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Scalable Synthesis of Norbornadienes via *in situ* Cracking of Dicyclopentadiene Using Continuous Flow Chemistry

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The norbornadiene (NBD)-quadricyclane (QC) photoswitch has recently attracted attention due to its use in molecular solar thermal energy systems (MOST). Normally for device testing, several grams are needed. One way of synthesizing NBDs efficiently is through the Diels-Alder reaction between alkynes and cyclopentadiene. However, scaling up the reaction can be troublesome in a research lab environment. Also, dicyclopentadiene needs cracking before utilization which is a time-consuming step. Here, we developed a method where we both scale up the synthesis in a single reaction step that involves both *in situ* cracking of dicyclopentadiene and the direct reaction of cyclopentadiene with acetylene derivatives using a tubular coiled stainless steel flow reactor. As a proof-of-concept, we synthesized six different NBD compounds and scaled the synthesis to produce 87 g of a novel NBD in 9 h. The NBD is further characterized, showing promising properties for MOST applications. Our new method shows that flow chemistry is an attractive technique for the fast and efficient synthesis of large quantities of NBDs, needed to develop future real-life devices and applications.

Introduction

Norbornadiene (NBD), a photoswitching molecule, has received increasing attention during the past decade due to its ability to store energy by isomerization to its meta-stable form, quadricyclane (QC). The system is currently evaluated for possible use as a molecular solar thermal energy storage system (MOST).[1] Several examples of 2,3-disubstituted NBDs with electron-accepting and electron-donating groups on one of the double bonds have been investigated for MOST purposes.[2] Among synthetic routes towards NBDs, one of the most attractive ways is through the Diels-Alder reaction between cyclopentadiene (CP) **1** and a substituted alkyne. The synthesis is usually a two-step procedure since CP is very reactive and, therefore, upon storage exists mainly as a dimer, dicyclopentadiene **2**. Through thermal cracking of the dimer, a *retro* Diels-Alder reaction occurs and results in the CP monomer **1**, which can be used for further reactions, as in this case, another Diels-Alder reaction resulting in an NBD (Figure 1).

An interesting example of cracking the dimer was demonstrated by Dinda M, *et al.*,[3] who used solar thermal energy to drive the thermodynamically uphill reaction from dicyclopentadiene to CP. The cyclopentadiene was utilized in a second reaction step in a solar thermal driven reaction with 4-phenylbut-3-yn-2-one **3** to synthesize 3-phenylbicyclo[2.2.1]hepta-2,5-dien-2-yl)ethan-1-one **4**, a 2,5 norbornadiene derivative in a yield of 75 % (Figure 2).

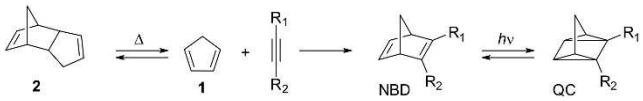

Figure 1. Two-step procedure towards a 2,5-substituted norbornadiene, starting with cracking of the dimer, dicyclopentadiene **2**, to receive CP **1**, followed by the Diels-Alder reaction with an alkyne (R_1, R_2 = various substituents) to NBD and photoisomerization from NBD to the QC form.

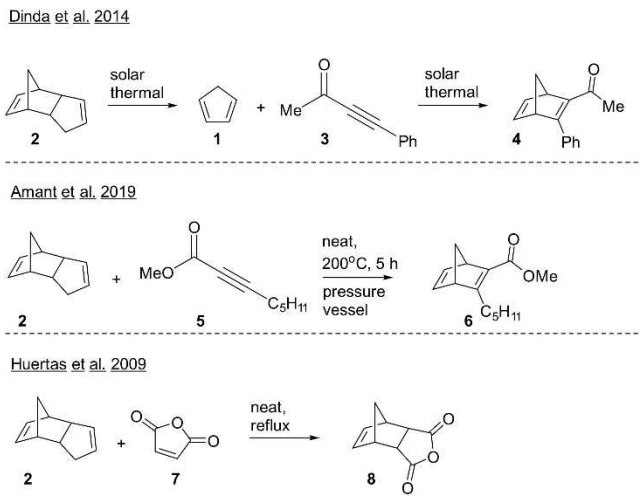

Figure 2. Examples of traditional batch synthesis using solar thermal energy for cracking dicyclopentadiene by Dinda et al.[3] and in situ cracking and reaction of dicyclopentadiene by Amant et al.[4] and Huertas et al.[5]

