Substituted Cyclopropylamines from Pyridinium Ylide: Complexes of Pentacarbonyl **Tungsten and Enamines**

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Abstract: Enamines derived from cyclic ketones react very easily with a series of pyridinium ylide complexes of tungsten pentacarbonyl (CO)₅W⁻–C(R)(H) Py⁺ to give either at room temperature (for R = Ph) or at 40°C (for R = alkyl) substituted cyclopropylamines as mixtures of stereoisomers.

Key words: enamines, cyclopropanation, aminocyclopropanes, tungsten ylides

Cyclopropanes are important building blocks in organic synthesis; those bearing an amino group are part of a variety of biologically active compounds or their precusors.¹ Whereas a few classical entries in the synthesis of cyclopropylamines already existed,²⁻⁶ new access to such structures appeared recently in the literature.^{7,8}

The purpose of this paper is to describe a new approach to highly substituted aminocyclopropanes which broadens the range of accessible derivatives of this family of compounds. This new approach relies on the reaction of shelfstable pyridinium ylide complexes of the general structure $(CO)_5W-C(R)(H)$ Pyridine⁺(1), the preparation of which from Fischer-type alkoxycarbene complexes of tungsten and dihydropyridines has recently been outlined.⁹ These N-ylide complexes result from the stabilization of alkylidene complexes of W(0) by pyridine. Although they react only sluggishly with simple olefins to give cyclopropanes, satisfactory results were observed in the case of more nucleophilic olefins such as enol ethers.⁹ We surmised that enamines might be the substrates of choice for such cyclopropanation reactions due to the nucleophilic character of their double bond. And this was indeed the case. Thus, when a slight excess of an enamine in dichloromethane was added to a solution of the benzylidene ylide complex in the same solvent, a fast consumption of the ylide was observed by TLC. That the reaction took place instantaneously was confirmed by ¹H NMR spectroscopy: in the case of the enamine **3a**, derived from cyclopentanone and morpholine, the formation of a 1:1 mixture of two isomeric cyclopropylamines was observed. This was also the case for the enamine 4b derived from cyclopentanone and pyrrolidine (Table 1).

In the first experiment leading to **7a.b**, separation of the two isomers was easily achieved by column chromatography on silica gel, the exo-isomer obtained in 48% yield being the less polar compound, whereas the more polar endo-isomer was isolated in 30% yield. Their geometry was assessed on the grounds of the coupling constants between the two vicinal hydrogens on the cyclopropane, which is higher for the endo-isomer (cis-relationship) than



R= Ph, X= CH_2CH_2 , n= 1 (5a, b); n= 2 (6a, b) $X = CH_2O$, n = 1 (7a, b); n = 2 (8a, b) $X = CH_2$, n = 1 (9b); n = 2 (10a, b) R= Me, X= CH₂CH₂, n= 1 (11a, b); n= 2 (12a)

 $X = CH_2O$, n = 1 (13a, b) $X = CH_2$, n = 1 (14a)

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R=(CH_2)_3Ph, X=CH_2CH_2, n=1 (15a, b)
               X = CH_2O, n = 1 (16a, b)
X = CH_2, n = 1 (17a)
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R= $(CH_2)_4CH(OMe)_2$, X= CH₂, n= 1 (18)

Scheme 1

for the exo-isomer (trans-relationship). Application of the same separation technique to the cyclopropylamines obtained from enamine 4a led to an unexpected result: only one cyclopropylamine, the endo-isomer could be isolated in 45% yield. The fate of the exo-isomer could, however, be established since a second product, the known 2-benzylcyclopentanone was also isolated in 46% yield.¹⁰ Thus a rearrangement of the exo-isomer, induced by silica gel, followed by hydrolysis, had taken place. A similar behaviour was observed for the cyclopropylamines derived from the enamine of cyclohexanone. It led, after chromatography to a mixture of cyclopropylamines (21% exo, 41% endo) together with 21% of the rearranged/hydrolyzed product, 2-benzylcyclohexanone:¹¹ thus only partial hydrolysis/rearrangement of the exo-isomer took place. No such rearrangements were however observed in the cases of the cyclopropylamines derived from the pyridinium ylides **1b** and **1c** $[R = Me, (CH_2)_3Ph]$ which were easily purified by chromatography on silica gel.

