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Divergent Reactivity of D-A Cyclopropanes under PTC Conditions, Ring-Opening vs. Decyanation Reaction

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Abstract: The divergent reactivity of D-A cyclopropane, under PTC conditions, is herein reported. Thus, a ring-opening or a decyanation reaction can be achieved by reacting 2-arylcyclopropane-1,1-dicarbonitriles **1** with thioacetic acid in different reaction conditions. The use of solid Cs_2CO_3 leads unexpectedly to the synthesis of new D-A cyclopropane derivatives via a decyanation reaction, followed by diastereoselective acetylation, whereas the use of an aqueous solution of Cs_2CO_3 results in a typical ring-opening reaction with the formation of *S*-thiolate products. Therefore, the use of tailored reaction conditions allows one to obtain either cyclic or open-chain products in moderate to good yields.

Keywords: D-A cyclopropane; decyanation; PTC; thioacetic acid

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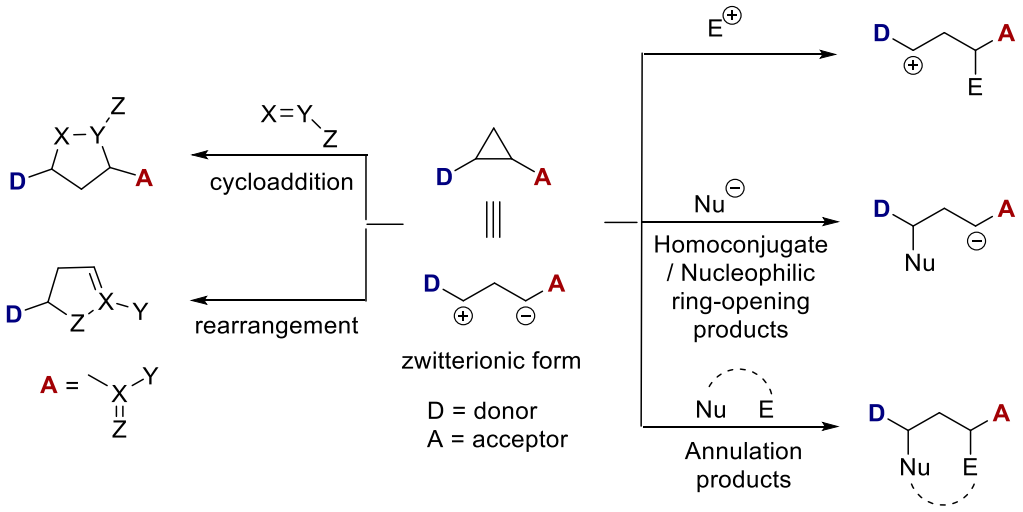
1. Introduction

Cyclopropane is the smallest possible saturated cyclic structure with a ring strain (Baeyer strain energy) of about 110–115 kJ mol^{-1} [1]. At the same time, the C-C bonds of an unsubstituted cyclopropane are rather kinetically inert and, despite the strain, the molecule does not tend to give up on its cyclic structure. This energy barrier, however, descends significantly in activated cyclopropanes where donor (D) and acceptor (A) groups are installed vicinally in a three-membered ring system. The relatively weak chemical bond between the donor- and acceptor-substituted carbon atoms of the cyclopropane may be rationalized by a zwitterionic relationship (a 1,3-dipole) in which the negative and positive charges are stabilized by the acceptor and donor substituent(s), respectively (Scheme 1). The acceptor groups are often carbonyl derivatives, such as esters, ketones, and nitriles, whereas electron-rich aryls, alkenyl and heteroatoms are typically used as donor groups. Generally, two acceptor groups in a geminal position, which guarantee better activation, are employed. Reissig suggested referring to them as "donor–acceptor-substituted cyclopropanes" [2,3], which was later reduced to donor-acceptor D-A cyclopropanes.

The synergistic "push–pull" effect of vicinal charge-stabilizing groups boosts the high polarization of the C-C bond, allowing ring rupture under mild conditions. It also favours a multitude of different reactions with both nucleophiles and electrophiles, including moderately active ones, as well as diverse ambiphilic reagents. Nucleophilic attack occurs at the donor end, leading to homoconjugated products, while the electrophilic one occurs at the acceptor end to afford cation equivalents for further transformations. The ring-opening reaction of D-A cyclopropanes has evolved into an effective strategy to assemble functionalized carbon scaffolds. Moreover, with suitable reacting partners containing both nucleophilic and electrophilic sites, cascade reactions may also proceed through ring-opening and annulative ring-closure in what is a formal cycloaddition [3–5].



Scheme 1. Reactivity of D-A cyclopropanes.

Cycloadditions of activated D-A cyclopropanes with dipolarophiles, 1,3-dipoles, or dienes represent a valuable tool for accessing highly functionalized five-, six-, or seven-membered-ring systems [6–8] (Scheme 1). Rearrangements that result in ring enlargement with the insertion of the acceptor in a cyclic structure are also possible [9].

Early synthetic applications of activated cyclopropanes were published in the 1960s and 1970s, and the first "golden age" for D-A cyclopropanes was entered in the 1980s, when all the fundamental reaction types were reported [10,11]. In 2014, Werz [12] and France [13] reviewed the 2000s as the second "golden age" of D–A cyclopropanes. Studies of their reactivity and catalytic asymmetric reactions of D–A cyclopropanes were next summarized in several reviews [5,14–20].

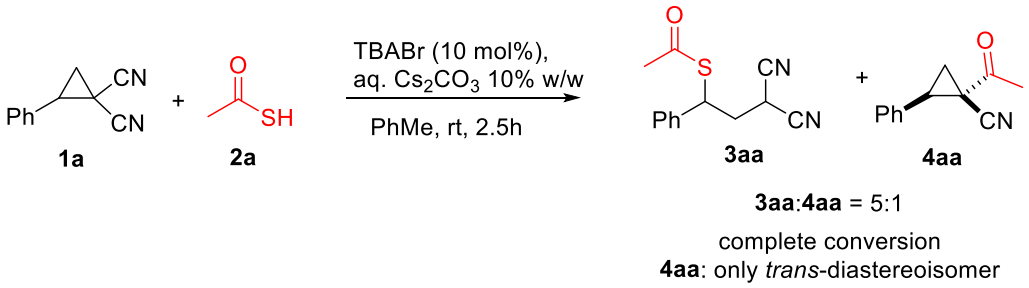
D-A cyclopropanes may be activated by (i) thermal activation [21,22], (ii) Lewis or Brønsted acid/base-mediated activation [23,24], and (iii) low-valent transition metal catalysis [25–28]. Recently, few reports regarding organocatalytic activation have been reported [23,29–31]. However, to the best of our knowledge, the reactivity of D-A cyclopropanes has never been studied under phase-transfer catalysis (PTC) [32–35]. Having maturated a broad expertise in the use of PTC in recent years [36–43], and inspired by the versatility of DA-cyclopropanes, we decided to study their reactivity with nucleophiles under PTC conditions.

2. Results

We started our investigation using 2-phenylcyclopropane-1,1-dicarbonitrile **1a** as a model of D-A cyclopropane compounds, tetra-*n*-butylammonium bromide (TBABr) as a PTC catalyst, and a 10% *w*/*w* Cs_2CO_3 aqueous solution as the base. After some disappointing results using indole, diphenylphosphite, thiols, ene-carbamates, and sulfoxonium ylides as nucleophiles, which did not lead to the formation of the expected products, we observed reactivity when using thioacetic acid **2a** as a reaction partner.

Surprisingly, besides product **3aa**, derived from the expected ring-opening of the D-A cyclopropane, we observed the formation of compound **4aa** as a single *trans*-diastereoisomer [44], obtained by the formal replacement of one of the cyano groups with an acetyl moiety, in a 5:1 ratio favouring **3aa** (Scheme 2).

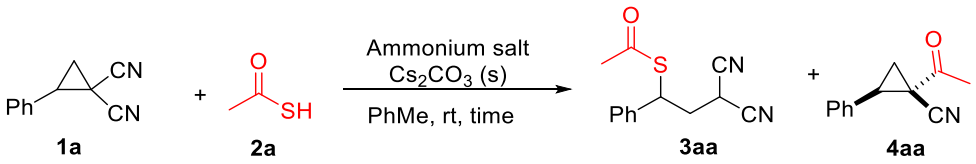
We next started an optimization process of the reaction conditions in order to selectively direct the reaction to the formation of the new cyclopropane derivative **4aa**, derived by a non-reductive decyanation reaction, or towards the open-chain product **3aa**, indeed achieved by the conventional reactivity of D-A cyclopropanes.



Scheme 2. Reaction conditions: **1a** 0.1 mmol, thioacetic acid; **2a** 0.15 mmol, 1 mL 10% *w*/*w* Cs_2CO_3, TBABr (10 mol%), PhMe 1 mL (0.1 M).