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Some examples of *in situ* cracking using the traditional batch synthesis of the dimer in a Diels-Alder reaction towards NBDs or similar derivatives have also been reported in the literature (Figure 2). One example, using high temperatures of 200 °C in pressure vials Amant, *et al.*[4] obtained methyl-3-pentylbicyclo[2.2.1]hepta-2,5-diene-2-carboxylate **6** in 50% yield by reacting methyl 2- octynoate **5** with dicyclopentadiene **2**.[4] Another example from Huertas, *et al.*[5] shows that the reaction of dicyclopentadiene **2** with dienophiles such as maleic anhydride **7** and unsaturated esters generates Diels-Alder adducts, like 4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1,3-dione **8** (Figure 2) using traditional batch synthesis.

Nevertheless, many interesting and successful NBD syntheses exist,[1a,6] mainly achieved using traditional batch synthesis, which may be impractical when larger amounts of one molecule are needed. An alternative synthetic technique that is recently gaining importance is continuous-flow synthesis. It is a relatively new technology with increasing interest since it has several possible advantages. By performing a reaction in a stream, the narrow channels in the reactor provide a high surface-to-volume ratio which improves heat and mass transfer, leading to better control and reproducibility of the reaction.[7] The technique potentially also enables *in-line* analysis and automation. One of the greatest advantages of continuous flow synthesis over batch is the ability to scale up a given synthesis without significant limitations associated with the equipment size, stirring, or temperature control. Scale-up can be achieved simply by running the continuous flow reaction under optimized conditions for a longer time.[7b]

With regards to cycloaddition reactions, several examples using flow techniques are reported in the literature.[8] A variety of different Diels-Alder reactions was investigated in flow.[9] Hornung *et al.* reported on the investigation and up-scaling of the Diels-Alder reaction of myrcene with acrylic acid in two different types of flow reactors, a tubular and a plate-type, and compared it to a batch stirred tank, and achieved shorter reaction times as well as a more uniform reaction using the flow technique.[9c]

Concerning norbornadienes in flow, a two-step continuous flow procedure has been developed to generate 2-bromo-2,5-norbornadienes **9** with a functional group at the 3-position starting from unsubstituted norbornadiene (Figure 3).[10] However, it was necessary to add several reagents separately at different stages of the reaction procedure while keeping the microreactor at specific low temperatures, which requires two cooling units.

Several investigations of Diels-Alder reactions using CP as a precursor in flow techniques are reported and highlight the accompanying difficulties for up-scaling due to polymerization of the highly active CP.[11] Li, Yu, and coworkers reported on the synthesis of methanonaphthalene **12** through a Diels-Alder reaction of CP and an *in situ* generated nitro-aryne prepared from 2-amino-6-nitrobenzoic acid **10** and isoamyl nitrite **11** via a continuous flow setup (Figure 3).[9d] Continuous and concurrent distillation and cracking of the dicyclopentadiene through *retro* Diels-Alder reaction to result in CP using a Hickman distillation apparatus were combined in line with a flow reactor

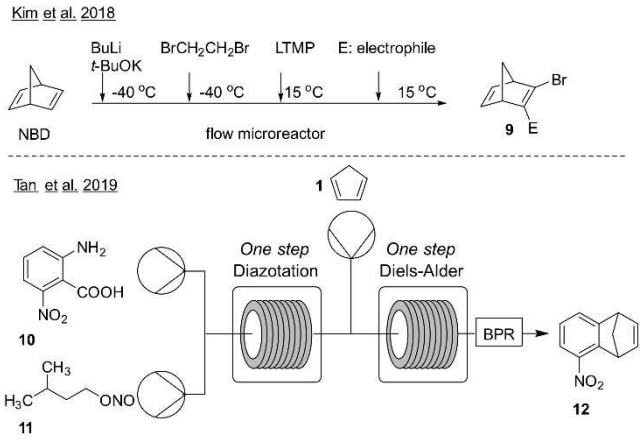


Figure 3. Flow examples by Kim et al..[10] starting from unsubstituted norbornadiene and by Tan et al.[9d] for a combination of Diazotation and Diels-Alder reaction using CP **1** using a back-pressure regulator (BPR).

setup.[12] Regarding the cracking of dicyclopentadiene, *retro* Diels-Alder reactions performed in continuous flow techniques from molecular systems containing CP or cyclohexadiene units[13] have been reported and illustrated *in situ* cracking of dicyclopentadiene **2** in flow.

