Showcasing research from the laboratories of Prof. Johnson and Prof. Sigman, Department of Chemistry, MIT and University of Utah, respectively, USA.

Tricyclononenes and tricyclononadienes as efficient monomers for controlled ROMP: understanding structure–propagation rate relationships and enabling facile post-polymerization modification

Living ring-opening metathesis polymerization of a library of tricyclic olefins was investigated for comparison to traditional bicyclic ROMP monomers, providing new insights into monomer reactivity and useful new monomers for macromolecular synthesis.

As featured in:

Chemical Science

See Jeremiah A. Johnson et al., Chem. Sci., 2024, 15, 8334.
Tricyclononenes and tricyclononadienes as efficient monomers for controlled ROMP:
understanding structure–propagation rate relationships and enabling facile post-
polymerization modification†

Landon J. Kilgallon, a Timothy P. McFadden, b Matthew S. Sigmanb and Jeremiah A. Johnsond,a

Ruthenium-initiated ring-opening metathesis polymerization (ROMP) remains an
indispensable tool in the polymer chemist’s toolbox. Tricyclononenes (TCN) and tricyclononadienes
(TCND) represent under-explored classes of monomers for ROMP that have the potential to both
advance fundamental knowledge (e.g., structure-polymerization kinetics relationships) and serve as
practical tools for the polymer chemist (e.g., post-polymerization functionalization). In this work, a library
of TCN and TCND imides, monooesters, and diesters, along with their exo-norbornene counterparts,
were synthesized to compare their behaviors in G3-initiated ROMP. Real-time1H NMR was used to study
their polymerization kinetics; propagation rates (kp) were extracted for each monomer. To understand
the relationships between monomer structure and ROMP propagation rates, density functional theory
methods were used to calculate a variety of electronic and steric parameters for each monomer. While
electronic parameters (e.g., HOMO energy levels) correlated positively with the measured kp values,
steric parameters generally gave improved correlations, which indicates that monomer size and shape
are better predictors for kp than electronic parameters for this data set. Furthermore, the TCND diester—
which contains an electron-deficient cyclobutene that is resistant to ROMP—and its polymer p(TCND)
are shown to be highly reactive toward DBU-catalyzed conjugate addition reactions with thiols,
providing a protecting- and activating-group free strategy for post-polymerization modification.

Introduction

Ruthenium-initiated ring-opening metathesis polymerization
(ROMP) is an invaluable tool in the polymer chemist’s repertoire
due to the commercial availability of fast-initiating ruthenium initiators and various strained olefin monomers,
its wide functional group tolerance, and the ease in which complex polymers may be synthesized in a rapid and controlled
manner. Grubbs 3rd-generation pyridine-ligated pre-catalysts (G3) are most frequently used for living ROMP due to their
fast initiation rates.1 Moreover, exo-norbornenes (NB) are often

† Electronic supplementary information (ESI) available. CCDC 2326835, 2326836 and 2351614. For ESI and crystallographic data in CIF or other electronic format see DOI: https://doi.org/10.1039/d4sc01986e
they offer facile routes to post-polymerization modification that are not possible for common exo-NBs. Finally, this study presents the first application of computed steric parameters to correlate monomer structure with propagation rates in ROMP, providing insights into the predictive design of future ROMP monomers.

## Results/discussion

### TCN and TCND monomer synthesis

Quadricyclane was prepared by photochemical isomerization of norbornadiene in batches of up to 17 g and yields up to >90% (ESI† Section 2). Heating quadricyclane in the presence of maleic anhydride gave TCN exo-anhydride 1 as a mixture of anti and syn diastereomers (67 : 33 anti : syn) in quantitative yield (Fig. 2a). Crystallization led to enrichment of the anti-1 to 78 : 22 anti : syn (69% yield); further isolation of pure diastereomers was conducted following a subsequent synthetic step. TCN diester TCN-(CO$_2$Me)$_2$ was prepared by acid-catalyzed esterification of 1 with methanol. The TCN imides TCN-NB$_n$anti, TCN-NCy, and TCN-NHex were prepared by condensation of 1 with benzylamine, cyclohexylamine, and n-hexylamine, respectively, in an analogous fashion to Warrener’s procedure for preparing the N-methyl TCN imide from 1 and methylamine. All of these TCNs were crystalline solids wherein crystallization afforded the anti-isomer in a >95 : 5 anti : syn ratio in each case.