It was immediately understood that performing the reaction in the same reaction conditions but using solid Cs_2CO_3 instead of the corresponding aqueous solution, the ratio between the two compounds **3aa** and **4aa** could be reversed in favour the new cyclopropane derivative **4aa** (Table 1, entry 1). We next evaluated different ammonium salts, as reported in Table 1: tetramethylammonium hydroxide hydrate (TMAOH × $5H_2O$) afforded only traces of product **4aa** and **3aa**, whereas promising results were obtained by performing the reaction with tetra-*n*-butylammonium iodide (TBAI), trimethyloctadecylammonium bromide (TMODABr), or timethylbenzylammonium chloride (TMBACl), (entries 3–5). TMODABr gave a slightly lower degree of selection between products **3aa** and **4aa** (entry 4) but a higher yield value. No products were obtained in the absence of an ammonium salt (entry 6). An increase or decrease in the concentration of the reaction mixture resulted in lower yield values (entries 7 and 8). Interestingly, when performing the reaction with a slight excess of substrate **1a** (entry 9) a yield increase and a better selectivity were obtained (compare entries 3 and 9). Lastly, a prolonged reaction time (entry 10) achieved slightly increased conversion, but meanwhile eroding the selectivity.

Table 1. Ammonium salt screening [1].

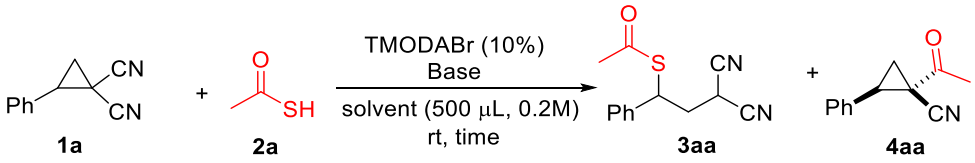


Entry	Ammonium Salt (10 mol%)	Solvent (M)	T (° C)	t (h)	NMR Yield of 4aa (%) [2]	Ratio 4aa/3aa [3]
1	TBABr	PhMe (500 µL, 0.2 M)	r.t.	2.5	32	11/1
2	TMAOH × $5H_2O$	PhMe (500 µL, 0.2 M)	r.t.	2.5	trace	14/1
3	TBAI	PhMe (500 µL, 0.2 M)	r.t.	2.5	34	17/1
4	TMODABr	PhMe (500 µL, 0.2 M)	r.t.	2.5	46	14/1
5	TMBACl	PhMe (500 µL, 0.2 M)	r.t.	2.5	10	>20/1
6	//	PhMe (500 µL, 0.2 M)	r.t.	2.5		
7	TMODABr	PhMe (250 µL, 0.4 M)	r.t.	2.5	19	10/1
8	TMODABr	PhMe (1000 µL, 0.1 M)	r.t.	2.5	31	>20/1
9 [4]	TMODABr	PhMe (500 µL, 0.2 M)	r.t.	2.5	52	>20/1
10 [4]	TMODABr	PhMe (500 µL, 0.2 M)	r.t.	18	45	7/1

[1] Reaction conditions: **1a** (0.1 mmol), thioacetic acid (0.15 mmol), cat. (10 mol%), solid Cs_2CO_3 (0.12 mmol) in PhMe, rt, 2.5 h; [2] determined by ^{1}H-NMR using *m*-dinitrobenzene as internal standard; [3] determined by ^{1}H NMR on the crude reaction mixture; [4] **1a** (0.15 mmol), thioacetic acid (0.1 mmol), cat. (10 mol%), Cs_2CO_3 (0.12 mmol) in PhMe (500 µL), rt, 2.5 h.

Subsequently, the screening of different bases (Table 2, entries 1–4), solvents (entries 5–10), and temperatures (entries 11, 12) was carried out. Cs_2CO_3 was confirmed as the best base, whereas better results were obtained using THF as a solvent (entry 9). Increasing the temperature to 60 °C (entry 11) resulted in a lower yield, while conducting the reaction at 0 °C (entry 12) for 18 h afforded product **4aa** in a comparable yield.

Table 2. Reaction condition screening [1].

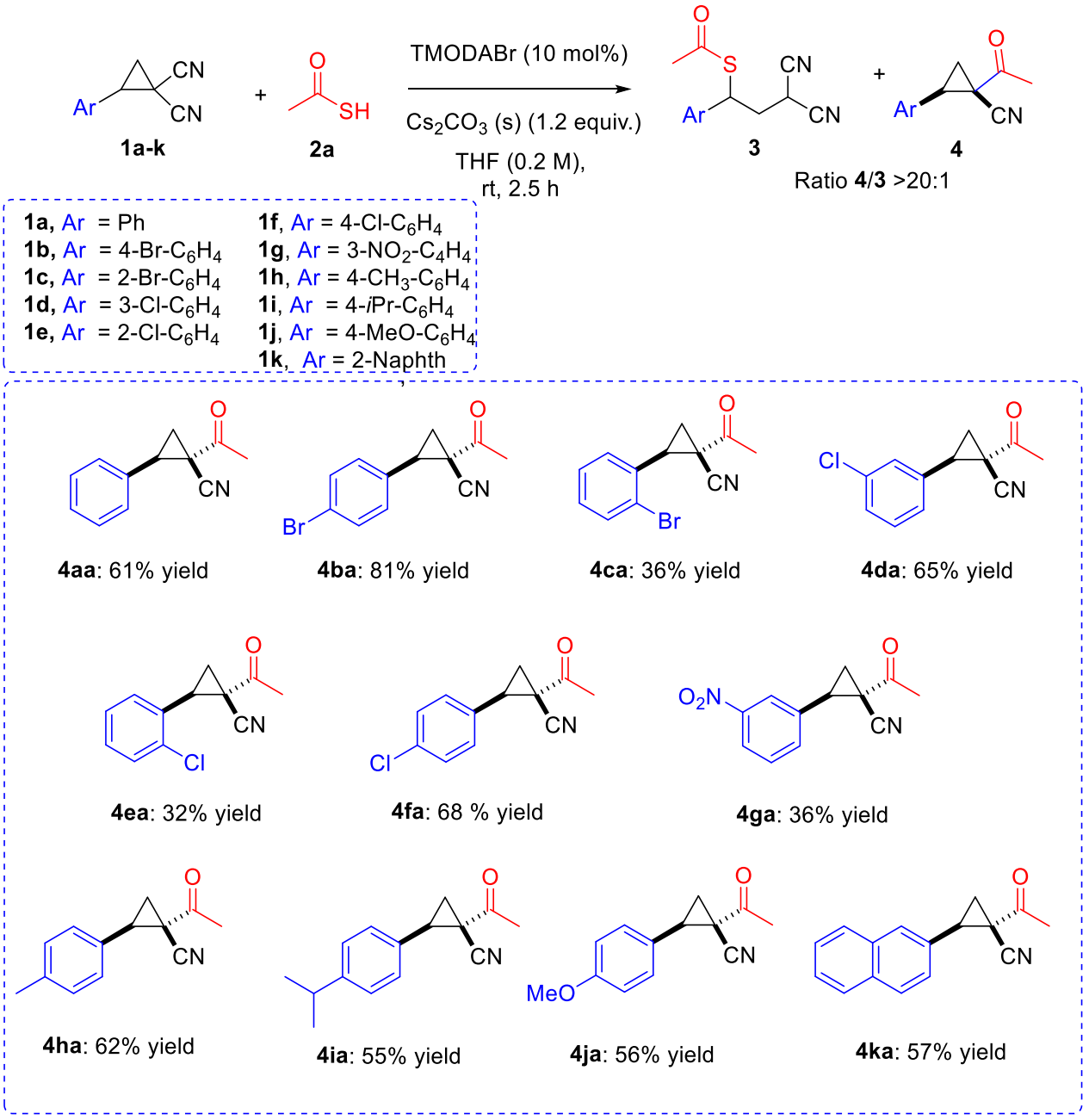


Entry	Base	Solvent	T (° C)	t (h)	NMR Yield (%) [2]	Ratio 4aa/3aa [3]
1	Cs_2CO_3(s)	PhMe	r.t.	2.5	52	>20/1
2	K_2CO_3(s)	PhMe	r.t.	2.5	19	>20/1
3	$KHCO_3$(s)	PhMe	r.t.	2.5	7	>20/1
4	K_3PO_4(s)	PhMe	r.t.	2.5	29	>20/1
5	Cs_2CO_3(s)	CH_2Cl_2	r.t.	2.5	50	>20/1
6	Cs_2CO_3(s)	EtOAc	r.t.	2.5	39	>20/1
7	Cs_2CO_3(s)	Et_2O	r.t.	2.5	28	>20/1
8	Cs_2CO_3(s)	MTBE	r.t.	2.5	43	>20/1
9	**Cs_2CO_3(s)**	**THF**	**r.t.**	**2.5**	**69**	**>20/1**
10	Cs_2CO_3(s)	2-Me-THF	r.t.	2.5	46	>20/1
11	Cs_2CO_3(s)	THF	60	2.5	23	>20/1
12	Cs_2CO_3(s)	THF	0	18	60	>20/1

[1] **1a** (0.15 mmol), thioacetic acid (0.1 mmol), TMODABr (10 mol%), base (0.12 mmol) in solvent (500 μL), 2.5 h; [2] determined by ^{1}H NMR using *m*-dinitrobenzene as internal standard; [3] determined by ^{1}H NMR on the crude reaction mixture.

