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THE EFFECT OF SUBSTITUENTS ON THE PYRIDINE RING IN THE DIASTEREOSELECTIVE CYCLOPROPANATION REACTION OF PYRIDINIUM YLIDES BEARING AN 8-PHENYLMENTHYL ESTER GROUP†

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Abstract – The reaction between β-substituted methylidenemalononitriles and the ylide from (-)-8-phenylmenthyl α-pyridiniumacetate, which affords activated cyclopropanes bearing two cyano groups and one carboxylic ester group, was examined. The *trans* isomer was obtained in up to 91:9 diastereoselectivity under optimized solvent conditions for the *t*-butyl substituted substrate. The selectivity increased to 96:4 upon using 4-methoxypyridine in the place of pyridine, whereas selectivities were generally lower for *N*,*N*-diethylnicotinamide. The major 4-pyridyl substituted cyclopropane was determined to be *trans*-1*R* by X-Ray structural analysis.

INTRODUCTION

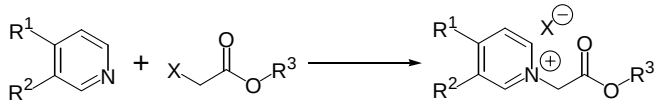
Due to their intrinsic ring strain, cyclopropane compounds have been known to exhibit unique reactivity.[1] Therefore, cyclopropane derivatives have been utilized as synthetic building blocks for further transformation.[2] The cyclopropyl group has also been found in compounds of biological interest.[3] As for the asymmetric synthesis of cyclopropanes, high levels of catalytic asymmetric induction have been achieved in metal-carbenoid reactions with aryl and electron-rich olefins.[4] For electron-deficient olefins, Michael type reactions have been more effective and most successful examples have been limited to

† This paper is dedicated to Professor Barry M. Trost on the occasion of his 65th birthday.

reactions involving stoichiometric asymmetric sources.[5] For cyclopropanes bearing two strongly electron-withdrawing groups such as carbonyl groups or the like, only a few successful catalytic processes have been disclosed.[5c,e-h] Activated cyclopropanes bearing multiple numbers of electron-withdrawing groups, have attracted our interest because of their unique reactivity.[6] However, asymmetric synthesis of such compounds by the use of Michael acceptors with two electron withdrawing groups has essentially been an unexplored area. Pyridinium ylides, which were originally prepared by Kröhnke[7] and are commonly used in cycloaddition reactions, have also found use in the cyclopropanation reaction giving product with exclusive *trans* geometry.[8] Some time back, we had found pyridine to react with activated cyclopropanes to give adducts with betaine structure, which incidentally are analogous to the anticipated intermediates in this cyclopropanation process.[6d,f] In order to develop an asymmetric version, we decided to utilize the 8-phenylmenthyl group,[9] which we also have found to be effective as a chiral auxiliary.[10] In preliminary work, we found the reaction to give cyclopropane products with selectivity up to 86:14.[11] In this full account we disclose improved selectivity attained as a result of further scrutiny of the reaction solvent and investigations on pyridinium ylides bearing substitution on the pyridine ring (4-methoxypyridine and *N*,*N*-diethylnicotinamide).

RESULTS AND DISCUSSION

In addition to pyridine, to examine effects of pyridine core substituents, we decided to undertake 4-methoxy as the electron-donating group and 3-amide as the electron-withdrawing group. The pyridinium salts examined for the cyclopropanation reactions were prepared by treating (-)-menthyl or 8-phenylmenthyl chloroacetate with the appropriate pyridines, as shown in Scheme 1. In the case of the 8-phenylmenthylnicotinic amide derivative, the corresponding α-bromoacetate was utilized instead of the chloride, since the desired pyridinium salt could not be obtained under the same conditions.

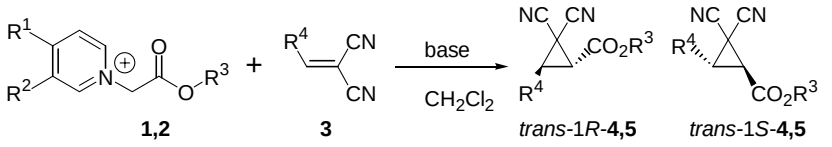


1a: R^1=H, R^2=H, R^3=menthyl, X=Cl, y. 82%
1b: R^1=H, R^2=$CONH_2$, R^3=menthyl, X=Cl, y. 97%
1c: R^1=H, R^2=$CONBn_2$, R^3=menthyl, X=Cl, y. 83%
1d: R^1=H, R^2=$CONEt_2$, R^3=menthyl, X=Cl, y. 82%
2a: R^1=H, R^2=H, R^3=8-phenylmenthyl, X=Cl, y. 94%
2b: R^1=MeO, R^2=H, R^3=8-phenylmenthyl, X=Cl, y. 71%
2c: R^1=H, R^2=$CONEt_2$, R^3=8-phenylmenthyl, X=Br, y. 89%

Scheme 1.

The ^{1}H NMR spectrum of the pyridinium salts bearing the phenylmenthyl group (**2a-c**) showed the presence of cation-π (or π-π) stacking interaction.[12] This was evident by the large high field shift for one of the methylene protons to δ 3.65 (**2b**), 3.89 (**2a**), and 4.03 (**2c**) from δ *ca.* 6, the value for the other methylene proton in **2a-c**. Both methylene protons for **1a-d**, which do not bear a phenyl group in the

chiral auxiliary, were also δ *ca.* 6. These high field chemical shift values show that the magnitude of the shift was larger for electron rich pyridinium salts. Although not as significant, this shielding effect was also obvious in the 2- and 6- protons of the pyridine ring by comparing signals of **1a** (δ 9.40) with **2a** (δ 9.10) and **1d** (δ 9.05 and 9.57) with **2c** (δ 8.68 and 9.10). These observations imply the possibility of phenyl π-stacking as a face-discriminating element.



3a: R^4=Ph
3b: R^4=4-$O_2NC_6H_4$
3c: R^4=4-pyridyl
3d: R^4=2-ClC_6H_4
3e: R^4=1-naphthyl
3f: R^4=*n*-butyl
3g: R^4=*s*-butyl
3h: R^4=*i*-propyl
3i: R^4=*t*-butyl
3j: R^4=adamanthyl

4a: R^4=Ph, R^3=menthyl
5a: R^4=Ph, R^3=8-phenylmenthyl
5b: R^4=4-$O_2NC_6H_4$, R^3=8-phenylmenthyl
5c: R^4=4-pyridyl, R^3=8-phenylmenthyl
5d: R^4=2-ClC_6H_4, R^3=8-phenylmenthyl
5e: R^4=1-naphthyl, R^3=8-phenylmenthyl
5f: R^4=*n*-butyl, R^3=8-phenylmenthyl
5g: R^4=*s*-butyl, R^3=8-phenylmenthyl
5h: R^4=*i*-propyl, R^3=8-phenylmenthyl
5i: R^4=*t*-butyl, R^3=8-phenylmenthyl
5j: R^4=adamanthyl, R^3=8-phenylmenthyl

Scheme 2.