To the best of our knowledge, no methods for synthesizing NBDs on a larger scale through the combination of *in situ* cracking of dicyclopentadiene and Diels-Alder reaction using continuous flow have been reported. Since MOST-device testing requires larger quantities of norbornadienes, we became motivated to investigate continuous flow chemistry for the possibilities of a one-step method for large-scale synthesis of NBDs with *in situ* cracking of dicyclopentadiene.

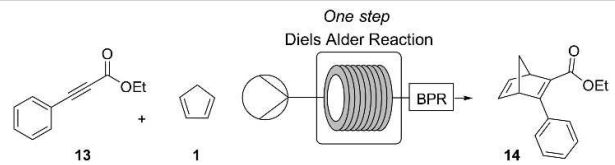
Herein we report the development of a flow synthesis of a library of 2,3-disubstituted NBD molecules using *in situ* cracking of dicyclopentadiene. Further, as our method starts from the already mixed starting materials in the solution, there is no need to add different reagents separately during the reaction. Although the method combines two reactions usually carried out at different temperatures, we combined both into one step kept at one single temperature, which displays an easy-to-follow and simplified method without any intervention of the experimentalist during the reaction. We further characterize a novel NBD in terms of MOST properties; hence the absorption profile, stability of the photoisomer, and the quantum yield of the photoisomerization process were measured.

Results and Discussion

Optimization

As a starting point, the reaction conditions for the Diels-Alder reaction were screened in batch using both conventional heating and microwave-assisted heating (Table S1, SI). Ethyl-3-phenylpropiolate **13** and CP **1** were chosen as model systems for optimizing the reaction parameters (Table 1). The highest

Table 1. Optimization of reaction conditions for Diels-Alder reaction between ethyl-3-phenylpropiolate **13** and cyclopentadiene **1** in toluene in a 5 mL stainless steel coiled tube flow reactor.



Entry[a]	c1 [M]	T [°C]	Flow rate [mL/min]	t_{res} [min]	P [bar]	Conv. [%]
1	3	160	0.20	25	2.9	22
2	3	200	0.20	25	4.9	35
3	3	200	0.07	75	5.5	80
4	3	200	0.04	120	4.5	78
5	3	200	0.08	60	5.8	83
6	3	250	0.08	60	–	–
7	3	200	0.11	45	0	17
8	3	200	0.11	45	5.7	80
9	3	200	0.17	30	5.6	82
10	2.2	200	0.17	30	5.5	87
11	3	200	0.17	30	5.5	48

[a] Fixed parameters: Concentration of **13** (c13), 2 M. Variable parameters: Concentration of **1** (c1), temperature (T), flow rate, residence time (t_{res}), and pressure (P) were varied. The conversion (Conv.) of **14** was monitored by ^{1}H-NMR.

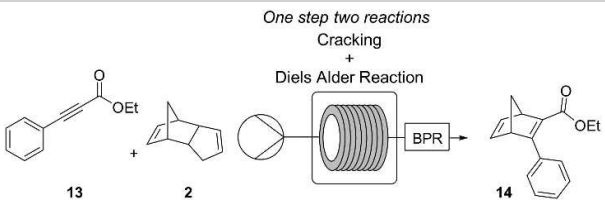
conversion yields of NBD were around 95% and obtained when 1.51 equivalents of CP were added in either toluene or *p*-xylene at 160 °C for 68 or 48 hours, respectively. These experiments show that high temperatures are required for the formation of the NBD. Another conclusion to be drawn from the optimization was that it is a fine balance of the amount of CP that should be added to the reaction mixture. Few equivalents provide low yields, but so does too large amounts of CP due to the possibility of forming side products (Figure S5 and Figure S6, SI). Adding catalysts such as BHT to enable reaction at lower temperatures did mainly result in isolation of starting material (Table S1, SI). With this information in hand, our next step was to optimize the reaction conditions in a continuous flow reactor. We selected toluene as solvent since it can be removed more easily after the reaction than other even higher boiling solvents. For the flow set up (Figure S3, SI), we used a system from Vapourtec, in which one of the pumps was used as a back-pressure regulator (BPR). The back-pressure, which essentially is a pressure higher than ambient, enables higher temperatures beyond the ambient boiling point of the solvent. Flow reaction parameters, such as flow rate, temperature, the residence time (t_{res}) of the reaction mixture within the flow reactor, and the pressure were studied during the screening. The results are presented in Table 1.