Having chosen the optimal reaction conditions for the selective obtainment of the decyaneted product **4** (Table 2, entry 9), we then moved to evaluate the generality of the reaction. As reported in Scheme 3, moderate to good yields and very good selectivity (ratio **4**/**3** > 20:1) could be obtained for all the D-A cyclopropane derivatives **1b–h** employed regardless of the presence of electron-withdrawing or electron-donating substituents on the *para*-position of the aromatic ring (55–81%). The presence of *orho*-substituents on the aromatic ring was detrimental for the obtainable yields, while variable results were obtained with *meta*-substituted substrates. All new D-A cyclopropane derivatives **4** were obtained as single *trans*-diastereoisomers. Unfortunately, when thiobenzoic acid **2b** was used in place of thioacetic acid, the corresponding decyanated cyclopropane derivatives were not obtained.

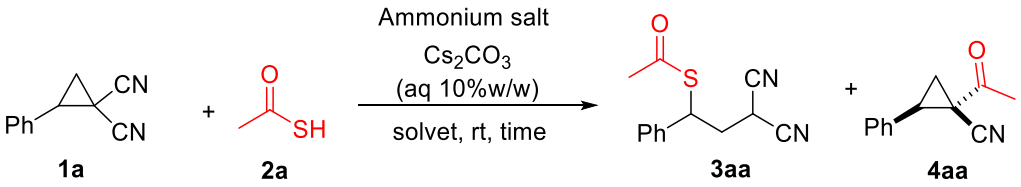
In addition, a screening of the reaction conditions for the selective obtainment of the ring-opening of D-A cyclopropanes **1** was performed. We restarted an optimization process of the reaction conditions in order to selectively direct the reaction towards the formation of the ring-opening product **3aa** derived by a nucleophilic attack at the donor end of D-A cyclopropane **1a**.



Scheme 3. Substrate scope of product **4**.

As previously mentioned, the use of an aqueous solution favoured the formation of product **3aa** (Scheme 2). Moving from TBABr to TBAI (Table 3, entries 1 and 3), both selectivity and conversion improved. Better results were obtained working at 0 °C overnight (entries 4 and 5); a further improvement was also achieved using EtOAc as a solvent (entry 6). On the contrary, different ammonium salts besides TMODABr, different aqueous bases (K_2CO_3, Na_2CO_3, and $NaHCO_3$), and other solvents (THF, CH_2Cl_2, Et_2O, and TBME) tested were not conducive to any further improvements.

Table 3. Reaction condition screening [1].



Entry	Ammonium Salt	Solvent (M)	T (° C)	t (h)	NMR Yield 3aa (%) [2]	Ratio 3aa/4aa [3]
1	TBABr	PhMe (1000 µL, 0.1 M)	r.t.	2.5	20	5/1
2	TBABr	PhMe (500 µL, 0.1 M)	r.t.	2.5	20	11/1
3	TBAI	PhMe (500 µL, 0.2 M)	r.t.	2.5	23	>20:1
4	TBABr	PhMe (500 µL, 0.2 M)	0	48	43	>20:1
5	TBAI	PhMe (500 µL, 0.2 M)	0	48	46	>20:1
6	**TBAI**	**EtOAc (500 µL, 0.2 M)**	**0**	**48**	**64**	**>20:1**

[1] **1a** (0.1 mmol), thioacetic acid (0.1.5 mmol), ammonium salt (10 mol%), Cs_2CO_3 (1 mL 10% *w*/*w*) in solvent (x µL), 2.5 h; [2] determined by ^{1}H NMR using *m*-dinitrobenzene as internal standard; [3] determined by ^{1}H NMR on the crude reaction mixture.

Having selected the optimal reaction conditions as the ones reported in Table 3 entry 6, we moved on to test the generality of the reaction.

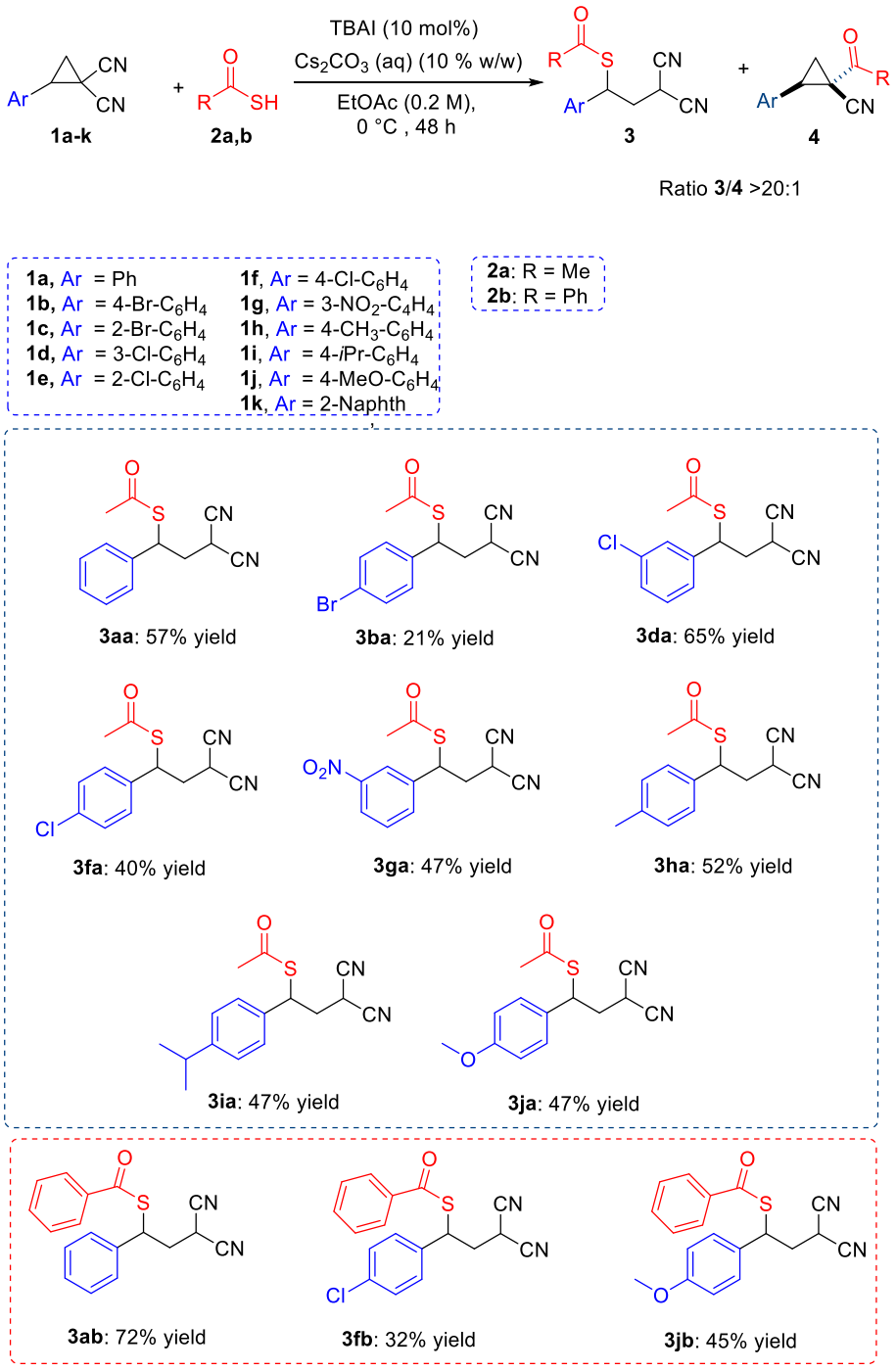
As reported in Scheme 4, moderate to good yields and very good selectivity (ratio **3**/**4** >20:1) could be obtained for the D-A cyclopropane derivatives **1a, 1b, 1d, 1f, 1g–j**, regardless of the presence of electron-withdrawing or electron-donating substituents on the aromatic ring. Thus, the presence of an EWG on *para*-position (**1b**, **1f**) considerably lowered the yield, whereas the presence of an EDG on *para*-position (**1h**, **1i** and **1j**) led to comparable results with respect to **1a**. No reactivity was observed in these reaction conditions, with D-A cyclopropanes **1c** and **1e** bearing a halogen in the *ortho*-position of the aromatic ring, probably due to a too-high steric constraint nearby the C2 of the cyclopropane ring where the nucleophilic attack had to occur.

The same reaction protocol was successfully employed with thiobenzoic acid **2b**, obtaining products **3ab**, **3fb**, and **3jb** in good or moderate yields.

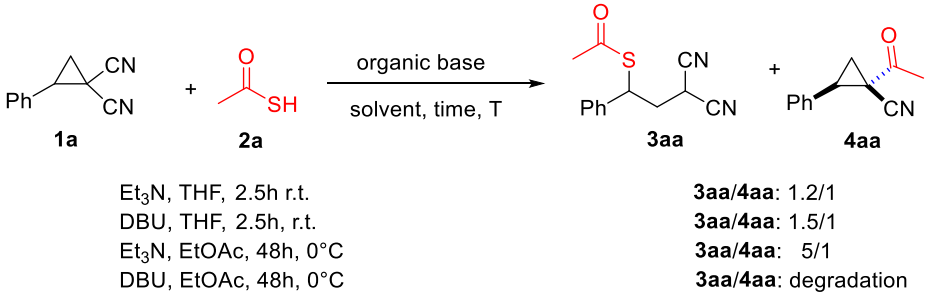
It is interesting to observe that the use of an organic base such as Et_3N or DBU, although allowing the reaction, led to the formation of a mixture of product **3aa** and **4aa** without the selectivity obtainable in PTC conditions (Scheme 5).