We also sought TCN-NB$_n$syn for comparison to its anti-diastereomer (Fig. 2b). While TCN-NB$_n$syn and TCN-NB$_n$anti may potentially be separable by chromatography, we identified a kinetic resolution method that leveraged the large difference in imidation rates between the syn (slow) and anti (fast) amic acids formed upon initial ring-opening of 1, ultimately giving TCN-NB$_n$syn in 4% yield over 2 steps with >98 : 2 d.r. (ESI† Section 2). The relative configurations of TCN-NB$_n$syn and TCN-NB$_n$anti were unambiguously determined by single-crystal X-ray diffraction (Fig. 2b). TCND derivatives TCND-(CO$_2$Me)$_2$ and TCND-CO$_2$Me were synthesized by direct cycloaddition of quadricyclane with dimethyldiacetaldicarboxylate and methyl propiolate, respectively (Fig. 2a).

We note that upon storage under ambient atmosphere for extended periods, TCND-(CO$_2$Me)$_2$ yellows and a new product is observed via $^1$H NMR spectroscopy. A small sample of this impurity was isolated chromatographically; its $^1$H NMR spectrum contained no olefinic resonances and its high-resolution mass spectrum suggested a mass 16 Da (i.e., 1 oxygen atom) larger than TCND-(CO$_2$Me)$_2$. Single-crystal X-ray analysis of the saponified derivative of this impurity revealed its identity to be the exo-epoxidized variant of TCND-(CO$_2$Me)$_2$ (ESI† Section 11). Thus, we recommend storage of uninhibited TCND-(CO$_2$Me)$_2$ under inert atmosphere, as is often done for olefinic monomers, to avoid its oxidative decomposition.

Finally, for comparison of ROMP propagation rates (vide infra), exo-NB analogs of each TCN and TCND were synthesized following previously reported procedures. All monomers and intermediates were isolated non-chromatographically, and the key intermediates towards TCNs (1) and TCNDs
(quadricyclane) were synthesized on the 16 g and 17 g scales, respectively. Notably, the melting temperatures for all but one (TCND-CO₂Me) of the TCNs and TCNDs synthesized in this study were greater than their exo-NB analogs (from 10 °C to >150 °C higher), presumably due to their multicyclic, comparably rigid structures. In particular, all of the TCNs studied here have melting points >40 °C above room temperature, making them generally easy to handle and purify (crystallization).

ROMP of TCN and TCND monomers

Each TCN and TCND described above (200 equiv.) was exposed to G3 (1 equiv.) in CDCl₃ solvent to initiate ROMP. Reactions of TCNs were allowed to proceed for 15 minutes before quenching and precipitating twice from methanol, giving p(TCN) in good yields (Table 1). Size exclusion chromatography (SEC) revealed low dispersities (D) and number-average molar masses (M_n) close to theoretical values for all p(TCN) samples (Fig. 3a–d). SEC analysis of p(TCND-CO₂Me) prepared under the same conditions (i.e., 15 min reaction time) showed a minor high molecular weight shoulder peak at 2 × M_n indicative of cross-linking, as was also reported for Mo-initiated ROMP of this monomer (Fig. 3e).³ Quenching the ROMP reactions after a shorter time (2 min) using the same batch of TCND-CO₂Me or a freshly distilled sample of TCND-CO₂Me (discarding the first and last ~10–15% of the distillate) substantially decreased the size of this shoulder peak. Notably, conversion was unaffected by decreasing the reaction time to 2 min, as evidenced by the similar SEC traces, suggesting that this monomer is highly reactive. Moreover, these results indicate that the cyclobutene component of TCND-CO₂Me remains largely intact under these ROMP conditions, providing an opportunity for further modification post-polymerization (vide infra).