We started with a temperature of 200 °C, which provided a higher conversion than 160 °C for a flow rate of 0.2 mL/min and a residence time of 25 min (entries 1 and 2). The conversion increased from 35% to 80% by prolonging the residence time to 75 min (entry 3), which resulted in a lower flow rate (0.07 mL/min). Further prolongation to 120 minutes (0.04 mL/min flow rate) seemed not to affect the conversion (entry 4) any further. Reduction of the residence time to 60 min (flow rate: 0.08 mL/min) but increasing the back-pressure to 5.8 bar gave a slightly better conversion. Further increasing of the temperature to 250 °C resulted in degradation of the starting material. The back-pressure has a significant effect on the outcome. By increasing the back-pressure from 0 bar to 5.7 bar, in otherwise identical settings (T = 200 °C, residence time: 45 min, flow rate 0.11 mL/min), the conversions went from 17% to 80% (entry 7 and 8). By keeping the back-pressure at around 5.5 bar, the residence time could be shortened while a high conversion of around 80% (compare entry 1 with entries 8 and 9) remained. However, a slight increase of the temperature to 220 °C lowered the conversion to 48% instead of 87%. The conversion was further increased to 87% by decreasing the concentration of cyclopentadiene to 2.2 M from 3 M, which agrees with the in-batch experiments (Table S1, SI).

Additionally, we performed a small study of the cracking of the dicyclopentadiene in flow (Table S3 and Figure S8, SI). A temperature of 200 °C, a back-pressure of 9 bar, and a residence time of 30 min gave a conversion of 38%. This result seemed to be very promising since the dimer and dicyclopentadiene stay in equilibrium. We further speculated that CP would be consumed if an alkyne is added to the reaction mixture, thus shifting the equilibrium towards forming more CP, according to the principle of *Le Chatelier*.

The next step was to optimize the Diels-Alder procedure with *in situ* cracking of **2** (Table 2). Again, the temperature was set to 200 °C, the residence time to 30 min (flow rate 0.17 mL/min), and toluene was chosen as the solvent, based on the previous investigations. Parameters such as concentrations of **13** and **2** and different ratios of the two starting materials were varied along with the pressure. Entries 1–3 show that too many equivalents of **2** resulted in lower conversion. The back-pressure of around 5 bar, which provided good conversion in the Diels-Alder reaction before (Table 1), resulted in a conversion of around only 50% for this one-step two-reactions approach.

Table 2. Optimization of reaction conditions for Diels-Alder reaction between ethyl-3-phenylpropiolate **13** and dicyclopentadiene **2** in toluene in a 5 mL stainless steel coiled tube flow reactor.



Entry[a]	Ratio 2:13	c13 [M]	c2 [M]	P [bar]	Conv. [%]
1	0.5	2.5	1.2	5.3	52
2	1.2	2.5	3.0	4	39
3	0.6	2.5	1.5	5	51
4	1.0	2.0	2.0	9	92
5	1.0	1.0	1.0	9	88
6	1.0	0.5	0.5	9	82

[a] Fixed parameters: Temperature (T), 200 °C, and residence time (t_{res}), 30 min. Variable parameters: Concentration of **13** (C13), the concentration of **2** (C2), and back-pressure (P). The conversion (Conv.) of **14** was monitored by ^{1}H-NMR.

Therefore, the back-pressure was increased to 9 bar (Table 2, entries 4–6), and the ratio between **2** and **13** was set to 1 while the concentrations were varied from 0.5 M to 2 M. The conversion increased from 82% to over 88% to even 92% from 0.5 M to 2 M concentration. As we speculated, while the conversion for the cracking reaction of dicyclopentadiene was only around 38%, the overall conversion in the combined reaction was impressively better.

We assume that upon forming the CP **1** through *in situ* cracking and direct usage as a reactant for the Diels-Alder reaction with alkyne **13**, the reaction is driven towards the overall product side. That means that considering the principle of *Le Chatelier*, which applies here as the cracking of **2** to **1** and the back-dimerization of CP **1** to dicyclopentadiene **2** is an equilibrium; the equilibrium is pushed to the side of CP **1**, as this reacts immediately and thus the overall reaction is facilitated.

Furthermore, we conducted a small study to evaluate the effect of the concentration in the Diels-Alder reaction (Table S4, SI). The main conclusion from the study was that higher concentration (higher than 1.7 M of the alkyne) could cause lower yields due to lower solubility of both the alkyne and, in this case, the product NBD **15**, causing clogging in the flow reactor.