Table 1. Reaction of **2a** with **3a**

entry	solvent	base	temp (°C)	yield (%)	diastereomeric ratio[a]	entry	solvent	base	temp (°C)	yield (%)	diastereomeric ratio[a]
1	EtOH	Et_3N	50	69	79:21	13	Et_2O	Et_3N	0	72	80:20
2	EtOH	Et_3N	0	59	79:21	14	Et_2O	NaH	0	56	75:25
3	*i*-PrOH	NaH	0	17	83:17	15	Et_2O	*t*-BuOK	0	20	76:24
4	DMF	NaH	0	57	68:32	16	Et_2O	KHMDS	0	42	72:28
5	DMSO	NaH	rt	32	74:26	17	toluene	NaH	0	48	78:22
6	MeCN	NaH	0	27	81:19	18	toluene	KHMDS	0	36	72:28
7	THF	Et_3N	0	100	67:33	19	CH_2Cl_2	Et_3N	0	78	83:17
8	THF	Et_3N-LiCl	0	88	70:30	20	CH_2Cl_2	LiH	0	97	83:17
9	THF	*n*-BuLi	0	75	68:32	21	CH_2Cl_2	NaH	0	76	83:17
10	THF	NaH	0	60	68:32	22	CH_2Cl_2	*t*-BuOK	0	77	82:18
11	THF	*t*-BuOK	0	81	68:32	23	CH_2Cl_2	KHMDS	0	79	82:18
12	THF	KHMDS	0	65	69:31	24	CF_3CH_2OH	Et_3N	0	59	88:12

[a] Determined by ^{1}H NMR spectrum of the diastereomeric mixture.

In the cyclopropanation reaction, only the *trans* product was obtained in all of the reactions carried out regardless of the pyridinium salt used, as evident by the characteristic cyclopropane vicinal proton coupling constant of *ca.* 8.5 Hz and NOE measurements. First examined was the reaction between phenylmethylidenemalononitrile (**3a**) and (**1a**). The diastereoselectivity turned out to be disappointing with

the ratio not exceeding 61:39 upon trials in several solvents, thus indicating the ineffectiveness of the menthyl group as a chiral auxiliary.

Results of the detailed examination of **3a** with **2a** are provided in Table 1. As a general trend, the change in selectivity was minimal upon changing the base. However, a small but obvious difference was observed upon changing the solvent. No apparent trend could be deduced from the results. In terms of both yield and diastereoselectivity, the optimal solvent was CH_2Cl_2 (83:17). As for selectivity alone, CF_3CH_2OH (88:12) was better.

In the case of *t*-butylmethylidenemalononitrile (**3i**), screening showed DMSO and MeCN to be choice solvents. Thus, the scope in terms of substrate was examined in CH_2Cl_2, MeCN, and CF_3CH_2OH, as given in Table 2. Although alkyl substrates of small size tended to give products of lower diastereoselectivity, **3i** exhibited selectivity as high as 91:9.

Table 2. Reaction of **2a** with conjugated alkenes **3a-j** using Et_3N as base

entry	R^4		in CH_2Cl_2		in MeCN		in CF_3CH_2OH	
			yield (%)	diastereomeric ratio[a]	yield (%)	diastereomeric ratio[a]	yield (%)	diastereomeric ratio[a]
1	Ph	**3a**	78	83:17	–[b]	–[b]	59	88:12
2	4-$O_2NC_6H_4$	**3b**	91	84:16	–[b]	–[b]	–[b]	–[b]
3	4-pyridyl	**3c**	82	84:16	–[b]	–[b]	–[b]	–[b]
4	2-ClC_6H_4	**3d**	91	86:14	–[b]	–[b]	–[b]	–[b]
5	1-naphthyl	**3e**	98	89:11	–[b]	–[b]	–[b]	–[b]
6	*n*-Bu	**3f**	97	72:28	83	74:26	52	77:23
7	*i*-butyl	**3g**	96	75:25	86	56:44	48	76:24
8	*i*-propyl	**3h**	93	66:34	72	75:25	47	78:22
9	*t*-butyl	**3i**	99	86:14	82	91:9	52	87:13
10	adamantyl	**3j**	100	76:24	–[b]	–[b]	–[b]	–[b]

[a] Determined by ^{1}H NMR spectrum of the diastereomeric mixture. [b] Reaction was not carried out.

The absolute stereochemistry of major **5c**, *trans*-2,2-dicyano-3-(4-pyridyl)cyclopropanecarboxylate, was established by X-Ray structural analysis to be of 1*R*,3*S* configuration. Other diastereomers were neither separable nor crystalline. The ORTEP representation of the molecular structure is shown in Figure 1. Interestingly, this stereochemistry is opposite to that assigned to *trans*-2,2-dicyano-3-(4-pyridyl)-cyclopropanecarboxamide with a 8-phenylmenthylamine as the chiral auxiliary.[13] The major product for the reactions of the other substrates with the ester based ylide were assumed to have analogous stereochemistry to major **5c**.

The solid-state structure of major **5c** showed the proton at the base of the carboxylic group to be located in the shielding region of the phenyl group of the chiral auxiliary. This happened to be in good agreement with its solution structure speculative from its ^{1}H NMR spectrum. The chemical shift of this proton observed at δ 3.68 for both diastereomers of **4a**, with the menthyl chiral auxiliary, were shifted upfield to

δ 2.04 (major) and 2.00 (minor) for **5a**. The fact that there is essentially no difference in chemical shift between diastereomers here indicates that in the solution structure of the minor isomer, the relative spatial relationship between the chiral auxiliary and the three membered ring core is the same as that for the major isomer. Thus, it follows that just by exchanging the substituents on the two other cyclopropane carbons in Figure 1, we obtain the solution structure of minor **5c**. This would put the proton at the base of the aryl group just outside the rim of the 8-phenylmenthyl phenyl group and in the deshielding region, showing good agreement with the downfield shift of this proton (δ 3.36) relative to that of the major isomer (δ 3.02) and corresponding signals (δ 3.12 and 3.13) of **4a**.

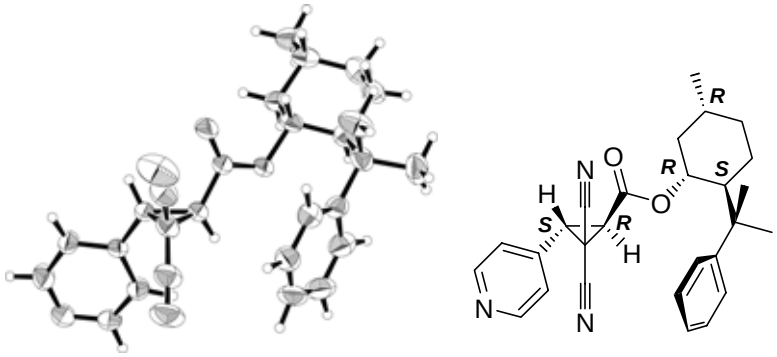


Figure 1. ORTEP drawing of the major 4-pyridyl product (**5c**)

Table 3. Reaction of **2b** with Et_3N as base

entry	R^4		solvent	yield (%)	diastereomeric ratio[a]
1	Ph	**3a**	CH_2Cl_2	50	69:31
2	*n*-Bu	**3f**	CH_2Cl_2	55	74:26
3	*i*-butyl	**3g**	CH_2Cl_2	77	67:33
4	*i*-propyl	**3h**	CH_2Cl_2	63	63:27
5	*t*-butyl	**3i**	CH_2Cl_2	64	93:7
6	*t*-butyl	**3i**	MeCN	64	96:4