While the synthesis of p(TCND-CO₂Me) appeared to be no different than for the other samples prepared here, the polymer product did not re-dissolve after the first precipitation. We
hypothesized that polymer-associated residual Ru led to cross-linking reactions upon precipitation; the addition of excess pyridine (∼2000 equiv. relative to G3) to the quenched ROMP reaction suppressed this cross-linking (ESI† Section 3), enabling NMR and SEC analysis of p(TCND-CO₂Me); however, SEC analysis showed a significant high molecular weight shoulder (Fig. 3f). Notably, while cyclobutene 1-carboxylic esters, like the cyclobutene fragment of TCND-CO₂Me, cannot homopolymerize via G3-initiated ROMP, they are known to slowly form ene-carbenes that are kinetically stabilized by intramolecular chelation. Thus, we propose that ROMP of TCND-CO₂Me occurs first through rapid polymerization of its NB-like alkene followed by slow cross-linking of its cyclobutene pendants, which are more sterically accessible than for TCND-(CO₂Me)₂ above.

1H NMR spectroscopy was used to characterize the structures of these p(TCN)s and p(TCND)s in more detail (Fig. 4). Resonances associated with each of the monomer protons could be identified in the polymers. Compared to p(exo-NB) analogs (ESI† Section 3), the backbone olefinic protons of p(TCN)s and p(TCND)s were slightly skewed toward the Z configuration: E : Z ranged from 48 : 52 to 37 : 63 for p(exo-NB)s while p(TCN)s and p(TCND)s ranged from 37 : 63 to 30 : 70 (Table 1). The spectrum of p(TCND-CO₂Me) contained an extra downfield resonance at 6.8 ppm that we attribute to the olefinic proton of the cyclobutene. Otherwise, the spectra generally resembled those of their p(exo-NB) counterparts, with the addition of two proton resonances in the carbocyclic region (∼1.4 ppm–3.5 ppm) for the p(TCN)s.

We anticipated that TCN and TCND monomers would display controlled polymerization behavior due to their high

Table 1 Characterization of p(TCN)s and p(TCND)s prepared by G3-initiated ROMP

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Mₘ (theo.)</th>
<th>Mₘ (SEC)</th>
<th>D</th>
<th>Yield</th>
<th>E/Z ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>p(TCN-NBₙex)</td>
<td>56.0 kDa</td>
<td>52.2 kDa</td>
<td>1.02</td>
<td>97%</td>
<td>37 : 63</td>
</tr>
<tr>
<td>p(TCN-NCy)</td>
<td>54.4 kDa</td>
<td>54.2 kDa</td>
<td>1.02</td>
<td>95%</td>
<td>34 : 66</td>
</tr>
<tr>
<td>p(TCN-NHex)</td>
<td>54.8 kDa</td>
<td>52.2 kDa</td>
<td>1.02</td>
<td>92%</td>
<td>37 : 63</td>
</tr>
<tr>
<td>p(TCN-(CO₂Me)₂)</td>
<td>47.4 kDa</td>
<td>47.8 kDa</td>
<td>1.02</td>
<td>97%</td>
<td>33 : 67</td>
</tr>
<tr>
<td>p(TCND-(CO₂Me)₂)</td>
<td>47.0 kDa</td>
<td>49.5 kDa</td>
<td>1.04</td>
<td>92%</td>
<td>30 : 70</td>
</tr>
<tr>
<td>p(TCND-CO₂Me)</td>
<td>35.3 kDa</td>
<td>59.3 kDa</td>
<td>1.97</td>
<td>75%</td>
<td>37 : 63</td>
</tr>
</tbody>
</table>

a Monomer conversion was >98% in each case. b Theoretical Mₘ values were calculated assuming 100% monomer conversion. c SEC conditions: DMF (0.025 M LiBr) mobile phase, 60 °C, with differential refractive index and multi-angle light scattering detectors. A 100% mass recovery method was used to calculate Mₘ. d E/Z ratio was determined by the relative integrations of the trans (downfield) and cis (upfield) backbone olefinic protons in the polymers’ ¹H NMR spectra.35,36