As far as the mechanism of this new cyclopropanation reaction is concerned, it is likely that the first step of the cyclopropanation is a $S_N 2$ type reaction with the concerted formation of a carbon-carbon bond and displacement of

Table 1. Reactions Between Ylide Complexes and Enamines

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Starting	Products	R	n	Х	Reaction Conditions		Yield	exo: endo Patio ^b
materials					T (°C)	t (min)	(70)	Kano
1a + 2a	5a, 5b	Ph	1	CH ₂ CH ₂	20	5	70	1:1.9
1a + 2b	6a, 6b	Ph	2	$CH_{2}CH_{2}$	20	5	50	1:1.5
1a + 3a	7a, 7b	Ph	1	CH ₂ O	20	5	80	1.6:1
1a + 3b	8a, 8b	Ph	2	CH_2O	20	5	50	1.5:1
1a + 4a	9b	Ph	1	CH_2	20	5	91	$0:1^{c}$
1a + 4b	10a, 10b	Ph	2	CH_2	20	5	83	1:2
1b + 2a	11a, 11b	Me	1	CH_2CH_2	40	240	38	4.9:1
1b + 2b	12a	Me	2	CH_2CH_2	40	360	16	$1:0^{c}$
1b + 3a	13a, 13b	Me	1	CH_2O	40	420	56	1.6 : 1
1b + 4a	14a	Me	1	CH_2	40	90	32	$1:0^{c}$
1c + 2a	15a, 15b	(CH ₂) ₃ Ph	1	CH_2CH_2	40	210	72	1:1
1c + 3a	16a, 16b	$(CH_2)_3Ph$	1	CH_2O	40	300	67	3.8:1
1c + 4a	17a	$(CH_2)_3Ph$	1	CH_2	40	120	66	1:0
1d + 4a	18	$(CH_2)_4 CH(OMe)_2$	1	CH_2	40	420	67	1:0

^a All reactions were carried out in CH₂Cl₂.

^b Ratio of isolated products.

^c Detected by NMR of the reaction mixture.

pyridine by the interaction of the nucleophilic β -carbon of the enamine double bond with the quaternary carbon atom of the ylide complex (Scheme 2). Interaction of the negatively charged metal with the carbon of the iminium would then lead to two diastereomeric tungstacyclobutanes. Reductive elimination of the metal might finally give the two isomeric cyclopropylamines. The remarkable point is the ease by which the transfer of the alkylidene group to the double bond takes place giving in high to medium yields a large range of substituted cyclopropylamines. This contrasts strongly with the observed reaction of alkoxycarbene complexes of the Fischer-type which led only in very modest yields and under rather harsh conditions to mixtures of cyclopropylamines and ring-opened products.¹²



Although polymerization rather than cyclopropanation is observed in the case of enamines derived from linear ketones, no limitations as far as the nature of the R group in the ylide complexes is concerned have been observed up to now: support to this comes from the transformation of



1d $[R = (CH_2)_4 CH(OMe)_2]$ into the cyclopropylamine **18** in 67% yield.

All reactions were carried out under Ar in predried glassware. Ylide complexes **1a**, **1b** and **1c** were prepared according to the literature procedure.⁹ CH₂Cl₂ was dried by distillation over P₂O₅ and was stored and transferred under Ar. Enamines were prepared from commercially available ketones and amines according to the literature procedures.^{13,14} Column chromatography was performed with Merck silica gel (70–230 mesh) using various ratios of light petroleum ether CH₂Cl₂ and light petroleum ether/Et₂O as eluents. Instrumental analyses: NMR spectra were recorded on Bruker AC200 or ARX400 instruments, in CDCl₃ or C₆D₆. Chemical shifts (δ) are listed in ppm relative to TMS and coupling constants (*J*) are given in Hertz (Table 2).

Aminocyclopropanes 5–18; General Procedure:

Enamine 2–4 (2 mmol) was added to a solution of the ylide complex 1 (0.5 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred until complete consumption of the ylide complex (temperatures and time of reaction are gathered in Table 1). The solvent was evaporated under vacuum and the residue was transferred onto a column of silica gel. Elution with petroleum ether/ CH_2Cl_2 mixtures gave complex W(CO)₅Py and with petroleum ether/ Et_2O mixtures the aminocyclopropanes.

1-(6-Phenylbicyclo[3.1.0]hex-1-yl)piperidines:

5a: *exo*-isomer; $R_f 0.92$ (EtOAc/cyclohexane, 20:80); light petroleum ether/Et₂O (98:2) as eluent; yield: 24%.

5b: *endo*-isomer; R_f 0.44; light petroleum ether/Et₂O (90:10) as eluent; yield: 46%.

HRMS: *m/z* Obsd (Calcd) for C₁₇H₂₃N⁺: 241.1830 (241.1829).

1-(7-Phenylbicyclo[4.1.0]hept-1-yl)piperidines:

6a: *exo*-isomer; $R_f 0.92$ (EtOAc/cyclohexane, 25:75); light petroleum ether/Et₂O (98:2) as eluent; yield: 20%.