[a] Determined by ^{1}H NMR spectrum of the diastereomeric

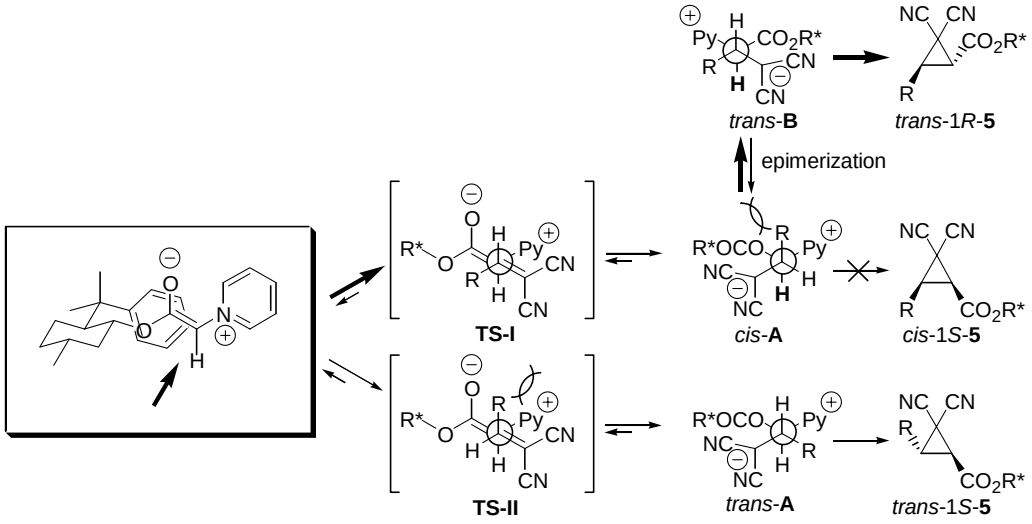
Table 4. Reaction of **2c** with Et_3N as base

entry	R^4		temp (°C)	yield (%)	diastereomeric ratio[a]
1	Ph	**3a**	0	80	80:20
2	Ph	**3a**	-40–0	74	73:27
3	Ph	**3a**	-78–0	72	73:27
4	*n*-Bu	**3f**	0	33	61:39
5	*i*-butyl	**3g**	0	45	68:32
6	*i*-propyl	**3h**	0	42	51:49
7	*i*-propyl	**3h**	-78	31	61:39
8	*t*-butyl	**3i**	0	36	80:20
9	*t*-butyl	**3i**	-78	30	81:19

[a] Determined by ^{1}H NMR spectrum of the diastereomeric mixture.

The cyclopropanation reaction can be rationalized to consist of the three following steps: (1) The formation of an enolate by deprotonation of the pyridinium salts, (2) the Michael addition of the enolate to the substituted methylidenemalononitrile (which should be a reversible process), and (3) ring closure by intramolecular S_N2 reaction of the stabilized carbanion bearing the two cyano groups with concomitant extrusion of the pyridyl group. An electron rich pyridine would be expected to accelerate the Michael addition step and retard the reverse process, thus reducing the possibility of stereochemical leakage by the latter. On the other hand, an electron deficient pyridine can be envisioned to rev up not only the

elimination (ring formation) step but also the retro-Michael process. This should allow the reaction to be carried out at lower temperatures, at which selectivity might rise. In order to see how these substituents actually effect the reactivity and selectivity, 4-methoxypyridine as an example for the former group of pyridines and nicotinamide as that for the latter were examined. As for the reaction of **2b**, an increase was observed for **5i**. Otherwise, the selectivity was lower. For the nicotinamide series, prior to the use of reagents bearing the 8-phenylmenthyl group, reagents **1b** ($R^2 = CONH_2$), **1c** ($R^2 = CONBn_2$), and **1d** ($R^2 = CONEt_2$), bearing a menthyl group were examined, and it was found that good reproducible yields were attained using **1d**. Thus, **2c** with the same amide on the pyridine ring was investigated. Although the reaction was found to proceed at temperatures as low as -78 °C, drops in selectivity were observed. Thus, the effect of substituents does not seem to be clear cut.



Scheme 3. Plausible mechanism

The mechanism involving selectivity can tentatively be assumed to be as follows. The enolate, in which the large pyridyl and 8-phenylmenthyloxy groups are in a *trans* relationship, is expected to be predominant upon deprotonation due to both steric factors and electrostatic interaction between the cationic pyridine and anionic oxide moieties. Reaction with the Michael acceptor is expected to occur upon the face of the enolate not sterically encumbered by the phenyl group of the 8-phenylmenthyl chiral auxiliary,[11-13] and considering dipole cancellation as the driving force, we come upon the process involving **TS-I** as the favored and thus the primary stereodetermining step. Upon ring closure to give the cyclopropane product, however, intermediate *cis*-**A** experiences severe steric hindrance due to interaction between the carboxylate group and the R group, and thus product formation is unfavorable. Due to the presence of the two carbanion stabilizing groups, intermediate *cis*-**A** should have a sufficient lifetime to allow for the carbon in between the pyridinium and carboxylate groups to undergo epimerization under the basic reaction conditions. This affords intermediate *trans*-**B**, in which hindrance in the ensuing cyclization process is alleviated, and thus gives the observed major stereoisomer *trans*-1*R*-**5**. Since the

product cyclopropane could not easily be deprotonated, it is difficult to assume the formation of the *cis* product followed by epimerization to the *trans* product. Unfortunately, NMR spectral monitoring of the reaction showed the presence of only starting materials and products, and no viable intermediates. Therefore, experimental verification of the mechanism is problematic at the moment. The minor isomer could arise from either **TS-II** or the enolate in which the two large groups are in a *cis* relationship.

Since pyridinium ylides are well known for their dipolar cycloadditions, there is a possibility of the initial reaction being a [3+2] reaction followed by C-C bond dissociation to give intermediates corresponding to **A** and **B**. However, we feel this pathway unlikely, since if secondary orbital interactions were operative to give endo-type products, then the opposite *trans*-1*S* stereoisomer would have been expected from the enolate depicted above.

In summary, we have presented the asymmetric synthesis of highly activated cyclopropanes by utilizing 8-phenylmenthyl α-pyridiniumacetates with diastereoselectivity up to 96:4. Substitution on the pyridine ring was found to alter the reaction rate, but lower temperature did not necessarily lead to higher selectivity. The selectivity here complements that found for analogous reactions involving the 8-phenylmenthylamine auxiliary.

EXPERIMENTAL

General

Melting points were measured on a Yanaco micro melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were measured on a JEOL JNM–LA500 spectrometer with chemical shifts given from ordinary standards. High resolution mass spectra were measured on a JEOL JMS-SX102A spectrometer under electron ionization conditions (70 eV) or fast atom bombardment conditions (glycerol as matrix). Elemental analyses (CHN) were carried out on a Perkin–Elmer 2400CHN elemental analyzer.

1-(*l*-Menthyloxycarbonylmethyl)pyridinium chloride (1a)

A mixture of *l*-menthyl chloroacetate (5.78 g, 25 mmol) and pyridine (2.2 mL, 26 mmol) was heated at 90 °C overnight. Recrystallization of the resulting solid from a mixture of methanol and ether gave 6.42 g (82%) of pyridinium salt (**1a**) as a colorless solid. mp 181-183 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.40 (d, *J* = 6.0 Hz, 2H), 8.50 (t, *J* = 8.0 Hz, 1H), 8.07 (t, *J* = 7.0 Hz, 2H), 6.31 (d, *J* = 17.0 Hz, 1H), 6.20 (d, *J* = 17.0 Hz, 1H), 4.79 (dt, *J* = 4.6, 10.9 Hz, 1H), 2.07-2.01 (m, 1H), 1.91-1.82 (m, 1H), 1.73-1.65 (m, 2H), 1.51-1.37 (m, 2H), 1.13-0.99 (m, 2H), 0.91 (t, 6H, *J* = 6.5 Hz), 0.92-0.83 (m, 1H), 0.75 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ165.4, 146.3, 146.1, 127.6, 77.7, 60.8, 46.5, 40.2, 33.6, 31.1, 25.7, 22.9, 21.6, 20.6, 15.9. Anal. Calcd for $C_{17}H_{26}NO_2Cl$: C, 65.48; H, 8.40; N, 4.49. Found: 65.31, H, 8.69, N, 4.23.