Fig. 3 (a–d) SEC traces of p(TCN)s. (e) Overlaid SEC traces of p(TCND-(CO₂Me)₂) when quenched after 15 min, 2 min, or after carefully distilling the monomer and quenching after 2 min (f) SEC trace of p(TCND-CO₂Me) after working up the polymer in the presence of excess pyridine.
ring strain and low likelihood of backbiting/chain transfer. In support of this hypothesis, $M_{n,SEC}$ values for $p(\text{TCN-NBn}_{\text{anti}})$ agreed well with the theoretical values and increased linearly as a function of conversion up to a degree of polymerization (DP) of 500 (Fig. 5a). Moreover, a plot of $\ln([\text{TCN-NBn}_{\text{anti}}]/[\text{TCN-NBn}_{\text{anti}}]_0)$ was linear as a function of time (Fig. 5b), and $D$ remained low throughout the polymerization (Fig. 5a), suggesting minimal irreversible termination or chain transfer. Finally, to demonstrate the active nature of the $p(\text{TCN-NBn}_{\text{anti}})$ Ru-alkylidene chain ends, a block copolymer $p(\text{TCN-NBn}_{\text{anti}})_{100}$-...
$b$-$p$(TCN-NHex)\textsubscript{100} was synthesized via sequential monomer addition (Fig. 5c). SEC analysis showed a clear peak shift to shorter retention time upon addition of TCN-NHex, suggesting complete chain extension; $D$ for the block copolymer remained low (1.02).

1$^H$ NMR spectroscopic kinetic investigations of TCN and TCND ROMP reactions

Real-time $^1$H NMR spectroscopy was used to evaluate the ROMP propagation kinetics for each monomer shown in Fig. 2 in the presence of pyridine (5 equiv. relative to G3; note: pyridine was added to retard the polymerization reactions sufficiently for $^1$H NMR analysis). For all monomers except TCND-CO$_2$Me, conversion was measured by comparison of the monomer signal to an added internal standard (mesitylene). The additional downfield olefin resonance of p(TCND-CO$_2$Me) overlapped with that of the internal standard; monomer conversion was measured by relative integration of the monomer signal to the backbone olefin signals in this case. Each polymerization followed pseudo-first order kinetics up to $\geq 95\%$ conversion, indicative of a controlled process (Fig. 6a–f). The propagation rates ($k_p$), obtained by linear fitting of $\ln([M]_0/[M])$ vs. time plots (Fig. 6, insets, and ESI† Section 4), spanned a factor of $\sim 13$ ($k_p = 0.094–1.259$ min$^{-1}$) for the monomers analyzed in this study (Table 2).

The $k_p$ values for imides TCN-NB\textsubscript{anti} TCN-NB\textsubscript{syn} TCN-NCy, and TCN-NHex were within $\sim 20\%$ of each other and were slightly lower than their exo-NB imide counterparts. A similar trend was observed for the monoesters, but to a larger extent: $k_p$ for NB-CO$_2$Me was 2.2-fold higher than for TCND-CO$_2$Me. Notably, however, the opposite trend was observed for the diester monomers; $k_p$ for TCND-(CO$_2$Me)$_2$ was greater than TCN-(CO$_2$Me)$_2$, which was greater than NB-(CO$_2$Me)$_2$.

Comparing across the imides, diesters, and monoesters, the imides had the lowest $k_p$ values without exception; the fastest imide (NB-NCy) had a $\sim 19\%$ lower $k_p$ than the slowest diester/monoester (NB-(CO$_2$Me)$_2$). This result agrees well with the trends reported for imide versus ester anchor groups for both small molecule monomers and macromonomers.\textsuperscript{5–7} Comparison of the monoesters and diesters shows that while the monoester TCND-CO$_2$Me and diester TCND-(CO$_2$Me)$_2$ propagate at nearly the same rate, NB-CO$_2$Me propagates 5.6 times faster than its diester counterpart NB-(CO$_2$Me)$_2$. Altogether, these results demonstrate that TCN and TCND monomers possess similar living behavior and G3-initiated ROMP $k_p$ values compared to traditional exo-NBs.

Fig. 6 (a–f) ROMP propagation kinetics of all TCN and TCND monomers in this study. The raw data are presented with an inset plot of $\ln([M]_0/[M])$ versus time. Each was run in triplicate, and error bars are plotted as $\pm$ SD in the raw data plots. Conditions: 95 mM monomer (200 equiv.), 2.4 mM pyridine (5 equiv.), 0.48 mM G3 (1 equiv.) and internal standard (mesitylene) in CDCl$_3$ at 25 °C.
Density functional theory (DFT) calculations of monomer electronic and steric parameters to predict $k_p$