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Table 2. NMR Data of Products 5–18

Prod- uct	¹ H NMR ^a δ, J (Hz)	δ^{13} C NMR ^a
5a	1.18–1.31 (m, 7 H, H-4', 3 CH ₂), 1.52 (dd, 1 H, <i>J</i> = 4.6, 4.6, H- 2), 1.59–1.68 (m, 3 H, H-4, H-5', H-3'), 1.75 (m, 1 H, H-5), 1.82 (d, 1 H, <i>J</i> = 4.6, H-6), 1.93 (m, 1 H, H-3), 2.27–2.36 (m, 4 H, 2 NCH ₂), 7.03–7.20 (m, 5 H, Ph)	21.5 (C-4), 23.3 (C-3), 24.8 (CH ₂), 26.3 (2 CH ₂), 27.5 (C-5), 31.7 (C-6), 33.9 (C-2), 50.7 (2 NCH ₂), 60.8 (C-1), 124.6, 126.9, 128.2, 139.9 (Ph)
5b	0.07 (m, 1 H, H-4'), 1.33 (m, 1 H, H-4), 1.47 (m, 2 H, CH ₂), 1.62 (m, 6 H, H-3', 2 CH ₂ , H-5'), 1.69 (m, 1 H, H-2), 1.91 (m, 1 H, H-3), 2.02 (m, 1 H, H-5), 2.28 (d, 1 H, <i>J</i> = 9.0, H-6), 2.67 (m, 2 H, CHHNCHH), 2.85 (m, 2 H, CHHNCHH), 7.21–7.32 (m, 5 H, Ph)	20.9 (C-5), 22.7 (C-4), 24.7 (CH ₂), 25.3 (C-3), 26.4 (2 CH ₂), 30.3 (C-2), 33.4 (C-6), 51.2 (2 NCH ₂), 59.2 (C-1), 125.9, 128.3, 128.5, 138.1 (Ph)
6a	1.20–1.45 (m, 11 H, 3CH ₂ , H-2, H-3, H-3', H-5, H-5'), 1.54– 1.62 (m, 1H, H-6'), 1.70–1.80 (m and d, 2 H, $J = 6.6$, H-7, H-4'), 1.95 (m, 1 H, H-4), 2.11 (m, 1 H, H-6), 2.25 and 2.46 (m, 2 H each, CH ₂ NCH ₂), 7.11–7.36 (m, 5 H, Ph)	21.4 (C-3), 22.6 (C-4, C-5), 24.2 (C-6), 24.9 (CH ₂), 26.2 (2 CH ₂), 29.2 (C-2), 36.8 (C-7), 49.5 (CH ₂ NCH ₂), 51.2 (C-1), 124.7, 127.0, 127.9, 140.6 (Ph)
6b	0.46 (m, 1 H, H-4'), 0.97 (m, 2 H, H-2, H-5'), 1.14 (m, 1 H, H-4), 1.30–1.41 (m, 2 H, H-5, H-6'), 1.46 (m, 2 H, CH ₂), 1.55–1.65 (m, 4 H, 2 CH ₂), 1.86–1.96 (m, 2 H, H-3, H-3'), 2.04 (m, 1 H, H-6), 2.10 (d, 1 H, $J = 8.7$, H-7), 2.71 (m, 4 H, 2 NCH ₂), 7.18–7.38 (m, 5 H, Ph)	18.1 (C-6), 21.4 (C-3), 21.8 (C-4), 22.7 (C-5), 23.9 (C-2), 24.7 (CH ₂), 26.4 (2 CH ₂), 32.7 (C-7), 46.8 (C-1), 49.4 (2 NCH ₂), 125.8, 128.2, 131.0, 138.3 (Ph)
7a	1.41 (m, 1 H, H-4'), 1.69 (dd, 1 H, $J = 4.3, 4.3, H-2$), 1.74–1.82 (m, 3 H, H-4, H-5', H-4), 1.87 (m, 1 H, H-5), 1.98 (d, 1 H, $J = 4.3, H-6$), 2.05 (m, 1 H, H-3'), 2.47–2.52 (m, 4 H, 2 NCH ₂), 3.43–3.55 (m, 4 H, 2 OCH ₂), 7.13–7.28 (m, 5 H, Ph)	23.5 (C-3), 28.5 (C-4), 29.3 (C-5), 31.6 (C-2), 33.1 (C-6), 49.6 (2 NCH ₂), 60.1 (C-1), 67.3 (2 OCH ₂), 121.4, 125.0, 127.1, 128.4 (Ph)
7b	0.08 (m, 1 H, H-4'), 1.36 (m, 1 H, H-4), 1.60–1.68 (m, 2 H, H-3', H-5'), 1.70 (m, 1 H, H-2), 1.91 (m, 1 H, H-5), 2.01 (m, 1 H, H-3), 2.28 (d, 1 H, $J = 8.7$, H-6), 2.70–2.75 (m, 2 H, CHHNCHH), 2.86–2.91 (m, 2 H, CHHNCHH), 3.74 (m, 4 H, OCH ₂), 7.21–7.42 (m, 5 H, Ph)	21.2 (C-4), 22.6 (C-3), 25.3 (C-5), 29.9 (C-6), 33.3 (C-2), 50.1 (2 NCH ₂), 59.1 (C-1), 67.5 (2 OCH ₂), 126.0, 128.3, 128.9, 137.6 (Ph)