To shed some light on this intriguing and unusual divergent behaviour of D-A cyclopropanes **1**, product **3aa** was reacted with TMODABr in THF in the presence of solid Cs_2CO_3. This experiment afforded product **4aa** via a retro-addition reaction and the subsequent decyanation of the restored D-A cyclopropane **1a** (Scheme 6a). On the contrary, it was not possible to react **4aa** in the standard reaction conditions to obtain the ring-opening product **3aa** (Scheme 6b), indicating that the decyanation pathway is irreversible.

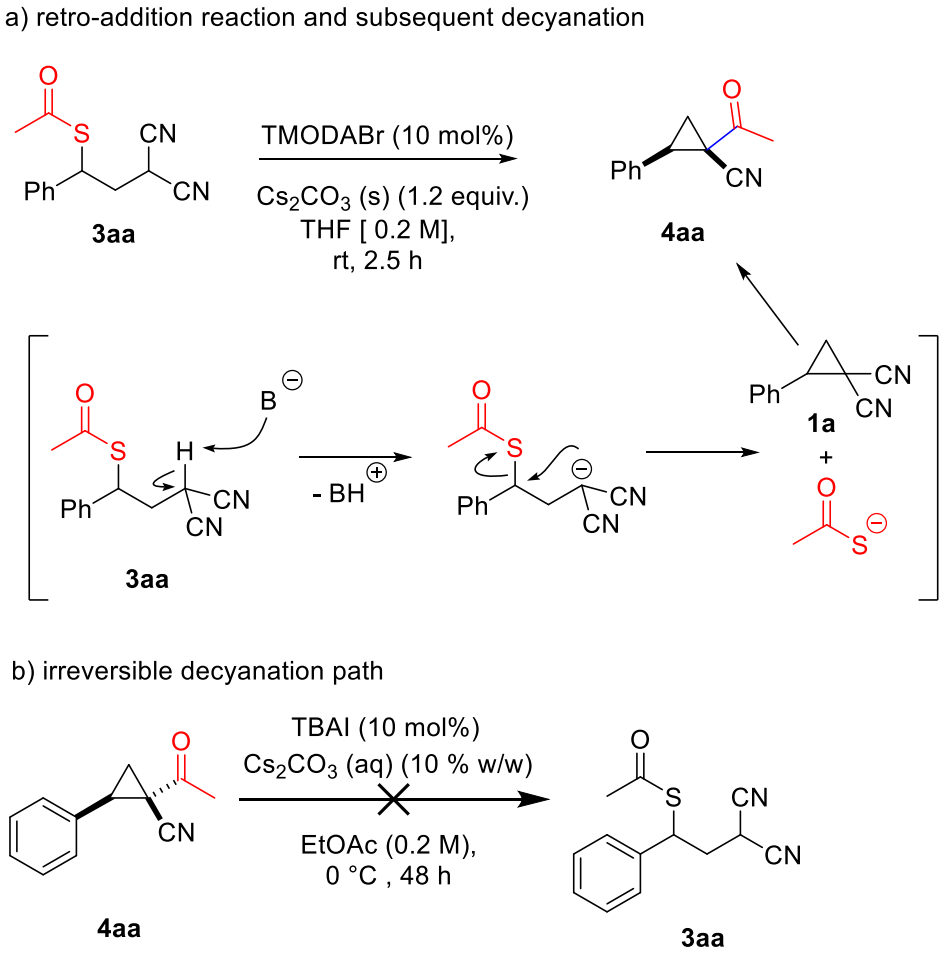
It is noteworthy that, using the first set of reaction conditions, namely solid Cs_2CO_3 and TMODABr, **4ka** was obtained in 57% yield, in addition to product **5ka** (12% yield) derived from the ring-opening of **4ka** itself (Scheme 7); no selectivity could be obtained using aqueous Cs_2CO_3 and TBAI, since a mixture of products **3ka**, **4ka**, and **5ka** was obtained.



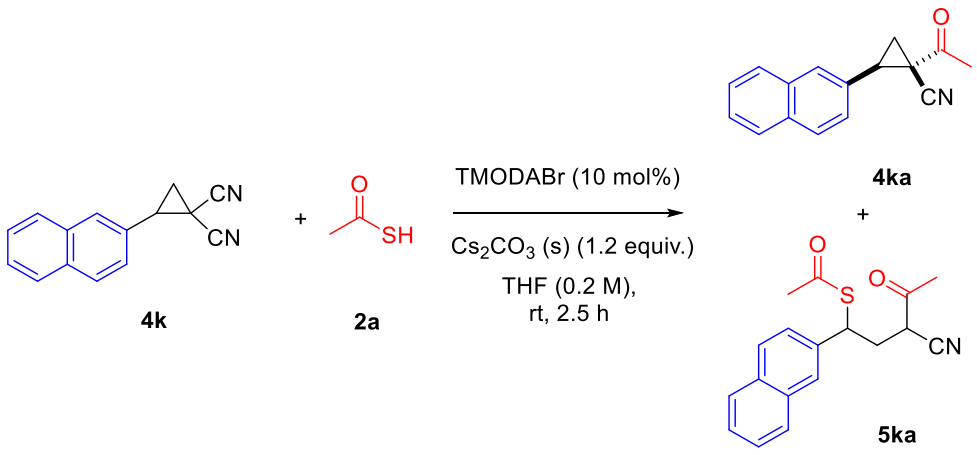
Scheme 4. Substrate scope of products **3**.



Scheme 5. Use of organic bases.



Scheme 6. (**a**) Conversion of product **3aa** in **4aa**; (**b**) stability of **4aa** under the reaction conditions.

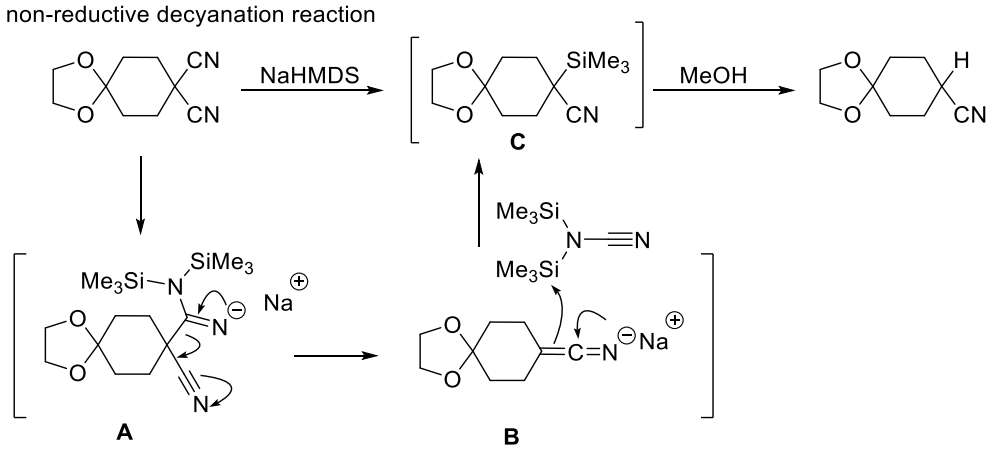


Scheme 7. Reactivity of **4k**.

The divergent behaviour of D-A cyclopropane **1** appeared to be strictly related to the typology of the base used, since the presence of solid Cs_2CO_3 allowed the unprecedented decyanation pathway to be activated in favour of the new cyclopropane derivative **4**, whereas an aqueous solution of the same base pushed the reaction towards the ring-opening product **3**. The extraction of water molecules into the organic phase in liquid–liquid systems probably decreases the reactivity of the thiolate by solvating it. On the other hand, in the solid–liquid mode, the anions are naked, and their reactivity is higher [45].

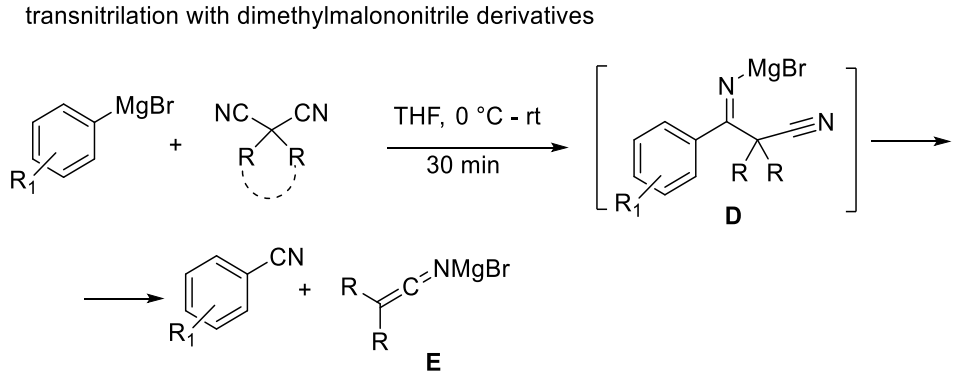
Moreover, the presence of a long aliphatic chain in the ammonium salt structure increased the selectivity between products **4** and **3**, possibly due to the onset of considerable steric hindrance nearby the C2 of the cyclopropane ring, or to an increase in the reactivity of the thiolate.