Matson and coworkers have proposed that the DFT-calculated HOMO energy levels of exo-NB monomers correlate well with their $k_p$ values in G3-initiated ROMP.\textsuperscript{5–8} To determine if TCNs and TCNDs follow this trend, the HOMO energies for each monomer shown in Fig. 2b were calculated using the M06-2X functional and dev2-TZVP basis set (with a conductor-like polarizable continuum model for chloroform) and plotted against the measured ln($k_p$) values (Fig. 7b). The HOMO energies ranged from $-183$ kcal mol$^{-1}$ to $-194$ kcal mol$^{-1}$, which falls within the range reported for other ROMP monomers ($-174$ kcal mol$^{-1}$ to $-197$ kcal mol$^{-1}$) calculated with the same functional and basis set.\textsuperscript{5,6,8} In agreement with Matson and coworkers, a positive correlation between $k_p$ values and HOMO energies was observed; however, NB-CO$_2$Me stands out as having a much larger $k_p$ value than its HOMO energy would predict. Notably, NB-CO$_2$Me is the only monosubstituted

<table>
<thead>
<tr>
<th>Monomer</th>
<th>$k_p$ (min$^{-1}$)</th>
<th>$t_{1/2}$ (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NB-NBn</td>
<td>0.157 ± 0.001</td>
<td>4.4</td>
</tr>
<tr>
<td>TCN-NBn$_{anti}$</td>
<td>0.117 ± 0.001</td>
<td>5.9</td>
</tr>
<tr>
<td>TCN-NBn$_{syn}$</td>
<td>0.122 ± 0.001</td>
<td>5.7</td>
</tr>
<tr>
<td>NB-NCy</td>
<td>0.183 ± 0.001</td>
<td>3.8</td>
</tr>
<tr>
<td>TCN-NCy</td>
<td>0.101 ± 0.001</td>
<td>6.9</td>
</tr>
<tr>
<td>NB-NHex</td>
<td>0.140 ± 0.001</td>
<td>5.0</td>
</tr>
<tr>
<td>TCN-NHex</td>
<td>0.094 ± 0.001</td>
<td>7.4</td>
</tr>
<tr>
<td>NB-(CO$_2$Me)$_2$</td>
<td>0.225 ± 0.001</td>
<td>3.1</td>
</tr>
<tr>
<td>TCN-(CO$_2$Me)$_2$</td>
<td>0.342 ± 0.001</td>
<td>2.0</td>
</tr>
<tr>
<td>TCND-(CO$_2$Me)$_2$</td>
<td>0.622 ± 0.007</td>
<td>1.1</td>
</tr>
<tr>
<td>NB-CO$_2$Me</td>
<td>1.259 ± 0.014</td>
<td>0.6</td>
</tr>
<tr>
<td>TCND-CO$_2$Me</td>
<td>0.564 ± 0.010</td>
<td>1.2</td>
</tr>
</tbody>
</table>

*Conditions: 95 mM monomer (200 equiv.), 2.4 mM pyridine (5 equiv.), 0.48 mM G3 (1 equiv.) and internal standard (mesitylene) in CDCl$_3$ at 25 °C.
norbornene (only one of the two \( \text{exo} \) positions is substituted) of the monomers studied here.

Grubbs\textsuperscript{3} and Matson also found that monosubstituted \( \text{exo-NBs} \) polymerize faster than disubstituted variants; Matson attributed this difference either to the possibility that monosubstituted monomers can form regioisomers where their substituents point away from the ruthenium center (a steric effect),\textsuperscript{7} or to electronic effects (HOMO level and HOMO/LUMO gap).\textsuperscript{8-9} While the chelating ability of NB monomer substituents has also been shown to significantly affect the activation parameters of polymerization and may slow the polymerization rate by ground-state stabilization in certain cases,\textsuperscript{4} the chelating ability of \( \text{exo-NB} \) monomers seems to have little correlation with their propagation rates.\textsuperscript{5} We note that \( \text{NB-CO}_2\text{Me} \) has a \( \sim 4 \)-fold larger \( k_p \) than \( \text{TCN-(CO}_2\text{Me)}_2 \) despite having nearly the same calculated HOMO energy (0.6 kcal difference), and that \( \text{TCN-(CO}_2\text{Me)}_2 \) and \( \text{TCND-CO}_2\text{Me} \) both have higher-lying HOMOs (by \( \sim 4 \) and \( \sim 6 \) kcal mol\(^{-1} \), respectively) than \( \text{NB-CO}_2\text{Me} \) but significantly lower \( k_p \) values. Overall, while HOMO energy is a useful tool for predicting ROMP reactivity for \( \text{exo-NB} \)-like scaffolds, other effects, such as steric effects near the propagation site, may impact the rate as well.