8a	1.21–1.49 (m, 5 H, H-2, H-3, H-3', H-5, H-5'), 1.64 (m, 1 H, H-6'), 1.74 (m, 1 H, H-4'), 1.80 (d, 1 H, $J = 6.4$, H-7), 1.95 (m, 1 H, H-4), 2.13 (m, 1 H, H-6), 2.53 (m, 4 H, 2 NCH ₂), 3.49 (m, 4 H, 2 OCH ₂), 7.12–7.34 (m, 5 H, Ph)	21.3 (C-3), 22.4 (C-4), 22.5 (C-5), 24.1 (C-6), 28.2 (C-2), 36.5 (C-7), 48.4 (2 NCH ₂), 50.3 (C-1), 67.3 (2 OCH ₂), 125.1, 127.2, 128.0, 129.9 (Ph)
8b	0.37 (m, 1 H, H-4'), 0.82–0.94 (m, 2 H, H-5, H-5'), 1.04 (m, 1 H, H-4), 1.26–1.38 (m, 2 H, H-2, H-6'), 1.85–1.75 (m, 2 H, H-3, H-3'), 1.92–1.99 (m, 2 H, H-6 and inside d, $J = 9.6$, H-7), 2.67 (m, 4 H, 2 NCH ₂), 3.62 (m, 4 H, 2 OCH ₂), 7.10–7.22 (m, 5 H, Ph)	18.8 (C-6), 21.8 (C-3), 22.3 (C-4), 23.1 (C-5), 24.1 (C-2), 32.9 (C-7), 46.9 (C-1), 49.1 (2 NCH ₂), 68.0 (2 OCH ₂), 126.6, 128.9, 135.6, 138.4 (Ph)
9b	0.10 (m, 1 H, H-4'), 1.34 (m, 1 H, H-4), 1.60–1.75 (m, 3 H, H-2, H-3', H-5'), 1.84 (m, 4 H, 2 CH ₂), 1.84–2.02 (m, 2 H, H-3, H-5), 2.35 (d, 1 H, $J = 9.1$ Hz, H-6), 2.78 (m, 2 H, CHHNCHH), 2.87 (m, 2 H, CHHNCHH), 7.20–7.35 (m, 5 H, Ph)	22.5 (C-4), 22.7 (C-3), 23.9 (CH ₂), 25.4 (C-5), 29.5 (C-2), 31.0 (C-6), 49.6 (2 NCH ₂), 55.0 (C-1), 125.9, 128.2, 129.0, 130.0 (Ph)
10a	$\begin{array}{l} 1.15-1.55 \ (m, 7 \ H, \ H-2, \ H-3', \ H-3, \ H-5', \ H-5), \ 1.60-1.80 \ (m, 3 \ H, \ H-4', \ CH_2), \ 1.74 \ (d, 1 \ H, \ J=6.2, \ H-7), \ 1.95 \ (m, 1 \ H, \ H-6'), \\ 2.00-2.10 \ (m, 2 \ H, \ H-4, \ H-6), \ 2.30 \ (m, 2 \ H, \ CHHNCHH), \ 2.57 \ (m, 2 \ H, \ CHHNCHH), \ 7.00-7.25 \ (m, 5 \ H, \ Ph) \end{array}$	20.0 (C-3), 21.7 (C-4), 21.8 (C-5), 22.9 (C-6), 23.0 (2 CH ₂), 27.4 (C-2), 35.3 (C-7), 44.9 (C-1), 45.9 (2 NCH ₂), 123.5, 126.0, 127.3, 139.8 (Ph)
10b	0.38 (m, 1 H, H-4'), 0.93 (m, 2 H, H-5', H-5), 1.08 (m, 1 H, H-4), 1.37 (m, 2 H, H-2, H-6'), 2.73 (m, 4 H, 2 CH ₂), 1.80–1.92 (m, 3 H, H-3', H-3, H-6), 2.05 (d, 1 H, $J = 10.0$, H-7), 2.90 (m, 4 H, 2 NCH ₂), 7.12–7.25 (m, 5 H, Ph)	19.4 (C-6), 21.4 (C-3), 22.0 (C-4), 23.2 (C-2, C-5), 24.1 (CH ₂), 31.4 (C-7), 41.8 (C-1), 48.1 (2 NCH ₂), 126.2, 128.5, 131.5, 138.5 (Ph)
11a	$\begin{array}{l} 0.86 \ (m, 1 \ H, \ H{-}6), \ 0.91 \ (m, 1 \ H, \ H{-}2), \ 1.23 \ (m, 1 \ H, \ H{-}4'), \ 1.39 \\ (d, 3 \ H, \ J = 6.0, \ CH_3), \ 1.50 \ (m, 2 \ H, \ CH_2), \ 1.58 \ (m, 1 \ H, \ H{-}4), \\ 1.64 \ (m, 1 \ H, \ H{-}3'), \ 1.66 \ (m, 4 \ H, \ 2 \ CH_2), \ 1.73 \ (m, 1 \ H, \ H{-}5'), \\ 1.79 \ (m, 1 \ H, \ H{-}3), \ 1.97 \ (m, 1 \ H, \ H{-}5), \ 2.57 \ (m, 2 \ H, \\ CHHNCHH), \ 2.72 \ (m, 2 \ H, \ CHHNCHH) \end{array}$	11.5 (CH ₃), 20.5 (C-6), 22.1 (C-4), 22.6 (C-5), 25.0 (CH ₂), 26.7 (2 CH ₂), 27.1 (C-3), 31.3 (C-2), 51.3 (2 NCH ₂), 57.2 (C-1)