Scope and up-scaling

With optimized conditions in hand, we aimed to broaden the scope of the reaction in continuous flow. A series of 6 norbornadienes (Figure 4) starting from their respective precursors (Figure S1, SI) were synthesized using the optimized reaction conditions. After that, they were purified by automated column chromatography and isolated in very satisfying yields (65%–98%). Comparing **14**–**18**, it seems that the procedure works even better when the ester group on C2 is exchanged by a nitrile or trifluoroacetyl group since the yields increases from 70% to more than 90%. The higher yields of the trifluoroacetyl-substituted compounds can be reasonably explained by higher reactivity due to electron demand and better solubility of the starting material in toluene, and thus the overall better conversion. Further, it was found that for more active alkynes, e.g., especially carrying the trifluoroacetyl unit, a shorter residence time (t_{res} = 15 min) was necessary.

Additionally, the nature of the functionality of the phenyl-substituent plays a role as well. Herein, either none or two ether moieties seem to provide not as good solubility in toluene as only one ether unit, resulting in lower isolated yields (**14** and **19**). Regarding future investigations of device testing and MOST application, we were especially interested in the novel norbornadiene **18**. Thus, we wanted to prepare a large amount of **18** and test the scalability of our method. 72.7 g of the respective alkyne and 43.2 g of dicyclopentadiene were reacted using continuous flow synthesis during a period of 9 h (Figure S4, SI), followed by purification using an automated chromatography system. We were able to isolate around 87.4 g of **18** in 97% isolated yield, serving as proof of principle that larger gram amounts of NBDs can be produced with our method within less than half a day.

Photophysical evaluation of novel norbornadiene 18
Norbornadiene **18** was evaluated as a MOST candidate (Figure S10, SI). The absorption profile of **18** has a good solar spectrum match with an absorption maximum at 381 nm and an absorption onset of 464 nm (Figure 5). An isosbestic point can be found at 293 nm in the UV/Vis spectra of NBD and its corresponding photoisomer, quadricyclane (QC) **20**, indicating a clean photoconversion. The quantum yield for the photoisomerization process was determined to 51%. The stability of QC was evaluated by measuring the rate constants of the back conversion at three different temperatures. The half-life of QC at 25 °C was determined to be 6.5 hours making this NBD/QC system suitable for short-time energy storage and quick release of energy for possible day to night storage applications.

Conclusion

We demonstrate here that upon utilization of flow chemistry, we were able to transfer the synthesis of technologically

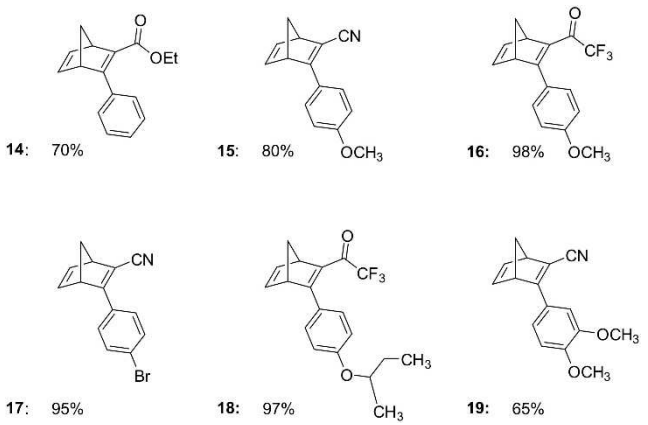


Figure 4. Norbornadienes with isolated yields synthesized with our newly developed procedure with *in situ* cracking.

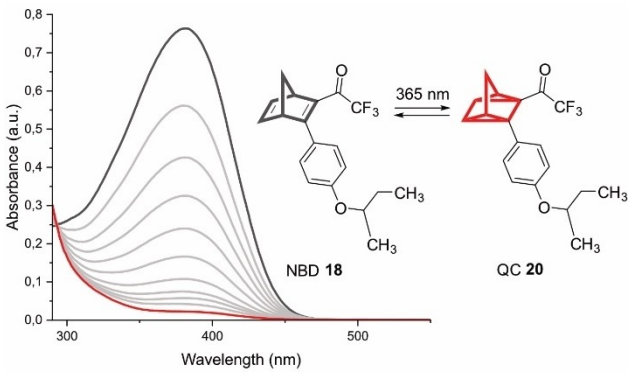


Figure 5. UV/Vis absorption spectra that show the stepwise conversion (light grey lines) of NBD **18** (dark grey line) to QC **20** (red line) in toluene upon irradiation and the respective photoisomerization reaction.