These findings led us to consider alternative readily-computed structural descriptors that may provide better correlations with ROMP monomer performance over a wider structure range, and may then also provide greater predictive power for the design of novel monomers. We began by collecting DFT-derived parameters from an AQME derived conformer ensemble\textsuperscript{41,42} using RDKit\textsuperscript{43} for each monomer. From the conformer ensemble, five representative conformers were selected to extract a range of steric and electronic parameters (Fig. 7a).\textsuperscript{44,45} The ensemble conformer properties were condensed to include the lowest energy conformer (low \( E \)), minimum (min), maximum (max), and Boltzmann derived parameter values. Additionally, we also extracted condensed properties from the conformer presenting the minimum percent buried volume (\( V_{\text{bur-min}} \)) parameter value at the active site olefinic carbon (\( C_1 \)), as we hypothesized that steric effects may be a driver of the observed rate differences. Percent buried volume probes the proximal steric environment by placing a 3 Å sphere at the site of interest and measuring the resulting overlap.\textsuperscript{46} The library of parameters was regressed against ln(\( k_p \)) to reveal a range of good correlations with various parameters describing steric effects (molar volume (MV), solvent accessible surface area (SASA) and Sterimol B\(_3\)). These correlations all resulted from the \( V_{\text{bur-min}} \) conformer values located at the active site olefinic carbon \( C_1 \). A representative correlation using Sterimol B\(_3\) is depicted in Fig. 7c. This parameter describes the display of steric information for how the adjacent olefinic carbon \( C_1 \) may present itself to the propagating Ru chain end (Fig. 7a). The other two strong correlations, MV and SASA, represent the shape of the monomer while accounting for the local environment defined by the \( V_{\text{bur-min}} \) conformer. Notably, the Sterimol B\(_3\) and the MV \( V_{\text{bur-min}} \) conformers were found to be collinear, and the same parameters derived from other conformers (i.e., low \( E \), min, and max values) do not perform nearly as well [ESI\textsuperscript{†} Section 13]. Overall, these data suggest that the overall size and shape of the monomer has a significant impact on polymerization kinetics.

Further derivatization of \( \text{TCN-(CO}_2\text{Me)}_2 \) and post-polymerization functionalization of \( \text{p(TCND-(CO}_2\text{Me)}_2) \)

In addition to their straightforward syntheses and good \( k_p \) values, \( \text{TCN-(CO}_2\text{Me)}_2 \) and \( \text{TCND-CO}_2\text{Me} \), and their corresponding polymers \( \text{p(TCND-(CO}_2\text{Me)}_2) \) and \( \text{p(TCND-CO}_2\text{Me}) \), offer unique opportunities for further derivatization and post-polymerization functionalization, respectively, compared to \( \text{exo-NBs} \). While their cycloaddition reactivity has been explored,\textsuperscript{45-47} we suspected that their strained, electron-deficient cyclobutene substituents would make them good electrophiles for conjugate addition reactions (e.g., “thiol-Michael” addition). To test this idea, \( \text{TCN-(CO}_2\text{Me)}_2 \) was exposed to dodecanethiol (1.0 equiv.) in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (10 mol\%) in CDCl\(_3\) for 30 min (Table 3, entry 1); 47% conversion to the conjugate addition product was observed under these conditions, while 0% conversion was observed in the absence of DBU. Polar

### Table 3 Conjugate addition of dodecanethiol to various conjugate acceptors

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conjugate acceptor</th>
<th>LUMO energy (kcal mol(^{-1}))</th>
<th>Solvent</th>
<th>DBU (mol%)</th>
<th>Conversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TCN-(CO\textsubscript{2}Me\textsubscript{2})</td>
<td>−30</td>
<td>CDCl(_3)</td>
<td>10%</td>
<td>47%</td>
</tr>
<tr>
<td>2</td>
<td>TCN-(CO\textsubscript{2}Me\textsubscript{2})</td>
<td>−30</td>
<td>DMF-d(_7)</td>
<td>1%</td>
<td>87%</td>
</tr>
<tr>
<td>3</td>
<td>DDM</td>
<td>−8</td>
<td>CDCl(_3)</td>
<td>10%</td>
<td>0%</td>
</tr>
<tr>
<td>4</td>
<td>TCND-CO\textsubscript{2}Me</td>
<td>−10</td>
<td>CDCl(_3)</td>
<td>10%</td>
<td>3%</td>
</tr>
</tbody>
</table>

© 2024 The Author(s). Published by the Royal Society of Chemistry
solvents are known to accelerate conjugate addition reactions
that involve polar mechanisms; when DMF-d₇ was used as the
solvent for this reaction, 87% conversion was achieved in
30 min using only 1 mol% DBU (Table 3, entry 2).