Prod- uct	1 H NMR ^a δ , J (Hz)	δ^{13} C NMR ^a
11b	0.90 (d, 3 H, $J = 6.8$, CH ₃), 1.19 (m, 1 H, H-6), 1.25–1.95 (m, 6 H, H-3', H-3, H-4', H-4, H-5', H-5), 1.31 (m, 2 H, CH ₂), 1.40 (m, 1 H, H-2), 1.52 (m, 4 H, 2 CH ₂), 2.40 (m, 2 H, CHHNCHH), 2.51 (m, 2 H, CHHNCHH)	8.9 (CH ₃), 25.2 (C-4, C-6), 25.3 (C-5), 25.7 (CH ₂), 27.3 (2 CH ₂), 27.6 (C-3), 30.4 (C-2), 52.0 (2 NCH ₂), 60.1 (C-1)
12a	$\begin{array}{l} 0.39\ (\mathrm{m},1\ \mathrm{H},\mathrm{H}\text{-}2), 0.45\ (\mathrm{m},1\ \mathrm{H},\mathrm{H}\text{-}7), 1.02\ (\mathrm{m},1\ \mathrm{H},\mathrm{H}\text{-}4'), 1.09\\ (\mathrm{d},3\ \mathrm{H},J=5.6,\ \mathrm{CH}_3), 1.13\ (\mathrm{m},1\ \mathrm{H},\mathrm{H}\text{-}5'), 1.20\ (\mathrm{m},1\ \mathrm{H},\mathrm{H}\text{-}5), 1.24\ (\mathrm{CH}_2), 1.28\ (\mathrm{m},1\ \mathrm{H},\mathrm{H}\text{-}4), 1.32\ (\mathrm{m},1\ \mathrm{H},\mathrm{H}\text{-}6'), 1.45\ (\mathrm{m},4\ \mathrm{H},2\ \mathrm{CH}_2), 1.58\ (\mathrm{m},1\ \mathrm{H},\mathrm{H}\text{-}3'), 1.76\ (\mathrm{m},1\ \mathrm{H},\mathrm{H}\text{-}3), 1.99\ (\mathrm{m},1\ \mathrm{H},\mathrm{H}\text{-}6), 2.45\ (\mathrm{m},4\ \mathrm{H},2\ \mathrm{NCH}_2) \end{array}$	13.0 (CH ₃), 22.4 (C-4), 23.0 (C-6), 23.3 (C-5), 24.8 (C-3), 25.6 (CH ₂), 26.0 (C-7), 27.2 (2 CH ₂), 27.3 (C-2), 50.6 (2 NCH ₂), 53.3 (C-1)
13a	0.73 (m, 1 H, H-2), 0.76 (m, 1 H, H-6), 1.07 (d, 3 H, $J = 6.0$, CH ₃), 1.14 (m, 1 H, H-4'), 1.51 (m, 1 H, H-5'), 1.59 (m, 1 H, H-3'), 1.64 (m, 1 H, H-3), 1.67 (m, 1 H, H-4), 1.86 (m, 1 H, H-5), 2.49 (dt, 2 H, $J = 11.2$, 4.6, CHHNCHH), 2.64 (dt, 2 H, $J = 11.2$, 4.6, CHHNCHH), 3.63 (t, 4H, $J = 4.6$, 2 OCH ₂)	11.56 (CH ₃), 20.3 (C-6), 22.0 (C-4), 22.8 (C-5), 27.0 (C-3), 30.8 (C-2), 50.2 (2 NCH ₂), 56.6 (C-1), 67.6 (2 OCH ₂)