We then tried to devise a sound mechanistic hypothesis accounting for the formation of the unusual product **4aa** in the reaction. In the literature, only one example of non-reductive decyanation reactions, of cyclic and acyclic disubstituted malononitriles, has been reported so far (Scheme 8) by Tanino [46] and co-workers, using sodium bis(trimethylsilyl)amide (NaHMDS) followed by methanol. The authors reported that the anionic intermediate **A** decomposes into α-cyano anion **B** and bis(trimethylsilyl)cyanamide, which readily undergoes an inter-molecular transfer of a silyl group. The reactive anion **B** is immediately captured by a silyl group to give **C.** The silyl group of **C** is then removed in the same pot simply by adding methanol to the reaction mixture.



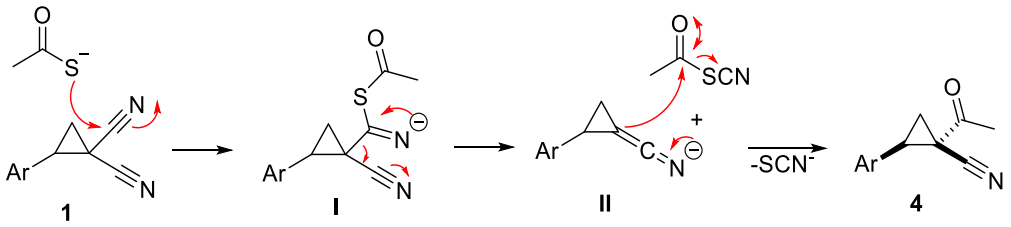
Scheme 8. Non-reductive decyanation reaction.

More recently, Reeves [47] and co-workers reported a transnitrilation of aryl Grignard and aryllithium reagents with dimethylmalononitrile derivatives via the intermediacy of imine **D** and the subsequent formation of ketimine **E** (Scheme 9).



Scheme 9. Transnitrilation reaction.

On this basis, we envisioned that the thiolate, formed by the deprotonation of thioacetic acid by the inorganic base, attacks the electrophilic carbon of one of the two cyano groups, with the subsequent formation of a cyano anion **I** that evolves to ketimine anion **II** by the elimination of acetyl thiocyanate. The anion **II** is then captured by an acetyl group to form cyclopropane **4** with the concomitant formation of thiocyanate. The acetyl group enters at the less hindered side of the α-cyano carbanion, that is, *trans* to the phenyl ring (Scheme 10).



Scheme 10. Mechanistic hypothesis.

A few controlling experiments were performed in order to verify the proposed mechanism. First of all, an $FeCl_3$ 1M aqueous solution was added to the reaction mixture conducted in the reaction condition to obtain product **4**, resulting in the development of an intense reddish-brown coloration, indicative of the formation of an iron complex with the thiocyanate ions present at the end of the reaction (Figure 1) [48].

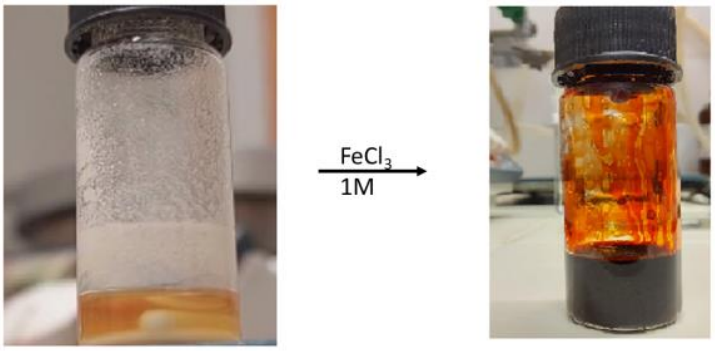
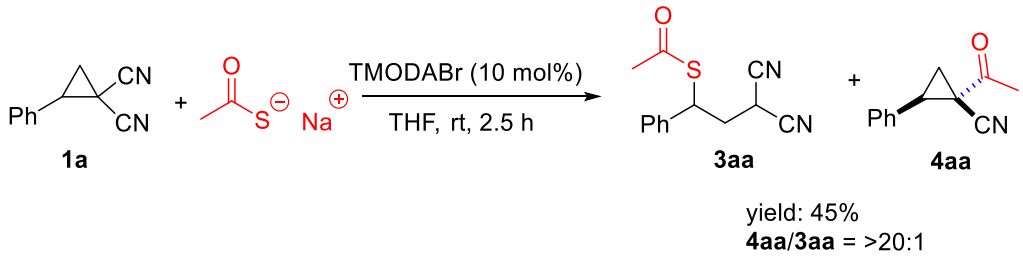


Figure 1. Visualization of thiocyanate by complexation with $FeCl_3$.

Next, D-A cyclopropane **1a** was reacted with sodium thioacetate as a nucleophile, leading to the acquisition of product **4aa** in a 45% yield (Scheme 11).



Scheme 11. Use of sodium thioacetate.

3. Materials and Methods

3.1. General Methods

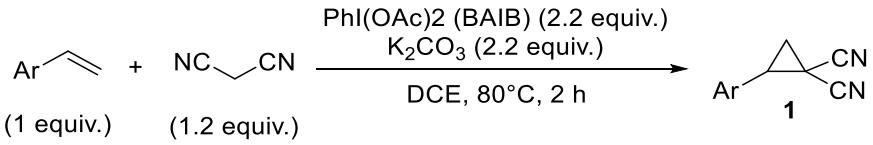
The 1H and ^{13}C NMR spectra were recorded on a Varian Mercury 400 spectrometer. Chemical shifts (δ) are reported in ppm relative to residual solvents signals [49] for ^{1}H and ^{13}C NMR. Signal patterns are indicated as follows: bs, broad singlet; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants (*J*) are given in Hertz (Hz). The ^{13}C NMR were acquired with the ^{1}H broad-band decoupled mode. Mass spectra were recorded using micromass LCT spectrometer using electrospray (ES) ionization techniques or FOCUS/DSQ using electron impact (EI) ionization techniques (relative intensities are given in brackets). The purification of reaction products was carried out by flash chromatography (FC) on silica gel (230–400 mesh) or by gravimetric chromatography using 70–230 mesh silica.

3.2. Materials

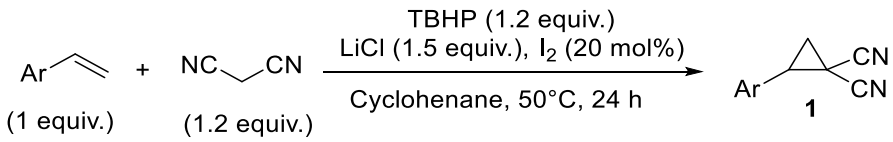
Analytical-grade solvents and commercially available reagents were used as received, unless otherwise noted.

Cyclopropane **1** was obtained from the corresponding styrene derivatives and malononitrile following a literature procedure using bisacetoxyiodobenzene (BAIB) and K_2CO_3 [50], as reported in Scheme 12a, or using iodine, LiCl, and tert-butyl hydroperoxide (TBHP) [51], as reported in Scheme 12b.

a) cyclopropanation with BAIB



b) cyclopropanation with I_2, LiCl and TBHO



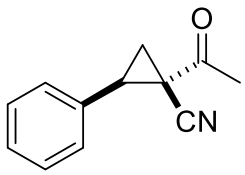
Scheme 12. Preparation of D-A cyclopronanes: route (**a**) [50], route (**b**) [51].

The corresponding styrene derivatives, if not commercially available, were obtained by Wittig reactions from aldehydes.

3.3. General Procedure for the Synthesis of Products *4*

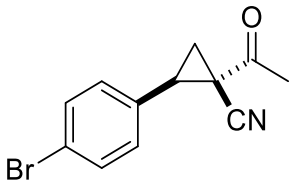
In a 4 mL vial equipped with a magnetic stirring bar, D-A cyclopropane **1** (1.5 equiv., 0.3 mmol) was dissolved in 1000 µL of THF. TMODABr (10 mol% 0.02 mmol, 7.8 mg), thioacetic acid (1.0 equiv, 0.2 mmol, 14.3 µL), and Cs_2CO_3 (1.2 equiv., 0.24 mmol, 78.2 mg) were added in this order. The resulting suspension was stirred for 2.5 h at room temperature and then directly pre-purified by a short plug on silica gel using DCM and Et_2O as eluents. After the evaporation of the solvent, the crude product was analysed by ^{1}H-NMR and then purified through chromatography on silica gel to afford the desired compounds **4** as single diastereoisomers.