Notably, dimethyl 2,3-dimethylmaleate (DDM), a less-
strained electrophile with a similar substitution pattern, did
not react under the CDCl₃ conditions described above (Table 3, entry 3), and TCND-CO₂Me reached only 3% conversion (Table 3, entry 4). These results correlate with the DFT calculated
LUMO energies (M06-2X/def-TZVP) for each molecule (Table 3), suggesting that the rigid structure of TCND-(CO₂Me)₂ paired with its two electron-withdrawing ester substituents make it a better electrophile for conjugate addition. Meanwhile, as
discussed above, these structural features are also key for (1)
ensuring a high ROMP $k_p$ (by avoiding steric hindrance asso-
ciated with diesters appended directly to the exo-NB) and (2)
avoiding undesired cross-linking during ROMP (as observed for
TCND-CO₂Me), making TCND-(CO₂Me)₂ a particularly prom-
ising monomer for further exploration.

We hypothesized that the electrophilicity of TCND-(CO₂Me)₂
would not change significantly after ROMP, rendering p(TCND-
(CO₂Me)₂) a similarly useful substrate for post-polymerization
conjugate addition reactions. This hypothesis was supported
by DFT calculations (M06-2X/def-TZVP); the LUMO energy of
a model substrate designed to mimic the p(TCND-(CO₂Me)₂)
backbone—the ethenolysis product of TCND-(CO₂Me)₂—was
very similar (−32 kcal mol⁻¹) to that of TCND-(CO₂Me)₂
(−30 kcal mol⁻¹). Moreover, nearly quantitative conjugate
addition was observed when p(TCND-(CO₂Me)₂) was exposed to
dodecanethiol (5 equiv.) and DBU (20 mol%) in DMF solvent for
1 h under ambient atmosphere (Table 4, entry 1). The reaction
solution became cloudy almost immediately after addition of
the DBU, suggesting rapid conjugate addition and limited
solubility of the functionalized polymer product in DMF.

Decreasing the number of equivalents of thiol to 2 (Table 4,

<table>
<thead>
<tr>
<th>Entry</th>
<th>H₂S₅C₁₂SH equiv.</th>
<th>DBU equiv.</th>
<th>Conversion</th>
<th>( ^{1} \text{H NMR} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>20 mol%</td>
<td>&gt;95%</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>20 mol%</td>
<td>&gt;95%</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>5 mol%</td>
<td>&gt;95%</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1.5</td>
<td>5 mol%</td>
<td>&gt;95%</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1.1</td>
<td>5 mol%</td>
<td>95%</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>1.1</td>
<td>2.5 mol%</td>
<td>93%</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1.2</td>
<td>5 mol%</td>
<td>&gt;95%</td>
<td></td>
</tr>
</tbody>
</table>

Conditions: p(TCND-(CO₂Me)₂) in DMF (50 mg mL⁻¹) at room
temperature. Dodecanethiol was added, followed by the addition of
DBU as a stock solution in DMF (1 : 9 v/v DBU : DMF) and was allowed
to react for 1 hour. Conversion was assessed by comparing the
integration of the backbone olefinic protons (4.8 ppm – 5.7 ppm)
versus the integration of the terminal –CH₃ of the dodecanethiol side-
chain (0.9 ppm).

Table 4  Optimization of post-polymerization modification of
p(TCND-(CO₂Me)₂) with dodecanethiol
entry 2) and lowering the catalyst loading to 5 mol% (Table 4, entry 3) did not affect the conversion. Reduction of the equivalents of thiol to 1.5 (Table 4, entry 4) did not affect conversion either; however, further decreasing the amount of thiol to 1.1 equiv. gave slightly reduced conversion (95%, Table 4, entry 5), which was reduced further with a lower catalyst loading of 2.5 mol% (93%, Table 4, entry 6). Over 95% conversion was achieved with 1.2 equiv. of thiol and 5 mol% DBU (Table 4, entry 7); these conditions were chosen as optimal for further studies.