3-Aminocarbonyl-1-(*l*-menthyloxycarbonylmethyl)pyridinium chloride (1b)

Colorless solid. mp 229-230 °C; ^{1}H NMR (500 MHz, D_2O) δ 9.34-9.31 (m, 1H), 8.96-8.94 (m, 1H), 8.91-8.88 (m, 1H), 8.14-8.01 (m, 1H), 4.77 (dt, *J* = 4.5, 11.0 Hz, 1H), 1.97-1.95 (m, 1H), 1.65-1.58 (m, 3H), 1.45-1.32 (m, 2H), 1.05-0.96 (m, 2H), 0.83 (d, *J* = 6.7 Hz, 3H), 0.83-0.75 (m, 1H), 0.78 (d, *J* = 7.0 Hz, 3H), 0.64 (d, *J* = 7.0 Hz, 3H), (4 signals lack due to overlap or deuteration by the solvent). ^{13}C NMR (125 MHz, CD_3OD) δ 166.0, 164.2, 148.5, 147.2, 145.3, 135.0, 128.4, 78.4, 47.6, 41.0, 34.4, 32.0, 26.5, 22.7, 21.6, 20.5, 15.9 (1 signal lacks due to overlap). HRMS (EI^+) calcd for $C_{18}H_{27}NO_3$ 319.2022, found 319.1992. Anal. Calcd for $C_{18}H_{27}N_2O_3Cl$: C, 60.92; H, 7.67; N, 7.89. Found: 61.13, H, 7.39, N, 7.75.

3-(*N,N*-Dibenzylaminocarbonyl)-1-(*l*-menthyloxycarbonylmethyl)pyridinium chloride (1c)

Colorless solid. mp 170-172 ˚C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.58 (d, 1H, *J* = 6.0 Hz), 9.14 (s, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 7.89 (dd, *J* = 6.5, 8.0 Hz, 1H), 7.44-7.23 (m, 8H), 7.14-7.02 (m, 2H), 6.31 (d, *J* = 17.0 Hz, 1H), 6.14 (d, *J* = 17.0 Hz, 1H), 4.81-4.70 (m, 3H), 2.28 (s, 2H), 2.01-1.95 (m, 1H), 1.87-1.78 (m, 1H), 1.72-1.63 (m, 2H), 1.49-1.35 (m, 2H), 1.09-0.96 (m, 2H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.88 (d, *J* = 7.0 Hz, 3H), 0.89-0.81 (m, 1H), 0.72 (d, *J* = 6.5 Hz, 3H),. ^{13}C NMR (500 MHz, $CDCl_3$) δ 165.4, 164.8, 147.7, 144.4, 143.6, 135.6, 129.1 (br), 129.0 (br), 128.6 (br), 128.0 (br), 127.5, 126.9 (br), 78.2, 61.3, 52.0, 49.4, 46.6, 40.6, 33.8, 31.4, 26.0, 23.1, 21.8, 20.7, 16.1 (3 signals lack due to peak broadening). HRMS (EI^+) calcd for $C_{32}H_{39}N_2O_3$ 499.2961, found 499.3001. Anal. Calcd for $C_{32}H_{39}N_2O_3Cl$: C, 71.82; H, 7.35; N, 5.24. Found: 71.96, H, 7.28, N, 5.25.

3-(*N,N*-Diethylaminocarbonyl)-1-(*l*-menthyloxycarbonylmethyl)pyridinium chloride (1d)

Colorless solid. mp 131-132˚C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.54-9.59 (m, 1H), 9.05 (s, 1H), 8.48 (t, *J* = 7.0, 1H), 8.16-8.22 (m, 1H), 6.33 (d, *J* = 17.0, 1H), 6.19 (d, *J* = 17.0, 1H), 4.79 (dt, *J* = 4.5, 11.0, 1H), 3.51-3.62 (m, 2H), 3.38-3.48 (m, 2H), 2.00-2.06 (m, 1H), 1.81-1.90 (m, 1H), 1.65-1.74 (m, 2H), 1.39-1.52 (m, 2H), 1.16-1.34 (m, 6H), 0.99-1.13 (m, 2H), 0.92 (d, *J* = 6.5, 3H), 0.91 (d, *J* = 7.0, 3H), 0.84-0.90 (m, 1H), 0.75 (d, *J* = 7.0, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.4, 163.4, 147.2, 144.0, 143.7, 135.9, 128.2, 77.8, 61.1, 46.4, 43.7, 40.2, 40.0, 33.6, 31.1, 25.7, 22.8, 21.6, 20.5, 15.9, 14.0, 12.4. HRMS (EI^+) calcd for $C_{22}H_{35}N_2O_3$ 375.2648, found 375.2648.

1-(8-Phenylmenthyloxycarbonylmethyl)pyridinium chloride (2a)

Colorless solid. mp 110-112˚C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.10 (d, *J* = 6.1 Hz, 2H), 8.48 (t, *J* = 7.3 Hz, 1H), 8.03 (t, *J* = 7.0 Hz, 2H), 7.41-7.36 (m, 4H), 7.22-7.19 (m, 1H), 6.18 (d, *J* = 16.5 Hz, 1H), 4.94 (dt, *J* = 4.5, 11.0 Hz, 1H), 3.89 (d, *J* = 17.0 Hz, 1H), 2.26-2.19 (m, 1H), 1.96-2.04 (m, 1H), 1.93-1.87 (m, 1H), 1.77-1.70 (m, 1H), 1.50-1.39 (m, 1H), 1.31 (s, 1H), 1.28-1.11 (m, 2H), 1.18 (s, 3H), 1.03-0.94 (m,

1H), 0.91 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 151.9, 146.2, 128.1, 127.9, 125.6, 125.4, 60.1, 49.5, 41.2, 39.4, 34.0, 31.2, 30.2, 26.0, 22.3, 21.5 (2 signals lack due to overlap). HRMS (EI^+) calcd for $C_{23}H_{30}NO_2$ 352.2277, found 352.2265.

4-Methoxy-1-(8-phenylmenthyloxycarbonylmethyl)pyridinium chloride (2b)

Colorless solid. mp 142-145°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 (d, *J* = 7.5 Hz, 2H), 7.41-7.34 (m, 6H), 7.24-7.17 (m, 1H), 5.73 (d, *J* = 17.5 Hz, 1H), 4.93 (dt, *J* = 4.5, 11.0 Hz, 1H), 4.14 (s, 3H), 3.65 (d, *J* = 17.5 Hz, 1H), 2.24-2.15 (m, 1H), 2.03-1.96 (m, 1H), 1.90-1.84 (m, 1H), 1.77-1.70 (m, 1H), 1.51-1.40 (m, 1H), 1.31 (s, 3H), 1.28-1.18 (m, 1H), 1.18 (s, 3H), 1.17-1.08 (m, 1H), 1.05-0.94 (m, 1H), 0.91 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.6, 165.9, 152.2, 140.4, 127.9, 125.4, 125.1, 118.3, 75.9, 55.8, 49.6, 41.4, 39.2, 34.1, 31.1, 30.8, 25.8, 21.5, 21.3 (1 signal lacks due to overlap). HRMS (EI^+) calcd for $C_{24}H_{32}NO_3$ 382.2382, found 382.2406. Anal. Calcd for $C_{24}H_{32}NO_3Cl$: C, 68.97; H, 7.72; N, 3.35. Found: 68.88, H, 7.63, N, 3.54.

