D. Gigmes, *Prog. Control. Radic. Polym. Mater. Appl.* **2012**, pp. 141–162.

[19] C. J. Hawker, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1456–1459.

[20] S. O. Hammouch, J. M. Catala, *Macromol. Rapid Commun.* **1996**, *17*, 149–154.

[21] Y. Miura, Y. Yoshida, *Macromol. Chem. Phys.* **2002**, *203*, 879–888.

[22] T. E. Kiovsky, *U. S. Patent 4,077,893 Star-Shaped Dispersant Viscosity Index Improver* **1978**.

[23] L. M. Van Renterghem, M. Lammens, B. Dervaux, P. Viville, R. Lazzaroni, F. E. Du Prez, *J. Am. Chem. Soc.* **2008**, *130*, 10802–10811.

[24] D. P. Yang, M. N. N. L. Oo, G. R. Deen, Z. Li, X. J. Loh, *Macromol. Rapid Commun.* **2017**, *38*, 1–25.

[25] N. Hadjichristidis, M. Pitsikalis, H. Iatrou, P. Driva, G. Sakellariou, M. Chatzichristidi, *Polymers with Star-Related Structures: Synthesis, Properties, and Applications*, Elsevier B. V. **2012**.

[26] K. A. Hansen, J. P. Blinco, *Polym. Chem.* **2018**, *9*, 1479–1516.

[27] G. Audran, P. Brémond, S. R. A. Marque, *Chem. Commun.* **2014**, *50*, 7921–7928.

[28] M. K. Brinks, M. Hirtz, L. Chi, H. Fuchs, A. Studer, *Angew. Chem.* **2007**, *119*, 5324–5326; *Angew. Chem. Int. Ed.* **2007**, *46*, 5231–5233.

[29] L. Tebben, A. Studer, *Angew. Chem. Int. Ed.* **2011**, *50*, 5034–5068; *Angew. Chem.* **2011**, *123*, 5138–5174.

[30] B. Schulte, M. Tsotsalas, M. Becker, A. Studer, L. De Cola, *Angew. Chem. Int. Ed.* **2010**, *49*, 6881–6884; *Angew. Chem.* **2010**, *122*, 7033–7036.

[31] T. Kothe, S. Marque, R. Martschke, M. Popov, H. Fischer, *J. Chem. Soc. Perkin Trans. 2* **1998**, 1553–1559.

[32] I. Wessely, V. Mugnaini, A. Bihlmeier, G. Jeschke, S. Bräse, M. Tsotsalas, *RSC Adv.* **2016**, *6*, 55715–55719.

[33] K. Jin, L. Li, J. M. Torkelson, *Adv. Mater.* **2016**, *28*, 6746–6750.

[34] Y. Higaki, H. Otsuka, A. Takahara, *Macromolecules* **2006**, *39*, 2121–2125.

[35] S. Telitel, Y. Amamoto, J. Poly, F. Morlet-Savary, O. Soppera, J. Lalevée, K. Matyjaszewski, *Polym. Chem.* **2014**, *5*, 921–930.

[36] H. Otsuka, K. Aotani, Y. Higaki, A. Takahara, *J. Am. Chem. Soc.* **2003**, *125*, 4064–4065.

[37] H. Otsuka, *Polym. J.* **2013**, *45*, 879–891.

[38] M. Becker, L. De Cola, A. Studer, *J. Mater. Chem. C* **2013**, *1*, 3287–3290.

[39] M. Herder, J.-M. Lehn, *J. Am. Chem. Soc.* **2018**, *140*, 7647–7657.

[40] Q. An, I. D. Wessely, Y. Matt, Z. Hassan, S. Bräse, M. Tsotsalas, *Polym. Chem.* **2019**, *10*, 672–678.

[41] Y. Jia, Y. Matt, Q. An, I. Wessely, H. Mutlu, P. Theato, S. Bräse, A. Llevot, M. Tsotsalas, *Polym. Chem.* **2020**, *11*, 2502–2510.

[42] L. Li, H. Ren, Y. Yuan, G. Yu, G. Zhu, *J. Mater. Chem. A* **2014**, *2*, 11091–11098.

[43] K. J. Msayib, N. B. McKeown, *J. Mater. Chem. A* **2016**, *4*, 10110–10113.

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