A variety of thiol nucleophiles was explored using these optimized conditions (Table 5); 1H NMR and SEC were used to measure conversion of each reaction, with the two methods showing agreement within ~15% in most cases. Incomplete conversion was observed for 4-tert-butylthiophenol and 2-naphthalenethiol under ambient (Table 5, entries 1 and 3) or inert (N2) atmosphere (Table 5, entries 2 and 4), which we attribute to the steric bulk of these thiols. Nearly quantitative functionalization was observed for methyl thioglycolate (Table 5, entries 5 and 6) regardless of atmosphere; however, the SEC peak shape for the product showed distinct broadening and tailing compared to the initial p(TCND-(CO2Me)2), which may be due to possible deleterious side-reactions promoted by the relatively acidic α-protons of the α-mercapto ester (ESI† Section 9). By contrast, 1-methyl-3-mercaptopropionate, a β-mercapto ester, underwent high conversion to give a polymer product with no significant change in peak shape (Table 5, entry 7). Finally, hexanethiol also gave high conversion under these conditions (Table 5, entry 8).

Conclusions

This work represents the first detailed study of the polymerization behavior of TCN and TCND monomers in G3-initiated ROMP. A variety of functional (imides, monoesters, and diesters) TCNs, TCNDs, and exo-NBs were synthesized and their ROMP propagation rates were measured to span a factor of ~13. To understand the relationship between monomer structure and propagation rate, the monomers were featurized using DFT to extract a variety of electronic and steric parameters and search for correlations with measured propagation rates. While simple electronic parameters (e.g., HOMO levels) positively correlated with monomer kprop, steric parameters that described the overall size and shape of the monomer were more strongly correlated with kprop. TCND-(CO2Me)2—which contains an electron-deficient cyclobutene—was discovered to be highly active towards DBU-catalyzed conjugate addition of dodecanethiol. This conjugate addition reaction was optimized on p(TCND-(CO2Me)2), and a variety of thiol nucleophiles were used to functionalize p(TCND-(CO2Me)2) in this post-polymerization modification reaction.

Overall, this study revealed that TCNs and TCNDs are a synthetically accessible class of ROMP monomers that do not compromise on activity or controlled polymerization behavior in comparison to other commonly used monomers (e.g. exo-NBs). In particular, TCND-(CO2Me)2 is a uniquely promising monomer due to its ease of synthesis (2 steps from commercial materials), fast ROMP kinetics, and its innate activity towards post-polymerization functionalization with thiols; we envision its future widespread use for functional polymer design. Finally, our experimental and computational study revealed that monomer steric parameters correlate most strongly with their measured propagation rates; these results offer the polymer chemist both the intuitive framework and computational tools for developing future novel ROMP monomers.

Data availability

The datasets supporting this article have been uploaded as part of the ESL†

Author contributions


Conflicts of interest

There are no conflicts of interest to declare.

Acknowledgements

This work was supported as part of the Center for Regenerative Energy-Efficient Manufacturing of Thermoset Polymeric Materials (REMAT), an Energy Frontier Research Center funded by the U.S. Department of Energy, Office of Science, Basic Energy Sciences under award #DE-SC0023457. Thanks to Dr Peter Müller of the MIT Chemistry Department X-Ray Diffraction Facility for crystal structure determination.

References

4 M. G. Hyatt, D. J. Walsh, R. L. Lord, J. G. Andino Martínez and D. Guironnet, Mechanistic and Kinetic Studies of the


31 R. N. Warrener, Dimethyl (1z,2z, 5b,6z)tricyclo[4.2.1.2.5]nona-3,7-dien-3,4-dicarboxylate, in Encyclopedia of Reagents for Organic Synthesis (EROS), 2004.


46 G. Jenner, High pressure sequential (π2 + π2 + π2) and (π2 + σ2 + σ2) cycloaddition reactions. Synthesis of polycyclic bisadducts from C5H8 hydrocarbons, Tetrahedron Lett., 1987, 28(34), 3927–3930, DOI: 10.1016/S0040-4039(00)96422-0.