1-acetyl-2-phenylcyclopropane-1-carbonitrile 4aa



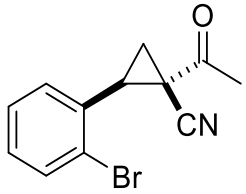
Following the general procedure and using cyclopropane **1a** (50 mg), product **4aa** was obtained in 61% yield (23 mg) after chromatographic purification on silica gel (3:1 = DCM: *n*-hexane as eluent) as a pale-yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.44–7.31 (m, 3H), 7.30–7.18 (m, 2H), 3.12 (t, *J* = 9.1 Hz, 1H), 2.58 (s, 3H), 2.21 (dd, *J* = 9.1, 4.9 Hz, 1H), 2.11 (dd, *J* = 8.4, 4.9 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 198.6, 133.1, 128.8 (2C), 128.6, 128.2 (2C), 118.3, 38.4, 30.3, 29.4, 24.7. **MS** (ESI) m/z: 208 $[M + Na]^+$ The *trans*-relative configuration of compound **4aa** was determined by a comparison with data in the literature [44] and by NOE experiments (see supplementary material). [44].

1-acetyl-2-(4-bromophenyl)cyclopropane-1-carbonitrile 4ba



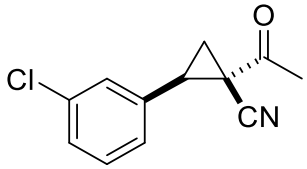
Following the general procedure and using cyclopropane **1b** (74 mg), product **4ba** was obtained in 81% yield (43 mg) after chromatographic purification on silica gel (2:1 = DCM: *n*-hexane as eluent) as a yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 7.50 (d, *J* = 8.3 Hz, 2H), 7.11 (d, *J* = 8.3 Hz, 2H), 3.05 (t, *J* = 8.7 Hz, 1H), 2.56 (s, 3H), 2.17 (dd, *J* = 9.1, 5.0 Hz, 1H), 2.03 (dd, *J* = 9.1, 5.0 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 198.2, 132.2, 131.9 (2C), 129.8 (2C), 122.7, 118.1, 37.4, 30.1, 29.4, 24.7. **MS** (ESI) m/z: 286, 288 $[M + Na]^+$.

1-acetyl-2-(2-bromophenyl)cyclopropane-1-carbonitrile 4ca



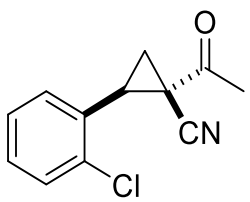
Following the general procedure and using cyclopropane **1c** (74 mg), product **4ca** was obtained in 36% yield (19 mg) after chromatographic purification on silica gel (3:1 = DCM: *n*-hexane as eluent) as a yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 7.65 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.33 (td, *J* = 7.5, 1.2 Hz, 1H), 7.27–7.22 (m, 1H), 7.17 (dt, *J* = 7.6, 1.3 Hz, 1H), 3.08 (t, *J* = 8.6 Hz, 1H), 2.63 (s, 3H), 2.26 (dd, *J* = 8.8, 4.9 Hz, 1H), 2.10 (dd, *J* = 8.5, 5.0 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 198.6, 133.5, 133.0, 130.3, 129.2, 127.8, 126.9, 117.9, 39.4, 29.3, 29.3, 24.3. **MS** (ESI) m/z: 286, 288 $[M + Na]^+$.

1-acetyl-2-(3-chlorophenyl)cyclopropane-1-carbonitrile 4da



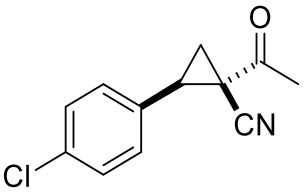
Following the general procedure and using s cyclopropane **1d** (60 mg), product **4da** was obtained in 65% yield (28 mg) after chromatographic purification on silica gel (3:1 = DCM: *n*-hexane as eluent) as a pale-yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 7.47 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.32 (td, *J* = 7.6, 1.8 Hz, 1H), 7.28 (td, *J* = 7.5,1.5, 1H), 7.18 (dd, *J* = 7.4, 1.8 Hz, 1H), 3.10 (t, *J* = 8.6 Hz, 1H), 2.62 (s, 3H), 2.26 (dd, *J* = 8.9, 4.9 Hz, 1H), 2.09 (dd, *J* = 8.4, 4.9 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 198.5, 136.4, 131.9, 130.0, 129.75, 129.0, 127.2, 118.0, 36.9, 29.2, 29.0, 23.8. **MS** (ESI) m/z: 242 $[M + Na]^+$.

1-acetyl-2-(2-chlorophenyl)cyclopropane-1-carbonitrile 4ea



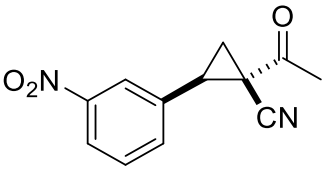
Following the general procedure and using cyclopropane **1e** (60 mg), product **4ea** was obtained in 32% yield (14 mg) after chromatographic purification on silica gel (3:1 = DCM: *n*-hexane as eluent) as a pale-yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 7.33–7.30 (m, 2H), 7.26–7.23 (bs, 1H), 7.13–7.10 (m, 1H), 3.07 (t, *J* = 8.7 Hz, 1H), 2.58 (s, 3H), 2.17 (dd, *J* = 9.1, 5.0 Hz, 1H), 2.06 (dd, *J* = 8.3, 5.0 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 198.2, 135.2, 134.7, 130.05, 128.8, 128.7, 126.2, 117.95, 37.2, 30.0, 29.5, 24.6. **MS** (ESI) m/z: 242 $[M + Na]^+$.

1-acetyl-2-(4-chlorophenyl)cyclopropane-1-carbonitrile 4fa



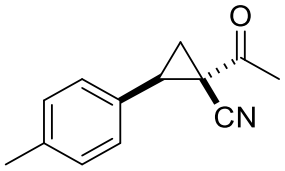
Following the general procedure and using cyclopropane **1f** (60 mg), product **4fa** was obtained in 68% yield (30 mg) after chromatographic purification on silica gel (3:1 = DCM: *n*-hexane as eluent) as a pale-yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 7.38–7.33 (m, 2H), 7.21–7.17 (m, 2H), 3.09 (t, *J* = 8.75 Hz, 1H), 2.58 (s, 3H), 2.20 (dd, *J* = 9.2, 5.0 Hz, 1H), 2.06 (dd, *J* = 8.3, 5.0 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 198.3, 134.6, 131.7, 129.5, 129.05, 118.1, 37.3, 30.1, 29.5, 24.8. **MS** (ESI) m/z: 242 $[M + Na]^+$.

1-acetyl-2-(3-nitrophenyl)cyclopropane-1-carbonitrile 4ga



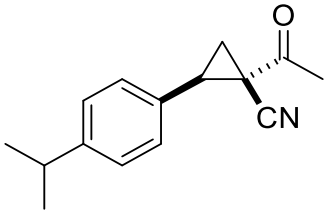
Following the general procedure and using cyclopropane **1g** (64 mg), product **4ga** was obtained in 36% (17 mg) yield after chromatographic purification on silica gel (4:1 = *n*-hexane: EtOAc as eluent) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.26–8.20 (m, 1H), 8.17–8.13 (m, 1H), 7.62–7.57 (m, 2H), 3.22 (t, *J* = 8.7 Hz, 1H), 2.62 (s, 3H), 2.25 (dd, *J* = 9.1, 5.2 Hz, 1H), 2.16 (dd, *J* = 8.2, 5.2 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 197.8, 148.4, 135.5, 134.0, 129.9, 123.6, 123.5, 117.6, 36.4, 29.9, 29.5, 24.6. **MS** (ESI) m/z: 253 $[M + Na]^+$.

1-acetyl-2-(p-tolyl)cyclopropane-1-carbonitrile 4ha



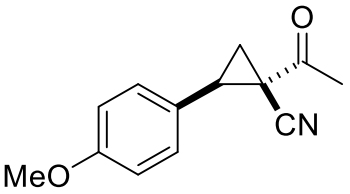
Following the general procedure and using cyclopropane **1h** (55 mg), product **4ha** was obtained in 62% (25 mg) yield after chromatographic purification on silica gel (4:1 = *n*-hexane: EtOAc as eluent) as a pale-yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.22–7.10 (m, 4H), 3.09 (t, *J* = 8.8 Hz, 1H), 2.57 (s, 3H), 2.35 (s, 3H), 2.19 (dd, *J* = 9.2, 4.9 Hz, 1H), 2.08 (dd, *J* = 8.4, 4.9 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 198.6, 138.5, 130.05, 129.5, 128.0, 118.5, 38.5, 30.4, 29.4, 24.7, 21.2. **MS** (ESI) m/z: 222 $[M + Na]^+$.

1-acetyl-2-(4-isopropylphenyl)cyclopropane-1-carbonitrile 4ia



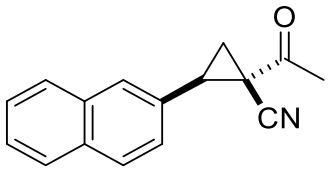
Following the general procedure and using cyclopropane **1i** (63 mg), product **4ia** was obtained in 55% yield (25 mg) after chromatographic purification on silica gel (4:1 = *n*-hexane: EtOAc as eluent) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.26–7.22 (m, 2H), 7.19–7.15 (m, 2H), 3.08 (t, *J* = 8.8 Hz, 1H), 2.91 (hept, *J* = 6.9 Hz, 1H), 2.57 (s, 3H), 2.20 (dd, *J* = 9.2, 4.8 Hz, 1H), 2.08 (dd, *J* = 8.4, 4.8 Hz, 1H), 1.24 (d, *J* = 6.9 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 198.6, 149.4, 130.4, 128.1, 126.9, 118.5, 38.5, 33.8, 30.3, 29.4, 24.9, 23.8, **MS** (ESI) m/z: 250 $[M + Na]^+$.