3-(*N,N*-Diethylaminocarbonyl)-1-(8-phenylmenthyloxycarbonylmethyl)pyridinium bromide (2c)

Pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.10 (d, *J* = 5.5 Hz, 1H), 8.68 (s, 1H), 8.48 (t, *J* = 8.0 Hz, 1H), 8.22 (t, *J* = 7.0 Hz, 1H), 7.42-7.33 (m, 4H), 7.30-7.22 (m, 1H), 5.92 (d, *J* = 17.0 Hz, 1H), 4.92 (dt, *J* = 4.5, 11.0 Hz, 1H), 4.03 (d, *J* = 17.0 Hz, 1H), 3.58 (d, *J* = 6.5 Hz, 2H), 3.40 (d, *J* = 6.5 Hz, 2H), 2.23-2.16 (m, 1H), 2.09-1.94 (m, 2H), 1.89 (d, *J* = 13.5 Hz, 1H), 1.73 (d, *J* = 13.5 Hz, 1H), 1.51-1.39 (m, 1H), 1.31 (s, 1H), 1.30 (s, 6H), 1.27-1.16 (m, 3H), 1.18 (s, 3H), 1.17-1.08 (m, 1H), 0.91 (d, *J* = 7.0 Hz, 3H), 1.02-0.90 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.3, 163.2, 151.8, 146.7, 144.0, 143.7, 136.3, 128.3, 128.2, 125.6, 125.5, 77.5, 60.7, 49.6, 44.2, 41.3, 40.3, 39.4, 34.1, 31.2, 30.5, 26.0, 22.0, 21.5, 14.4, 12.6. HRMS (EI^+) calcd for $C_{28}H_{39}N_2O_3$ 451.2961, found 451.2931.

8-Phenylmenthyl *trans*-2,2-dicyano-3-phenylcyclopropanecarboxylate (5a)

To a solution of pyridinium salt (**2a**) (42.5 mg, 0.110 mmol) and Et_3N (0.017 mL, 0.122 mmol) in CH_2Cl_2 (1.5 mL) cooled to 0 °C was added benzylidenemalononitrile (**3a**) (13.1 mg, 0.085 mmol) in CH_2Cl_2 (1.5 mL). After stirring the solution at this temperature for 15 h, the reaction was quenched with saturated NH_4Cl. The mixture was extracted with CH_2Cl_2, and the combined organic layer was washed with water, dried over anhydrous Na_2SO_4, and then the solvent was removed in vacuo. Purification by PTLC (SiO_2, hexane-ethyl acetate=5:2 v/v) gave 28.2 mg (78%, 83:17 diastereomeric mixture) of cyclopropane (**5a**) as a viscous oil. All other reactions were carried out in a similar manner. **5a**: Diastereomeric mixture, colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47-7.44 (m, 2H, minor), 7.40-7.36 (m, 7H, major), 7.30-7.27 (m, 2H, minor), 7.19-7.13 (m, 5H, minor), 7.12-7.06 (m, 3H, major), 6.94 (t, *J* = 7.3 Hz, 1H,

minor), 4.99 (dt, *J* = 4.5, 11.0 Hz, 1H), 3.43 (d, *J* = 8.5 Hz, 1H, minor), 3.11 (d, *J* = 8.5 Hz, 1H, major), 2.09-2.02 (m, 1H), 2.28-2.18 (m, 1H), 2.04 (d, *J* = 8.0 Hz, 1H, major), 2.00 (d, *J* = 8.0 Hz, 1H, minor), 1.93-1.84 (m, 1H), 1.80-1.73 (m, 1H), 1.55-1.45 (m, 1H), 1.35 (s, 3H, major), 1.30 (s, 3H, minor), 1.28-1.21 (m, 1H), 1.21 (s, 3H, major), 1.20 (s, 3H, minor), 1.17-0.92 (m, 2H), 0.94 (d, *J* = 6.5 Hz, 3H, minor), 0.90 (d, *J* = 6.5 Hz, 3H, major). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.1 (major), 163.8 (minor), 152.1 (major), 152.0 (minor), 129.6 (major), 129.1 (major), 129.0 (major), 128.2 (minor), 128.1 (major), 129.7 (minor), 129.1 (minor), 128.8 (minor), 128.3 (minor), 128.2 (major), 128.0 (minor), 125.7 (major), 125.3 (minor), 125.2 (major), 111.8 (both), 111.6 (minor), 111.5 (major), 77.4 (major), 77.2 (minor), 50.3 (major), 41.6 (minor), 41.5 (major), 39.3 (minor), 39.2 (major), 38.6 (minor), 38.3 (major), 34.3 (major), 33.3 (minor), 32.3 (major), 31.3 (major), 31.1 (major), 30.7 (minor), 26.0 (major), 21.7 (major), 21.4 (minor), 21.1 (major), 14.2 (minor), 14.1 (major). HRMS (EI^+) calcd for $C_{28}H_{30}N_2O_2$ 426.2307, found 426.2326.

8-Phenylmenthyl *trans*-2,2-dicyano-3-(4-nitrophenyl)cyclopropanecarboxylate (5b)

Diastereomeric mixture, colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.5 Hz, 2H, minor), 8.26 (d, *J* = 8.5 Hz, 2H, major), 7.39-7.33 (m, 4H, major), 7.34 (d, *J* = 8.0 Hz, 2H, minor), 7.30 (d, *J* = 9.2 Hz, 2H), 7.15-7.12 (m, 1H, major), 7.09-7.12 (m, 2H, minor), 6.94 (t, *J* = 7.3 Hz, 1H, minor), 5.01 (dt, *J* = 4.5, 11.0 Hz, 1H), 3.50 (d, *J* = 8.5 Hz, 1H, minor), 3.11 (d, *J* = 8.5 Hz, 1H, major), 2.30-2.22 (m, 1H), 2.08 (d, *J* = 8.5 Hz, major), 2.11-2.10m, 1H), 1.97 (d, *J* = 8.5 Hz, minor), 1.90-1.84 (m, 1H), 1.82-174 (m, 1H), 1.58-1.46 (m, 1H), 1.35 (s, 3H, major), 1.31 (s, 3H, minor), 1.31-1.23 (m, 1H), 1.21 (s, 3H), 1.17-0.96 (m, 2H), 0.95 (d, *J* = 6.5 Hz, 3H, minor), 0.91 (d, *J* = 6.5 Hz, 3H, major). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.4 (major), 163.1 (minor), 152.3 (minor), 152.3 (major), 148.6 (minor), 148.5 (major), 136.2 (major), 129.5 (major), 129.4 (minor), 128.1 (major), 127.9 (minor), 125.7 (major), 125.5 (minor), 125.4 (minor), 125.3 (major), 125.0 (minor), 124.2 (major), 124.1 (minor), 111.3 (major), 111.3 (minor), 111.1 (minor), 110.8 (major), 77.9 (major), 77.7 (minor), 50.1 (major), 50.1 (minor), 41.5 (minor), 41.4 (major), 39.3 (minor), 39.2 (major), 39.1 (minor), 36.9 (major), 36.3 (minor), 34.3 (major), 33.4 (minor), 32.5 (major), 31.3 (major), 31.3 (major), 31.0 (minor), 25.9 (major), 25.9 (minor), 21.7 (major), 20.9 (minor), 20.7 (major), 14.2 (major), 13.6 (minor). HRMS (EI^+) calcd for $C_{28}H_{29}N_3O_4$ 471.2171 , found 471.2136.