13b	$\begin{array}{l} 0.93 \ (\mathrm{d}, \ 3\ \mathrm{H}, \ J=6.8, \ \mathrm{CH}_3), \ 1.25 \ (\mathrm{m}, \ 1\ \mathrm{H}, \ \mathrm{H-2}), \ 1.32 \ (\mathrm{m}, \ 1\ \mathrm{H}, \ \mathrm{H-4}'), \ 1.42 \ (\mathrm{m}, \ 1\ \mathrm{H}, \ \mathrm{H-5}'), \ 1.45 \ (\mathrm{m}, \ 1\ \mathrm{H}, \ \mathrm{H-6}'), \ 1.70 \ (\mathrm{m}, \ 1\ \mathrm{H}, \ \mathrm{H-3}'), \ 1.75 \ (\mathrm{m}, \ 1\ \mathrm{H}, \ \mathrm{H-4}), \ 1.90 \ (\mathrm{m}, \ 1\ \mathrm{H}, \ \mathrm{H-5}), \ 2.04 \ (\mathrm{m}, \ 1\ \mathrm{H}, \ \mathrm{H-3}), \ 2.51 \ (\mathrm{dt}, \ 2\ \mathrm{H}, \ J=11.2, \ 4.6, \ CHHNCHH), \ 2.65 \ (\mathrm{dt}, \ 2\ \mathrm{H}, \ J=11.2, \ 4.6, \ CHHNCHH), \ 3.63 \ (\mathrm{t}, \ 4\ \mathrm{H}, \ J=4.6, \ 2\ \mathrm{OCH}_2) \end{array}$	7.8 (CH ₃), 20.0 (C-6), 23.9 (C-4), 24.4 (C-5), 26.3 (C-3), 28.8 (C-2), 49.9 (2 NCH ₂), 58.4 (C-1), 67.4 (2 OCH ₂)
14a	0.72 (m, 1 H, H-2), 0.79 (m, 1 H, H-6), 1.07 (d, 3 H, $J = 6.0$, CH ₃), 1.13 (m, 1 H, H-4'), 1.19 (m, 1 H, H-3'), 1.52 (m, 1 H, H-5'), 1.60 (m, 1 H, H-3), 1.70 (m, 4 H, 2 CH ₂), 1.79 (m, 1 H, H-5), 1.86 (m, 1 H, H-4), 2.57 (m, 2 H, CHHNCHH), 2.70 (m, 2 H, CHHNCHH)	11.8 (CH ₃), 20.3 (C-6), 22.0 (C-4), 22.3 (C-5), 24.4 (CH ₂), 27.1 (C-3), 31.2 (C-2), 49.2 (2 NCH ₂), 52.3 (C-1)
15a	0.67 (m, 1 H, H-6), 0.79 (m, 1 H, H-2), 1.10 (m, 1 H, H-4'), 1.36 (m, 2 H, CH ₂), 1.47 (m, 1 H, H-5'), 1.49 (m, 4 H, 2 CH ₂), 1.54 (m, 1 H, H-4), 1.58 (m, 2 H, CH ₂ -7), 1.64 (m, 1 H, H-3'), 1.72 (m, 1 H, H-3), 1.75 (m, 2 H, CH ₂ -8), 1.83 (m, 1 H, H-5), 2.42 (m, 2 H, CHHNCHH), 2.58 (m, 2 H, CHHNCHH), 2.61 (m, 2 H, CH ₂ -9), 7.15–7.28 (m, 5 H, Ph)	22.1 (C-4), 22.9 (C-5), 25.0 (CH ₂), 26.4 (C-7), 26.6 (2 CH ₂ , C-6), 27.2 (C-3), 30.1 (C-2), 32.1 (C-8), 36.3 (C-9), 51.3 (2 NCH ₂), 57.5 (C-1), 125.5, 128.2, 128.4, 143.3 (Ph)
15b	1.13 (m, 1 H, H-6), 1.22 (m, 2 H, CH_2 -7), 1.25 (m, 1 H, H-4'), 1.31 (m, 1 H, H-5'), 1.35 (m, 2 H, CH_2), 1.37 (m, 1 H, H-2), 1.39 (m, 1 H, H-3'), 1.50 (m, 4 H, 2 CH_2), 1.68 (m, 2 H, CH_2 -8), 1.70 (m, 1 H, H-4), 1.82 (m, 1 H, H-3), 1.95 (m, 1 H, H-5), 2.42 (m, 2 H, CH HNCHH), 2.55 (m, 2 H, CH_2 -9), 2.58 (m, 2 H, CH -HNCHH), 7.04–7.18 (m, 5 H, Ph)	20.1 (C-5), 23.4 (C-7), 24.4 (C-3), 24.9 (CH ₂), 26.6 (2 CH ₂), 27.1 (C-4), 29.8 (C-6), 32.1 (C-2), 32.4 (C-8), 36.1 (C-9), 50.4 (2 NCH ₂), 59.5 (C-1), 125.7, 128.3, 128.5, 142.7 (Ph)