relevant compounds, NBDs, from batch to flow, enabling continuous synthesis of compounds in a lab-scale setup. While traditional wet-chemical methods often lead to struggles in up-scaling due to the use of specific glassware, our flow chemistry method offered the possibility to synthesize NBDs at a rate of 0.029 mol/h (9.71 g/h) using a single 5 mL tubular coiled flow reactor. We note that with the demonstrated production rate, up to 85 kg/year (24 h for 365 days) of material could be produced. Up-scaling was shown exemplarily for a novel promising NBD candidate, which was further characterized for its photoswitching properties. This iso-butyl-protected phenol also gives opportunities for fast access to other similar compounds with optimized solubility by exchanging the substituent on the ether functionality. During the progress of our method development, we gained important insights into the cracking of dicyclopentadiene to cyclopentadiene, and we could use it *in situ* to the Diels-Alder synthesis, allowing both reactions in a single step in a flow reactor. Yields of the final product can be improved by this combined approach, whereas the cracking itself only gave moderate yields. Thus, we conclude that shifting the equilibrium of the cracking to the cyclopentadiene by its direct usage for the Diels-Alder reaction with the activated alkyne is reasonable and becomes evident (*Le Chatelier*). With this method in hand, future libraries of novel NBD systems can be generated efficiently, and real-time applications for energy storage could be realized. We are further investigating the use of larger flow reactors or even several reactors in parallel to further increasing the production rate. While the work-up in this study was done mainly by column chromatography, using an automated medium-pressure liquid chromatography (MPLC) device, we are currently studying the possibility of crystallization which is even more suitable for large-scale synthesis.

Experimental Section

General flow procedure: One flow stream is driven by the Vapourtec R4/R2+ containing a solution of the corresponding alkyne and dicyclopentadiene in toluene. The solution is pumped to a 5 mL reactor at 200 °C with 9 bar back-pressure (BP) that ensures the system was pressurized. Finally, the solvent was concentrated in vacuo to provide the desired crude mixture that was purified by flash chromatography.

Ethyl-3-phenylbicyclo[2.2.1]hepta-2,5-diene-2-carboxylate 14: Alkyne **13** (0.88 g, 0.83 mL, 5.0 mmol, 2 M), dicyclopentadiene (0.66 g, 0.67 mL, 5.0 mmol, 2 M) were mixed in 1.0 mL of toluene. All the solution was pumped to a 5 mL reactor at 200 °C with a flow speed of 0.167 mL/min, a residence time of 30 min. The solvent was evaporated, and the product was purified by flash chromatography by using dichloromethane/heptane (1:1) to afford the pure compound as a light-yellow oil (0.841 g, 3.50 mmol, 70%). ^{1}H NMR (400 MHz, MHz, $CDCl_3$) δ (ppm): 7.55–7.49 (m, 2H), 7.40–7.27 (m, 3H), 6.99 (dd, J = 4.7, 3.1 Hz, 1H), 6.92 (dd, J = 4.5, 3.1 Hz, 1H), 4.19–4.09 (m, 2H), 4.09–4.05 (m, 1H), 3.88–3.84 (m, 1H), 2.26 (dt, J = 6.6, 1.6 Hz, 1H), 2.07 (dt, J = 6.6, 1.6 Hz, 1H), 1.22 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 166.3, 165.5, 143.7, 140.8, 139.3, 135.7, 128.5, 127.8, 127.6, 70.6, 58.5, 53.0, 14.1. Data according to literature.[14]