8-Phenylmenthyl *trans*-2,2-dicyano-3-(4-pyridyl)cyclopropanecarboxylate (5c)

The diastereomers were separable by chromatography (SiO_2, hexane-ethyl acetate=4:1). Major-**5c**: colorless solid. mp 55-58 °C (hexane-CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.71-8.65 (m, 2H), 7.41-7.34 (m, 4H), 7.19-7.14 (m, 1H), 7.10-7.04 (m, 2H), 5.00 (dt, *J* = 4.5, 11.0 Hz, 1H), 3.02 (d, *J* = 8.0 Hz, 1H), 2.30-2.22 (m, 1H), 2.11-2.02 (m, 1H), 2.04 (d, *J* = 8.0 Hz, 1H), 1.87-1.83 (m, 1H), 1.81-1.75 (m,

1H), 1.56-1.46 (m, 1H), 1.35 (s, 3H), 1.33-1.23 (m, 1H), 1.21 (s, 3H), 1.10-0.96 (m, 2H), 0.91 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.4, 152.8, 150.4, 138.1, 128.1, 125.6, 125.2, 122.8, 111.7, 110.8, 77.7, 50.1, 41.4, 39.1, 36.4, 34.2, 31.9, 31.3, 31.2, 26.0, 21.6, 20.7, 14.0. HRMS (EI^+) calcd for $C_{27}H_{29}N_3O_2$ 427.2260, found 427.2275. Minor-**5c**: colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.85-8.68 (m, 2H), 7.29 (d, *J* = 7.5 Hz, 2H), 7.15-7.04 (m, 4H), 6.92 (t, *J* = 7.5 Hz, 1H), 4.98 (dt, *J* = 4.5, 11.0 Hz, 1H), 3.36 (d, *J* = 8.0 Hz, 1H), 2.20-2.27 (m, 1H), 2.10-2.02 (m, 1H), 1.93 (d, *J* = 8.0 Hz, 1H) , 1.97-1.86 (m, 1H), 1.82-1.75 (m, 1H), 1.57-1.47 (m, 1H), 1.30 (s, 3H), 1.29-1.21 (m, 1H), 1.19 (s, 3H), 1.13 (q, *J* = 12.0 Hz, 1H), 1.02 (m, 1H), 0.94 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.2, 152.2, 150.4, 137.9, 127.9, 125.3, 125.1, 122.9, 110.9, 110.8, 77.5, 50.1, 41.5, 39.3, 35.8, 34.3, 33.0, 31.3, 31.1, 25.9, 21.7, 20.9, 13.4. HRMS (EI^+) calcd for $C_{27}H_{29}N_3O_2$ 427.2260, found 427.2268.

8-Phenylmenthyl *trans*-2,2-dicyano-3-(2-chlorophenyl)cyclopropanecarboxylate (5d)

Diastereomeric mixture, colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55-7.47 (m, 1H), 7.44-7.33 (m, 3H), 7.32-7.25 (m, 3H), 7.13-6.92 (m, 2H), 5.02 (td, *J* = 10.7, 4.3 Hz, 1H), 3.59 (d, *J* = 8.2 Hz, 1H, minor), 2.94 (d, *J* = 8.2 Hz, 1H, major), 2.26 (ddd, *J* = 12.2, 10.7, 3.4 Hz, 1H), 2.12-2.03 (m, 1H), 2.11 (d, *J* = 8.2 Hz, 1H, minor), 2.10 (d, *J* = 8.2 Hz, 1H, major), 1.92-1.84 (m, 1H), 1.82-1.73 (m, 1H), 1.60-1.46 (m, 1H), 1.34 (s, 3H), 1.27 (dtd, *J* = 13.1, 12.2, 3.4 Hz, 1H), 1.22 (s, 3H, minor), 1.19 (s, 3H, major), 1.10 (ddd, *J* = 13.1, 12.2, 10.7 Hz, 1H), 1.01 (dtd, *J* = 13.1, 12.2, 3.4 Hz, 1H), 0.94 (d, *J* = 6.4 Hz, 3H, minor), 0.92 (d, *J* = 6.4 Hz, 3H, major); HRMS (EI^+) *m/z* calcd for $C_{28}H_{29}N_2O_2Cl$ 460.1918, found 460.1940.^{3}C NMR (125 MHz, $CDCl_3$) δ 163.7 (major), 163.6 (minor), 152.1 (major), 152.0 (minor), 136.2 (minor), 136.0 (major), 131.0 (minor), 130.9 (major), 130.2 (minor), 130.1 (major), 129.0 (major), 128.8 (minor), 128.3 (major), 128.1 (major), 128.0 (minor), 127.8 (minor), 127.2 (major), 127.0 (minor), 125.6 (major), 125.4, (minor), 125.2 (minor), 125.1 (major), 111.7 (major), 111.4 (minor), 111.3 (major), 111.3 (minor), 77.6 (minor), 77.5 (major), 50.0 (major), 50.0 (minor), 41.5 (minor), 41.5 (major), 39.4 (minor), 39.1 (major), 36.6 (major), 35.9 (minor), 34.3 (major), 33.6 (minor), 33.1 (major), 31.3 (major), 31.2 (major), 30.3 (minor), 26.1 (minor), 26.0 (major), 22.1 (minor), 21.7 (major), 20.9 (major), 20.9 (minor), 13.7 (major), 13.0 (minor) (2 minor alkyl signals lack due to overlap).

8-Phenylmenthyl *trans*-2,2-dicyano-3-(1-naphthyl)cyclopropanecarboxylate (5e)

Diastereomeric mixture, colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04-7.87 (m, 3H), 7.73-7.66 (m, 1H), 7.64-7.58 (m, 1H), 7.53-7.35 (m, 3H), 7.31-7.24 (m, 2H), 7.18-7.05 (m, 1H), 6.94-6.87 (m, 1H), 5.06 (td, *J* = 10.7, 4.3 Hz, 1H), 3.92 (d, *J* = 8.2 Hz, 1H, minor), 3.36 (d, *J* = 8.2 Hz, 1H, major), 2.34-2.24 (m, 1H), 2.28 (d, *J* = 8.2 Hz, 1H), 2.12-2.03 (m, 1H), 2.02-1.89 (m, 1H), 1.83-1.74 (m, 1H), 1.60-1.48 (m, 1H), 1.37 (s, 3H), 1.29 (dtd, *J* = 13.1, 12.2, 3.4 Hz, 1H), 1.21 (s, 3H), 1.14 (ddd, *J* = 13.1, 12.2, 10.7 Hz,