16a	0.66 (dt, 1 H, $J = 8.4$, 4.2, H-6), 0.73 (t, 1 H, $J = 4.2$, H-2), 1.08 (m, 1 H, H-4), 1.36 (m, 1 H, H-7'), 1.42–1.63 (m, 7H, H-3, H-3', H-4, H-5', H-7, CH ₂ -8), 1.78 (td, $J = 11.5$, 8.5, H-5), 2.42 (dt, 2 H, $J = 11.5$, 4.6, CHHNCHH), 2.57 (m, 4 H, CHHNCHH, CH ₂ -9), 3.53 (t, 4 H, $J = 4.6$, OCH ₂), 7.07–7.23 (m, 5 H, Ph)	22.0 (C-4), 23.1 (C-5), 26.3 (C-7), 26.7 (C-6), 27.2 (C-3), 29.7 (C-2), 32.1 (C-8), 36.2 (C-9), 50.3 (2 NCH ₂), 56.9 (C-1), 67.5 (2 OCH ₂), 125.6, 128.2, 128.4, 143.1 (Ph)
16b	1.03 (dt, 1 H, $J = 8.0$, 7.6, H-6), 1.15–1.37 (m, 6 H, H-2, H-3', H-4', H-5', CH ₂ -7), 1.74 (q, 2 H, $J = 7.9$, CH ₂ -8), 1.79–1.98 (m, 2 H, H-3, H-4), 2.05 (td, 1 H, $J = 11.4$, 6.0, H-5), 2.55 (dt, $J = 11.2$, 4.6, CHHNCHH), 2.64–2.73 (m, 4 H, CHHNCHH, CH ₂ -9), 3.67 (t, 4 H, $J = 4.6$, OCH ₂), 7.18–7.33 (m, 5 H, Ph)	20.6 (C-5), 23.3 (C-7), 24.4 (C-3), 26.9 (C-4), 29.2 (C-2), 31.5 (C-6), 32.3 (C-8), 36.1 (C-9), 49.9 (2 NCH ₂), 58.9 (C-1), 67.4 (2 OCH ₂), 125.7, 128.3, 128.4, 142.7 (Ph)
17a	0.67 (dt, 1 H, $J = 8.0$, 4.0, H-6), 0.84 (t, 1 H, $J = 4$, H-2), 1.15 (m, 1 H, H-4'), 1.40–1.80 (m, 11 H, H-3', H-3, H-4, H-5', H-5, CH ₂ -7, CH ₂ -8, CH ₂), 2.50–2.85 (m, 6 H, NCH ₂ , CH ₂ -9), 7.07–7.22 (m, 5 H, Ph)	22.0 (C-4), 22.6 (C-5), 24.5 (2 CH ₂), 26.7 (C-3, C-6), 27.3 (C-7), 30.1 (C-2), 32.3 (C-8), 36.2 (C-9), 49.3 (2 NCH ₂), 52.6 (C-1), 125.5, 128.2, 128.4, 143.3 (Ph)
18	0.65 (m, 1 H, H-6), 0.84 (m, 1 H, H-5), 1.18 (m, 1 H, H-3), 1.30– 1.80 (m, 6 H, 2 H-4, H-3, H-2), 1.85 (m, 1 H, H-2), 2.59 (m, 2 H, NCH ₂), 2.74 (m, 2 H, NCH ₃), 3.33 (s, 6 H, 2 OCH ₃), 4.39 (t, 1 H, <i>J</i> = 5.6 Hz, CH)	20.70 (CH ₂), 21.95 (CH ₂), 24.54 (2 CH ₂), 24.7 (CH ₂), 26.6 (C-6, C-4), 29.7 (CH ₂), 30.0 (CH ₂ , C-5), 32.63 (CH ₂), 49.8 (NCH ₂), 52.7 (OCH ₃), 104.7 (CHOCH ₃)