3-(4-methoxyphenyl)bicyclo[2.2.1]hepta-2,5-diene-2-carbonitrile 15: Alkyne **21** (6.42 g, 40.8 mmol, 1.0 M), dicyclopentadiene (5.423 g, 5.5 mL, 41.0 mmol, 1.0 M) were mixed in 34.5 mL of toluene. The solution was pumped to a 5 mL reactor at 200 °C with a flow speed of 0.167 mL/min, a residence time of 30 min. The solvent was evaporated, and the product was purified by flash chromatography by using EtOAc/petroleum ether (eluting 5% EtOAc) to afford the pure compound as a white solid (7.32 g, 32.8 mmol, 80%). ^{1}H NMR (400 MHz, MHz, $CDCl_3$) δ (ppm): 7.75-7.69 (m, 2H), 6.98–6.90 (m, 3H), 6.82 (dd, J = 4.7, 3.5 Hz, 1H), 4.15–4.06 (m, 1H), 3.90 (dt, J = 3.7, 1.6 Hz, 1H), 3.84 (s, 3H), 2.24 (dt, J = 6.8, 1.6 Hz, 1H), 2.16 (dt, J = 6.8, 1.6 Hz, 1H). ^{13}C NMR (100 MHz, MHz, $CDCl_3$) δ (ppm): δ 170.4, 161.2, 143.4, 140.0, 128.3, 126.0, 119.2, 114.4, 113.7, 70.8, 55.5, 54.8, 54.1. Data consistent with literature.[15]

2,2,2-trifluoro-3-(4-methoxyphenyl)bicyclo[2.2.1]hepta-2,5-dien-2-yl)ethan-1-one 16: Alkyne **25** (2.16 g, 9.47 mmol, 1.0 M), dicyclopentadiene (1.50 g, 1.52 mL, 11.4 mmol, 1.21 M) were mixed in 7.9 mL of toluene. The solution was pumped to a 5 mL reactor at 200 °C with a flow speed of 0.33 mL/min, a residence time of 15 min. The solvent was evaporated, and the product was purified by flash chromatography by using EtOAc/petroleum ether (eluting 5% EtOAc) to afford the pure compound as a yellow solid (2.72 g, 9.24 mmol, 98%). ^{1}H NMR (400 MHz, MHz, $CDCl_3$) δ (ppm): 7.82–7.67 (m, 2H), 6.99–6.86 (m, 4H), 4.21-4.16 (m, 1H), 3.99–3.95 (m, 1H), 3.86 (s, 3H), 2.24 (dt, J = 7.1, 1.6 Hz, 1H), 2.17 (dt, J = 7.1, 1.6 Hz, 1H). ^{13}C NMR (100 MHz, MHz, $CDCl_3$) δ (ppm): 178.2, 176.8 (q, J = 34 Hz), 161.8, 144.0, 139.7, 137.5, 130.8, 127.2, 117.0 (q, J = 293 Hz), 113.5, 69.1, 58.9, 55.6, 51.9 (q, J = 3.0 Hz). Data consistent with literature.[16]

2-(4-bromophenyl)-3-methylbicyclo[2.2.1]hepta-2,5-diene-2-carbonitrile 17: Alkyne **23** (2.50 g, 12.1 mmol, 1.0 M), dicyclopentadiene (1.76 g, 1.78 mL, 13.3 mmol, 1.1 M) were mixed in 10.2 mL of toluene. The solution was pumped to a 5 mL reactor at 200 °C with a flow speed of 0.167 mL/min, a residence time of 30 min. The solvent was evaporated, and the product was purified by flash chromatography by using dichloromethane/petroleum ether (1:1) to afford the pure compound as a light-yellow oil (3.13 g, 11.5 mmol, 95%). ^{1}H NMR (400 MHz, MHz, $CDCl_3$) δ (ppm): 7.62–7.52 (m, 4H), 6.94 (dd, J = 5.1, 3.0 Hz, 1H), 6.85 (dd, J = 4.9, 3.2 Hz, 1H), 4.11–4.06 (m, 1H), 3.98–3.92 (m, 1H), 2.28 (dt, J = 7.0, 1.7 Hz, 1H), 2.20 (dt, J = 6.9, 1.6 Hz, 1H). ^{13}C NMR (100 MHz, MHz, $CDCl_3$) δ (ppm): 169.7, 143.2, 140.3, 132.2, 132.0, 128.0, 124.5, 118.2, 117.9, 71.5, 55.2, 54.2. Data consistent with literature.[17]