1-acetyl-2-(4-methoxyphenyl)cyclopropane-1-carbonitrile 4ja



Following the general procedure and using cyclopropane **1j** (59 mg), product **4ja** was obtained in 56% yield (24 mg) after chromatographic purification on silica gel (3:1 = *n*-hexane: EtOAc as eluent) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.21–7.15 (m, 2H), 6.94–6.87 (m, 2H), 3.81 (s, 3H), 3.08 (dd, *J* = 9.1, 8.4 Hz, 1H), 2.57 (s, 3H), 2.20 (dd, *J* = 9.2, 4.9 Hz, 1H), 2.09–2.02 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 198.6, 160.0, 129.4, 125.0, 118.6, 114.2, 55.3, 38.5, 30.4, 29.4, 24.9. **MS** (ESI) m/z: 238 $[M + Na]^+$.

1-acetyl-2-(naphthalen-2-yl)cyclopropane-1-carbonitrile 4ka

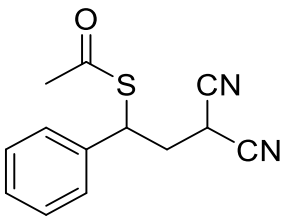


Following the general procedure and using cyclopropane **1k** (65 mg), product **4ka** was obtained in 57% yield (27 mg) after chromatographic purification on silica gel (3:1 = DCM: *n*-hexane as eluent) as an off-white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.93–7.76 (m, 3H), 7.76–7.69 (m, 1H), 7.57–7.44 (m, 2H), 7.36 (dd, *J* = 8.5, 1.9 Hz, 1H), 3.29 (t, *J* = 8.7 Hz, 1H), 2.61 (s, 3H), 2.33–2.22 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 198.55, 133.2, 133.1, 128.7, 127.9, 127.75, 127.5, 126.6, 126.55, 125.6, 118.4, 38.6, 30.3, 29.5, 24.8. **MS** (ESI) m/z: 258 $[M + Na]^+$.

*3.4. General Procedure for the Synthesis of Products **3***

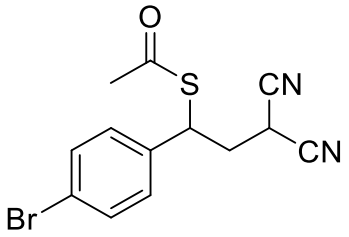
In a 4 mL vial equipped with a magnetic stirring bar, D-A cyclopropane **1** (1.0 equiv., 0.2 mmol) was dissolved in 1000 µL of EtOAc. TBAI (10 mol%, 0.02 mmol, 7.4 mg), thioacetic acid (1.5 equiv, 0.3 mmol, 21.4 µL), or thiobenzoic acid **2b** (1.5 equiv, 0.3 mmol, 36 µL) and Cs_2CO_3 (aq, 10% *w*/*w*, 500 µL) were added in this order. The resulting suspension was stirred for 48 h at 0 °C and then directly pre-purified by a short plug on silica gel using DCM and Et_2O as eluents. After the evaporation of the solvent, the crude product was analysed by ^{1}H-NMR and then purified through chromatography on silica gel to afford the desired compounds **3** as oils.

***S*-(3,3-dicyano-1-phenylpropyl) ethanethioate 3aa**



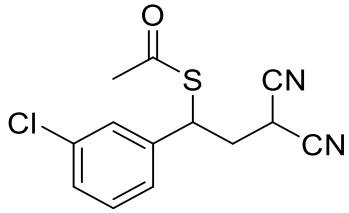
Following the general procedure and using cyclopropane **1a** (33.6 mg) and thioacetic acid **2a** (21.4 µL), product **3aa** was obtained in 57% yield (28 mg) after chromatographic purification on silica gel (3:1 = DCM: *n*-hexane as eluent) as a pale-yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 7.42–7.32 (m, 3H), 7.31–7.27 (m, 2H), 4.73 (dd, *J* = 9.3, 6.6 Hz, 1H), 3.53 (dd, *J* = 9.0, 6.4 Hz, 1H), 2.71 (ddd, *J* = 13.8, 9.0, 6.6 Hz, 1H), 2.58 (ddd, *J* = 13.8, 9.4, 6.4 Hz, 1H), 2.35 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 193.5, 136.9, 129.5, 128.9, 127.6, 111.9, 111.6, 44.8, 37.1, 30.4, 20.9. **MS** (ESI) m/z: 267 $[M + Na]^+$.

***S*-(1-(4-bromophenyl)-3,3-dicyanopropyl) ethanethioate 3ba**



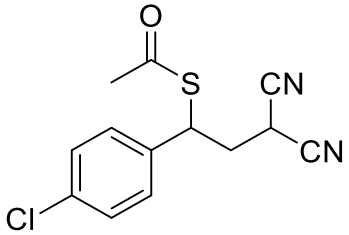
Following the general procedure and using cyclopropane **1b** (49.4 mg) and thioacetic acid **2a** (21.4 µL), product **3ba** was obtained in 21% yield (14 mg) after chromatographic purification on silica gel (3:1 = DCM: *n*-hexane as eluent) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.52 (d, *J* = 8.5 Hz, 2H), 7.19 (d, *J* = 8.5 Hz, 2H), 4.70 (dd, *J* = 8.9, 7.1 Hz, 1H), 3.59 (dd, *J* = 8.6, 6.9 Hz, 1H), 2.69 (ddd, *J* = 13.9, 8.6, 7.1 Hz, 1H), 2.56 (ddd, *J* = 13.9, 8.9, 6.9 Hz, 1H), 2.36 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 193.0, 136.4, 132.6, 129.3, 122.9, 111.7, 111.4, 44.2, 36.7, 30.4, 20.9. **MS** (ESI) m/z: 345, 347 $[M + Na]^+$.

***S*-(1-(3-chlorophenyl)-3,3-dicyanopropyl) ethanethioate 3da**



Following the general procedure and using cyclopropane **1d** (40 mg) and thioacetic acid **2a** (21.4 µL), product **3da** was obtained in 65% yield (36 mg) after chromatographic purification on silica gel (3:1 = DCM: *n*-hexane as eluent) as a pale-yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.35–7.28 (m, 3H), 7.24–7.18 (m, 1H), 4.72 (dd, *J* = 8.69, 7.24 Hz, 1H) 3.61 (dd, *J* = 8.43, 6.98 Hz, 1H), 2.69 (ddd, *J* = 13.9, 8.4, 7.3 Hz, 1H), 2.59 (ddd, *J* = 13.5, 8.7, 7.0 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.0, 139.45, 135.4, 130.8, 129.2, 127.7, 125.9, 111.7, 111.5, 44.32, 36.85, 30.46, 20.99. **MS** (ESI) m/z: 301 $[M + Na]^+$.

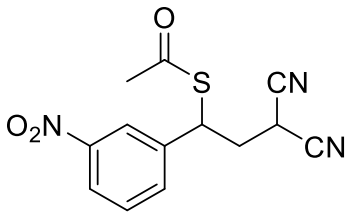
***S*-(1-(4-chlorophenyl)-3,3-dicyanopropyl) ethanethioate 3fa**



Following the general procedure and using cyclopropane **1f** (40 mg) and thioacetic acid **2a** (21.4 µL), product **3fa** was obtained in 40% yield (22 mg) after chromatographic purification on silica gel (3:1 = DCM: *n*-hexane as eluent) as a pale-yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.38–7.33 (m, 2H), 7.27–7.23 (m, 2H), 4.72 (dd, *J* = 8.9, 7.1 Hz, 1H), 3.58 (dd, *J* = 8.5, 6.85 Hz, 1H), 2.69 (ddd, *J* = 13.9, 8.6, 7.1 Hz, 1H), 2.56 (ddd, *J* = 13.9, 8.7,

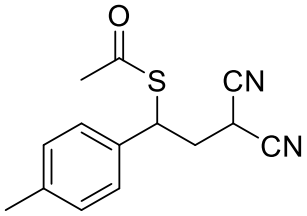
6.8 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.1, 135.9, 134.9, 129.7, 129.0, 111.7, 111.4, 44.2, 36.85, 30.5, 21.0. **MS** (ESI) m/z: 301 $[M + Na]^+$.

***S*-(3,3-dicyano-1-(3-nitrophenyl)propyl) ethanethioate 3ga**



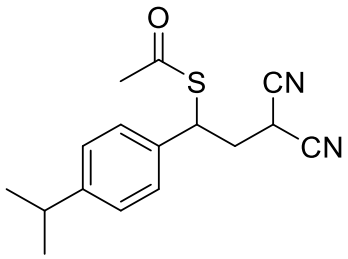
Following the general procedure using substrate **1g** (43 mg) and thioacetic acid **2a** (21.4 μL), product **3ga** was obtained in 47% yield (25 mg) after chromatographic purification on silica gel (4:1 = *n*-hexane: EtOAc as eluent) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.26–8.18 (m, 2H), 7.73–7.68 (m, 1H), 7.63–7.57 (m, 1H), 4.87 (t, *J* = 8.0 Hz, 1H), 3.76 (t, *J* = 7.5 Hz, 1H), 2.82–2.64 (m, 2H), 2.39 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 194.0, 161.2, 142.5, 133.1, 130.05, 123.3, 122.3, 116.9, 69.7, 51.8, 42.1, 29,4. **MS** (ESI) m/z: 312 $[M + Na]^+$.