1H), 1.03 (dtd, *J* = 13.1, 12.2, 3.4 Hz, 1H), 0.95 (d, *J* = 6.7 Hz, 3H, minor), 0.93 (d, *J* = 6.7 Hz, 3H, major); HRMS (EI^+) *m/z* calcd for $C_{32}H_{32}N_2O_2$ 476.2464, found 476.2445. ^{3}C NMR (125 MHz, $CDCl_3$) δ 164.2 (major), 164.1 (minor), 152.1 (major), 151.9 (minor), 133.7 (minor), 133.6 (major), 132.1 (minor), 131.9 (major), 130.7 (minor), 130.5 (major), 129.2 (minor), 129.1 (major), 128.1 (major), 128.1 (major), 128.0 (minor), 127.8 (minor), 127.7 (major), 127.7 (minor), 126.8 (minor), 126.8 (major), 125.9 (major), 125.7 (major), 125.7 (minor), 125.4 (minor), 125.3 (minor), 125.1 (major), 124.8 (major), 124.7 (minor), 122.5 (major), 122.4 (minor), 111.8 (major), 111.8 (minor), 111.7 (major), 111.5 (minor), 77.6 (minor), 77.5 (major), 50.2 (major), 50.0 (minor), 41.6 (minor), 41.5 (major), 39.5 (minor), 39.2 (major), 36.8 (major), 36.0 (minor), 34.3 (major), 34.3 (minor), 33.5 (minor), 32.7 (major), 31.4 (major), 31.2 (major), 30.2 (minor), 26.2 (minor), 26.0 (major), 22.4 (minor), 21.7 (major), 21.0 (major), 13.9 (major), 13.9 (minor) (2 minor alkyl signals lack due to overlap).

8-Phenylmenthyl *trans*-2,2-dicyano-3-butylcyclopropanecarboxylate (5f)

Diastereomeric mixture, colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.23 (m, major 5H + minor 4H), 7.12 (t, *J* = 7.0 Hz, 1H, minor), 4.92 (dt, *J* = 4.5, 11.0 Hz, 1H, major), 4.87 (dt, *J* = 4.5, 11.0 Hz, 1H, minor), 2.22-2.14 (m, 1H), 2.00 (dq, *J* = 13.7, 3.7 Hz, 1H, major), 1.96 (dq, *J* = 13.7, 3.7 Hz, 1H, minor), 1.93-1.85 (m, 1H), 1.84-1.79 (m, 1H, major), 1.76-1.71 (m, 1H), 1.69-1.65 (m, 1H, minor), 1.37 (d, *J* = 7.6 Hz, 1H, major), 1.56-1.18 (m, 8H+minor 1H), 1.31 (s, 3H, major), 1.30 (s, 3H, minor), 1.21 (s, 3H, minor), 1.20 (s, 3H, major), 1.09-0.87 (m, 3H), 0.94-0.85 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5 (major), 164.2 (minor), 152.1 (minor), 152.0 (major), 128.0 (major), 127.9 (minor), 125.6 (major), 125.4 (minor), 125.2 (major), 125.0 (minor), 112.5 (major), 112.4 (minor), 111.8 (both), 76.9 (major), 76.9 (minor), 50.2 (major), 50.1 (minor), 41.4 (major), 39.3 (minor), 39.2 (major), 35.4 (minor), 34.7 (major), 34.5 (major), 34.3 (major), 33.9 (minor), 31.3 (major), 30.8 (major), 30.1 (minor), 29.8 (minor), 29.7 (major), 29.6 (minor), 28.4 (major), 28.3 (minor), 26.0 (minor), 26.0 (major), 22.2 (minor), 22.1 (minor), 21.9 (major), 21.7 (major), 21.6 (minor), 21.3 (major), 13.8 (minor), 13.7 (major), 11.6 (major), 10.4 (minor). HRMS (EI^+) calcd for $C_{26}H_{34}N_2O_2$ 406.2620, found 406.2611.

8-Phenylmenthyl *trans*-2,2-dicyano-3-(2-methylpropyl)cyclopropanecarboxylate (5g)

Diastereomeric mixture, colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.25 (m, major 5H + minor 4H), 7.12 (t, *J* = 7.0 Hz, 1H, minor), 4.93 (dt, *J* = 4.6, 10.7 Hz, 1H, major), 4.87 (dt, *J* = 4.6, 11.0 Hz, 1H, minor), 2.23-2.14 (m, 1H), 2.02-1.98 (m, 1H), 1.94-1.69 (m, 3H), 1.57-1.45 (m, 2H), 1.32 (s, 3H, major), 1.30 (s, 3H, minor), 1.21 (s, 3H), 1.35-1.16 (m, 3H), 1.04 (d, *J* = 6.7 Hz, 3H, minor), 1.03 (d, *J* = 6.7 Hz, 3H, minor), 0.94 (d, *J* = 6.7 Hz, 3H, major), 0.91 (d, *J* = 6.7 Hz, 3H), 0.90 (d, *J* = 6.7 Hz, 3H, major), 1..10-0.90 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5 (minor), 164.2 (major), 152.1 (minor), 152.0

(major), 128.0 (major), 127.9 (minor), 125.6 (minor), 125.4 (major), 125.2 (major), 125.0 (minor), 112.5 (major), 112.4 (minor), 111.8 (both), 76.9 (major), 76.9 (minor), 50.2 (major), 50.1 (minor), 41.5 (minor), 41.4 (major), 39.4 (minor), 39.2 (major), 35.4 (minor), 34.7 (major), 34.5 (major), 34.3 (major), 33.9 (minor), 31.3 (major), 30.8 (major), 30.1 (minor), 29.8 (minor), 29.7 (major), 28.4 (major), 28.3 (minor), 26.0 (major), 26.0 (minor), 22.1 (minor), 22.0 (minor), 21.9 (major), 21.7 (major), 21.6 (minor), 21.3 (major), 13.8 (minor), 13.7 (major), 11.6 (major), 10.5 (minor). HRMS (EI^+) calcd for $C_{26}H_{34}N_2O_2$ 406.2620, found 406.2628.

8-Phenylmenthyl *trans*-2,2-dicyano-3-(2-methylethyl)cyclopropanecarboxylate (5h)

Diastereomeric mixture, colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.25 (m, major 5H + minor 4H), 7.16-7.12 (m, 1H, minor), 4.92 (dt, *J* = 4.5, 11.0 Hz, 1H, major), 4.89 (dt, *J* = 4.5, 11.0 Hz, 1H, minor), 2.21-2.13 (m, 1H), 2.03 (dd, *J* = 7.9, 10.7 Hz, 1H, minor), 1.99 (dq, *J* = 13.7, 3.7 Hz, 1H, major), 1.94-1.90 (m, 1H, minor), 1.86 (dq, *J* = 13.7, 3.7 Hz, 1H, minor), 1.81 (dd, *J* = 7.9, 10.7 Hz, 1H, major), 1.82-1.78 (m, 1H, major), 1.77-1.68 (m, 1H), 1.53-1.43 (m, 1H), 1.49 (d, *J* = 7.9, 1H, minor), 1.38 (d, *J* = 7.9, 1H, major), 1.32 (s, 3H, major), 1.30 (s, 3H, minor), 1.29-1.23 (m, 1H), 1.22 (s, 3H, minor), 1.21 (s, 3H, major), 1.20-1.15 (m, 2H), 1.13 (d, *J* = 6.5 Hz, 3H), 0.98 (d, *J* = 6.5 Hz, 3H), 1.08-0.93 (m,1H), 0.91 (d, *J* = 6.5 Hz, 3H, minor), 0.90 (d, *J* = 6.5 Hz, 3H, major). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5 (major)164.2 (minor), 151.9 (major), 151.8 (minor), 128.1 (major), 128.0 (minor), 125.7 (major), 125.3 (minor), 125.2 (major), 125.1 (minor), 112.5 (major), 112.4 (minor), 111.7 (minor), 111.7 (major), 77.4 (minor), 76.8 (major), 50.3 (major), 50.0 (minor), 41.7 (major), 41.4 (major), 40.7 (minor), 39.5 (minor), 39.2 (major), 35.5 (minor), 34.3 (major), 34.2 (major), 31.3 (major), 30.5 (minor), 29.9 (major), 29.7 (major), 29.2 (minor), 26.2 (minor), 26.0 (major), 23.4 (minor), 21.7 (major), 21.6 (major), 21.6 (minor), 21.0 (minor), 20.9 (major), 20.7 (minor), 20.6 (major), 11.6 (major), 10.4 (minor). HRMS (EI^+) calcd for $C_{25}H_{32}N_2O_2$ 392.2464, found 392.2487.