1-((1R,4S)-3-(4-(*sec*-butoxy)phenyl)bicyclo[2.2.1]hepta-2,5-dien-2-yl)-2,2,2-trifluoroethan-1-one 18: Alkyne **26** (10.0 g, 37.0 mmol, 1.0 M), dicyclopentadiene (5.87 g, 5.95 mL, 44.4 mmol, 1.27 M) were mixed in 29.1 mL of toluene. The solution was pumped to a 5 mL reactor at 200 °C with a flow speed of 0.33 mL/min, a residence time of 15 min. The solvent was evaporated, and the product was purified by flash chromatography by using EtOAc/petroleum ether (eluting 5% EtOAc) to afford the pure compound as a yellow oil under normal temperature and pressure (12.1 g, 36.0 mmol, 97%). ^{1}H NMR (400 MHz, MHz, $CDCl_3$) δ (ppm): 7.79–7.76 (m, 2H), 6.97–6.87 (m, 4H), 4.39 (h, J = 6.1 Hz, 1H), 4.20–4.18 (m, 1H), 4.00–3.97 (m, 1H), 2.23 (dt, J = 7.0, 1.6 Hz, 1H), 2.17 (dt, J = 7.1, 1.6 Hz, 1H), 1.82–1.61 (m, 2H), 1.32 (d, J = 6.1 Hz, 3H), 0.98 (td, J = 7.4, 0.9 Hz, 3H). ^{13}C NMR (101 MHz, MHz, $CDCl_3$) δ (ppm): 178.2, 176.5 (q, J = 34.0 Hz), 160.6, 143.8, 139.5, 137.0, 130.8, 126.6, 117.0 (q, J = 292 Hz), 114.8, 75.1, 68.8, 58.7, 51.7 (q, J = 3.0 Hz), 29.1, 19.2, 9.7. IR (ATR): $\tilde{\nu}$ = 2974, 2940, 2877, 1730, 1678, 1599, 1569, 1536, 1498, 1465, 1379, 1350, 1294, 1246, 1198, 1161, 1125, 1029, 1002, 988, 971, 923, 885, 834, 808, 768, 716, 636, 556 cm^{-1}. HRMS (ESI, +ve) calcd for $C_{19}H_{19}F_3O_2$ [$(M+H)^+$]: m/z = 337.1415; found 337.1414.

3-(3,4-dimethoxyphenyl)bicyclo[2.2.1]hepta-2,5-diene-2-carbonitrile 19: Alkyne **24** (1.62 g, 8.65 mmol, 0.5 M), dicyclopentadiene

(2.30 g, 2.3 mL, 17.4 mmol, 1.0 M) were mixed in 15.2 mL of toluene. The solution was pumped to a 5 mL reactor at 200 °C with a flow speed of 0.167 mL/min, a residence time of 30 min. The solvent was evaporated, and the product was purified by flash chromatography by using dichloromethane to afford the pure compound as a white solid (1.43 g, 5.65 mmol, 65 %). ^{1}H NMR (400 MHz, MHz, $CDCl_3$) δ (ppm): 7.46 (d, J = 2.1 Hz, 1H), 7.23 (dd, J = 8.4, 2.2 Hz, 1H), 6.94–6.86 (m, 2H), 6.84–6.79 (m, 1H), 4.13–4.09 (m, 1H), 3.92 (d, J = 5.6 Hz, 7H), 2.25 (dt, J = 6.8, 1.6 Hz, 1H), 2.16 (dt, J = 6.8, 1.6 Hz, 1H). ^{13}C NMR (100 MHz, MHz, $CDCl_3$) δ (ppm): 170.6, 150.9, 149.2, 143.3, 140.1, 126.3, 120.0, 119.2, 114.0, 110.9, 109.4, 70.8, 56.1, 54.8, 54.0. Data consistent with literature.[2c]

Further experimental details and spectral data can be found in the supporting information.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: Diels-Alder · Energy storage · Flow chemistry · Isomerization · Photochromism

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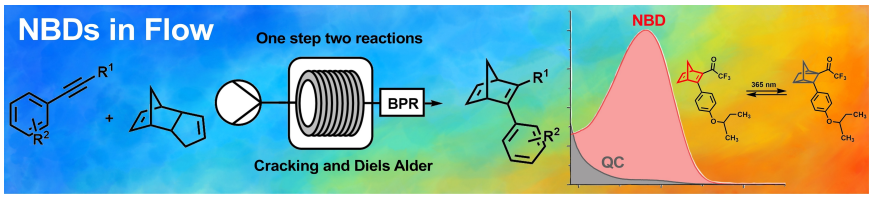

An efficient synthesis of norbornadienes (NBDs) was achieved using flow chemistry via a combination of two reactions in one step. *In situ* cracking of dicyclopentadiene followed by Diels Alder reaction with alkynes in a flow chemistry setup with back-pressure regulator (BPR) make larger quantities of the norbornadienes (NBD)-quadricyclane (QC) photoswitch pair accessible.