***S*-(3,3-dicyano-1-(*p*-tolyl)propyl) ethanethioate 3ha**



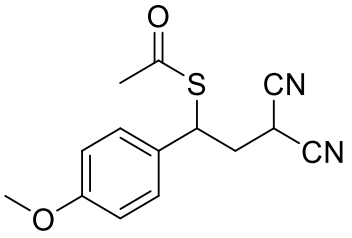
Following the general procedure and using cyclopropane **1h** (36 mg) and thioacetic acid **2a** (21.4 μL), product **3ha** was obtained in 52% yield (27 mg) after chromatographic purification on silica gel (4:1 = *n*-hexane: Et_2O as eluent) as a pale-yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.17 (br s, 4H), 4.70 (dd, *J* = 9.6, 6.5 Hz, 1H), 3.52 (dd, *J* = 9.2, 6.3 Hz, 1H) 2.71 (ddd, *J* = 13.6, 9.3, 6.5 Hz, 1H), 2.56 (ddd, *J* = 13.8, 9.6, 6.4 Hz, 1H), 2.34 (s, 3H), 2.33 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 193.6, 139.0, 133.8, 130.2, 127.5, 112.0, 111.6, 44.5, 37.15, 35.1, 30.4, 20.9. **MS** (ESI) m/z: 312 $[M + Na]^+$.

***S*-(3,3-dicyano-1-(4-isopropylphenyl)propyl) ethanethioate 3ia**



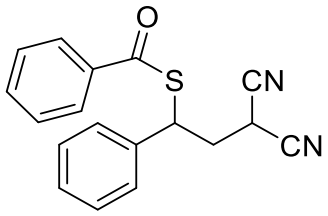
Following the general procedure using substrate **1i** (42 mg) and thioacetic acid **2a** (21.4 μL), product **3ia** was obtained in 47% yield (27 mg) after chromatographic purification on silica gel (6:1 = *n*-hexane: EtOAc as eluent) as a pale-yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.25–7.19 (m, 4H), 4.72 (dd, *J* = 9.6, 6.5 Hz, 1H), 3.53 (dd, *J* = 9.3, 6.25 Hz, 1H), 2.90 (hept, *J* = 6.9, 1H) 2.73 (ddd, *J* = 13.7, 9.3, 6.5 Hz, 1H), 2.60–2.51 (m, 1H) 2.36 (s, 3H), 1.24 (d, *J* = 6.9 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 193.6, 149.9, 134.05, 127.6, 127.5, 112.0, 111.6, 44.5, 37.2, 33.8, 30.4, 23.8, 20.9. **MS** (ESI) m/z: 309 $[M + Na]^+$.

***S*-(3,3-dicyano-1-(4-methoxyphenyl)propyl) ethanethioate 3ja**



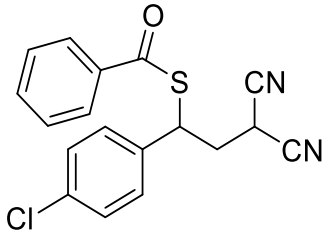
Following the general procedure using substrate **1j** (40 mg) and thioacetic acid **2a** (21.4 μL), product **3ja** was obtained in 47% yield (51 mg) after chromatographic purification on silica gel (4:1 = *n*-hexane: EtOAc as eluent) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.24–7.20 (m, 2H), 6.92–6.87 (m, 2H), 4.72 (dd, *J* = 9.7, 6.4 Hz, 1H), 3.81 (s, 3H) 3.53 (dd, *J* = 9.2, 6.2 Hz, 1H), 2.72 (ddd, *J* = 13.7, 9.2, 6.4 Hz, 1H), 2.54 (ddd, *J* = 13.7, 9.7, 6.25 Hz, 1H) 2.35 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 193.7, 159.9, 128.8, 128.6, 114.9, 112.0, 111.6, 55.35, 44.3, 37.2, 30.4, 20.9. **MS** (ESI) m/z: 297 $[M + Na]^+$.

***S*-(3,3-dicyano-1-phenylpropyl) benzothioate 3ab**



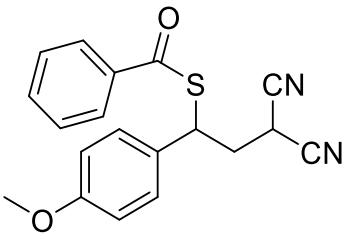
Following the general procedure using cyclopropane **1a** (33.6 mg) and thiobenzoic acid **2b** (36 μL), product **3ab** was obtained in 72% yield (44 mg) after chromatographic purification on silica gel (2:1 = DCM: *n*-hexane as eluent) as a pale-yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.97–7.90 (m, 2H), 7.64–7.56 (m, 1H), 7.53–7.31 (m, 7H), 4.97 (dd, *J* = 9.4, 6.5 Hz, 1H), 3.62 (dd, *J* = 9.0, 6.5 Hz, 1H), 2.86 (ddd, *J* = 13.8, 8.9, 6.5 Hz, 1H), 2.69 (ddd, *J* = 13.8, 9.4, 6.5 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 189.6, 137.0, 135.9, 134.1, 129.64, 129.61, 128.8, 127.8, 127.5, 112.0, 111.6, 44.8, 37.4, 21.0. **MS** (ESI)m/z: 329 $[M + Na]^+$.

***S*-(3,3-dicyano-1-(4-chlorophenyl)propyl) benzothioate 6fa**



Following the general procedure using cyclopropane **1f** (40 mg) and thiobenzoic acid **2b** (36 μL), product **3fb** was obtained in 32% yield (22 mg) after chromatographic purification on silica gel (1:1 = *n*-hexane: EtOAc as eluent) a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.95–7.90 (m, 2H), 7.64–7.58 (m, 1H), 7.52–7.42 (m, 2H), 7.42–7.32 (m, 4H), 4.95 (dd, *J* = 8.9, 7.0 Hz, 1H), 3.67 (dd, *J* = 8.5, 6.9 Hz, 1H), 2.83 (ddd, *J* = 13.9, 8.5, 7.0 Hz, 1H), 2.67 (ddd, *J* = 13.9, 9.0, 6.9 Hz, 1H). **MS** (ESI)m/z: 363 $[M + Na]^+$.

***S*-(3,3-dicyano-1-(4-methoxyphenyl)propyl) benzothioate 3jb**



Following the general procedure using **1j** (40 mg) and thiobenzoic acid **2b** (36 μL), product **3jb** was obtained in 45% yield (30 mg) after chromatographic purification on silica gel (2:1 = DCM: *n*-hexane as eluent) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.95–7.90 (m, 2H), 7.63–7.57 (m, 1H), 7.50–7.42 (m, 2H), 7.35–7.29 (m, 2H), 6.97–6.90 (m, 2H), 4.92 (dd, *J* = 9.7, 6.2 Hz, 1H), 3.82 (s, 3H), 3.61 (dd, *J* = 9.2, 6.2 Hz, 1H), 2.86 (ddd, *J* = 13.7, 9.2, 6.2 Hz, 1H), 2.64 (ddd, *J* = 13.7, 9.7, 6.3 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 189.8, 160.0, 136.1, 134.0, 129.0, 128.8, 128.6, 127.4, 114.9, 112.0, 111.6, 55.4, 44.3, 37.4, 21.0. **MS** (ESI)m/z: 359 $[M + Na]^+$.

4. Conclusions

In summary, the reactivity of some D-A cyclopropanes with thioacetic (and thiobenzoic) acid under PTC conditions was explored. This study, which constitutes a rare example of PTC reactions with cyclopropane substrates, led to the discovery of an unprecedented decyanation–acetylation reaction, affording 1-acetyl-1-cyano cyclopropanes **4**. This process was found to compete with a typical cyclopropane ring-opening reaction leading to adducts **3**. An investigation of the parameters affecting the two divergent pathways pointed to the nature of the inorganic base (solid vs. aqueous) as the key factor. With this insight, the screening of PT catalysts, solvents, and temperatures led to the creation of two complementary conditions, enabling excellent control over the product produced by the reaction. Thus, a series of cyclopropanes **4** were selectivity obtained in moderate to good yields using the first set of conditions, while the second set led to their ring-opened counterparts **3** with comparable results. Conversely, the low selectivity observed with common homogeneous organic bases in this reaction highlights the unique possibilities offered by the combination of PTC with D-A cyclopropanes.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/catal13040760/s1, NMR spectra of selected compounds.

Author Contributions: Conceptualization: G.D.B., L.B. and M.F.; methodology: G.D.B., P.V., L.B. and M.F.; writing—original draft preparation: M.F.; writing—review and editing: G.D.B., L.B. and M.F.; project administration: M.F. and L.B.; funding acquisition: M.F. and L.B. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement: Data is contained within the article or supplementary material.

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