8-Phenylmenthyl *trans*-2,2-dicyano-3-(1,1-dimethylethyl)cyclopropanecarboxylate (5i)

Diastereomeric mixture, colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.28 (m, major 4H + minor 5H), 7.16-7.12 (m, 1H, major), 4.88 (dt, *J* = 4.5, 11.0, 1H), 2.22-2.16 (m, 1H), 2.12 (d, *J* = 9.0 Hz, 1H, major), 1.94 (d, *J* = 9.0 Hz, 1H, minor), 1.99-1.86 (m, 2H), 1.75-1.70 (m, 1H), 1.65 (d, *J* = 9.0 Hz, 1H, major), 1.54 (d, *J* = 9.0 Hz, 1H, minor), 1.52-1.44 (m, 1H), 1.32 (s, 3H, minor), 1.30 (s, 3H, major), 1.22 (s, 3H, minor), 1.21 (s, 3H, major), 1.24-1.15 (m, 1H), 1.12-1.03 (m, 1H), 1.07 (s, 9H, major), 1.00 (s, 9H, minor), 0.99-0.94 (m, 1H), 0.90 (d, *J* = 6.5 Hz, 3H, major), 0.89 (d, *J* = 6.5 Hz, 3H, minor). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9 (minor), 164.4 (major), 152.0 (major), 151.9 (minor), 128.2 (minor), 128.1 (major), 125.7 (minor), 125.3 (major), 125.2 (minor), 125.1 (major), 112.9 (minor), 112.9 (major), 112.3

(major), 112.2 (minor), 77.1 (major), 76.9 (minor), 50.4 (minor), 49.9 (major), 45.5 (minor), 44.4 (major), 41.4 (major), 41.3 (minor), 39.4 (major), 39.2 (minor), 34.3 (major), 32.8 (major), 31.3 (major), 31.3 (minor), 30.3 (minor), 30.2 (minor), 30.2 (major), 29.9 (major), 27.8 (major), 27.8 (minor), 26.1 (major), 26.1 (minor), 22.5 (major), 21.9 (minor), 21.7 (minor), 21.6 (major), 9.0 (minor), 7.9 (major). HRMS (EI^+) calcd for $C_{26}H_{34}N_2O_2$ 406.2620, found 406.2593.

8-Phenylmenthyl *trans*-2,2-dicyano-3-(1-adamanthyl)cyclopropanecarboxylate (5j)

Diastereomeric mixture, colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43-7.25 (m, 4H), 7.20-7.12 (m, 1H), 4.88 (td, *J* = 10.7, 4.3 Hz, 1H), 2.23-2.13 (m, 1H), 2.10-1.99 (m, 3H), 1.96 (d, *J* = 8.8 Hz, 1H, major), 1.80 (d, *J* = 8.8 Hz, 1H, minor), 1.94-1.86 (m, 1H), 1.80-1.66 (m, 9H), 1.71 (d, *J* = 8.8 Hz, 1H, major), 1.59 (d, *J* = 8.8 Hz, 1H, minor), 1.66-1.59 (m, 1H), 1.59-1.52 (m, 4H), 1.51-1.44 (m, 1H), 1.32 (s, 3H, minor), 1.31 (s, 3H, major), 1.26-1.14 (m, 1H), 1.22 (s, 3H, minor), 1.21 (s, 3H, major), 1.07 (ddd, *J* = 13.1, 12.2, 10.7 Hz, 1H), 0.96 (ddd, *J* = 13.1, 11.9, 3.4 Hz, 1H), 0.91 (d, *J* = 6.7 Hz, 3H, major), 0.90 (d, *J* = 6.7 Hz, 3H, minor); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0 (minor), 164.6 (major), 151.9 (major), 151.8 (minor), 128.1 (major), 128.1 (minor), 125.6 (minor), 125.3 (major), 125.2 (minor), 125.2 (major), 113.2 (minor), 113.2 (major), 112.5 (major), 112.4 (minor), 77.3 (major), 76.8 (minor), 50.5 (minor), 49.6 (major), 45.7 (minor), 44.6 (major), 41.4 (major), 41.3 (minor), 40.2 (minor), 40.1 (major), 39.4 (major), 39.3 (minor), 36.3 (major), 36.2 (minor), 34.4 (minor), 34.3 (major), 31.9 (minor), 31.9 (major), 31.4 (major), 31.3 (major), 30.1 (minor), 29.8 (minor), 29.7 (minor), 28.0 (major), 28.0 (major), 26.1 (major), 26.1 (minor), 22.8 (major), 22.1 (minor), 21.7 (minor), 21.6 (major), 7.9 (minor), 6.8 (major) (1 minor alkyl signal lacks due to overlap). HRMS (EI^+) *m/z* calcd for $C_{32}H_{40}N_2O_2$ 484.3090, found 484.3090.

X-Ray crystallographic analysis of major 5c

Diffraction data for major **5c** was collected on a Mac Science DIP2030 imaging plate instrument equipped with graphite-monochromated Mo *K*α radiation (λ = 0.71073 Å). Unit cell parameters were determined by autoindexing several images in each data set separately with the DENZO program. For each data set, rotation images were collected in 3° increments with a total rotation of 180 ° about ϕ. Data were processed by using the SCALEPACK program. The structures were solved by a direct method and refined by full-matrix least-squares methods with the TeXsan program. All non-hydrogen atoms were refined with anisotropic thermal parameters and all hydrogen atoms were included in the refinement at calculated positions (C-H = 1.0 Å) riding on their carrier atom with isotropic thermal parameters. The solvent molecule CH_2Cl_2 was calculated as a disordered molecule. Crystallographic data for major-**5c**: colorless plates; $C_{27}H_{29}N_3O_2$+CH_2Cl_2; mol wt. 512.48; orthorhombic, $P2_12_12_1$, a= 10.5260(5) Å, b= 12.1580(5) Å, c = 22.1240(7) Å, V = 2831.3(2) Å^3, Z=4, D_{calc}=1.202 g cm^{-3}, 2028 reflections used with

$I>2(I)$ out of 3704, $R = 0.087$, $R_w = 0.134$, GOF = 1.38, max shift in final cycle, 0.05, final diff map, max, 0.29 e $Å^{-3}$. Crystallographic data for the X-Ray structure of major-**5c** has been deposited with the Cambridge Crystallographic Data Centre as CCDC-279681. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB12 1EZ, UK (fax: +44-(0)1223-336033 or email: deposit@ccdc.cam.ac.uk).

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