^a Solvent for **5–10**, **12–14**, **16–18**: CDCl₃. Solvent for **11**, **15**: C₆D₆.

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6b: *endo*-isomer; $R_f 0.52$; light petroleum ether/Et₂O (90:10) as eluent; yield: 30%.

HRMS: m/z Obsd (Calcd) for $C_{18}H_{25}N^+$: 255.1988 (255.1989).

1-(6-Phenylbicyclo[3.1.0]hex-1-yl)morpholines:

7a: *exo*-isomer; $R_f 0.65$ (EtOAc/cyclohexane, 20:80); light petroleum ether/Et₂O (98:2) as eluent; yield: 48%.

7b: *endo*-isomer R_f 0.24; light petroleum ether/Et₂O (90:10) as eluent; yield: 30%.

HRMS: m/z Obsd (Calcd) for $C_{16}H_{21}NO^+$: 243.1623 (243.1623).

1-(7-Phenylbicyclo[4.1.0]hept-1-yl)morpholines:

8a: *exo*-isomer; $R_f 0.77$ (EtOAc/cyclohexane, 25:75); light petroleum ether/Et₂O (98:2) as eluent; yield: 30%.

8b: *endo*-isomer; $R_f 0.40$; light petroleum ether/Et₂O (90:10) as eluent; yield: 20%.

HRMS: m/z Obsd (Calcd) for $C_{17}H_{23}NO^+$: 257.1780 (257.1780).

 $\label{eq:loss} \begin{array}{l} 1\mbox{-}(6\mbox{-}Phenylbicyclo[3.1.0]hex\mbox{-}1\mbox{-}yl)pyrrolidine: \\ \textbf{9b:} endo\mbox{-}isomer; R_f\mbox{ 0.10; light petroleum ether/Et}_2O\ (60\mbox{-}40)\ as eluent; yield: 45\%. \end{array}$

HRMS: m/z Obsd (Calcd) for $C_{16}H_{21}N^+$: 227.1674 (227.1674).

*2-Benzylcyclopentanone*¹⁰ (rearranged product): Light petroleum ether/Et₂O (98:2) as eluent; yield: 46%.

1-(7-Phenylbicyclo[4.1.0]hept-1-yl)pyrrolidines:

10a: *exo*-isomer; $R_f 0.74$; light petroleum ether/Et₂O (94:6) as eluent; yield: 21%.

10b: *endo*-isomer: $R_f 0.10$; light petroleum ether/Et₂O (60:40) as eluent; yield: 41%.

HRMS: m/z Obsd (Calcd) for $C_{17}H_{23}N^+$: 241.1829 (241.1830).

2-Benzylcyclohexanone¹¹ (rearranged product): Light petroleum ether/Et₂O (98:2) as eluent; yield: 21%.

1-(6-Methylbicyclo[3.1.0]hex-1-yl)piperidines:

11a: *exo*-isomer; $R_f 0.93$; light petroleum ether/ Et_2O (99:1) as eluent; yield: 32%.

11b: *endo*-isomer; $R_f 0.27$; light petroleum ether/ Et_2O (96:4) as eluent; yield: 6.5%.

HRMS: m/z Obsd (Calcd) for $C_{12}H_{21}N^+$: 179.1677 (179.1674).

1-(7-Methylbicyclo[4.1.0]hept-1-yl)piperidine:

12a: *exo*-isomer; $R_f 0.85$; light petroleum ether/Et₂O (98:2) as eluent; yield:16%.

HRMS: m/z Obsd (Calcd) for $C_{13}H_{23}N^+$: 193.1830 (193.1830).

1-(6-Methylbicyclo[3.1.0]hex-1-yl)morpholines:

13a: *exo*-isomer; $R_f 0.86$; light petroleum ether/Et₂O (99:1) as eluent; yield: 34.5%.

13b: endo-isomer; $R_f 0.45$: light petroleum ether/Et₂O (96:4) as eluent; yield: 21.5%.

MS: $m/z = (M^+ - CH_3, 166).$

 $\label{eq:loss} \begin{array}{l} $I-(6-Methylbicyclo[3.1.0]hex-1-yl)pyrrolidine:$$ 14a: exo-isomer; R_f 0.42; light petroleum ether/Et_2O$ (94:6) as eluent; yield: 24\%. \end{array}$

MS: $m/z = (M^+ - CH_3, 150).$

 $\label{eq:loss} \begin{array}{l} 1-\{6-(3-Phenylprop-1-yl)bicyclo[3.1.0]hex-1-yl]piperidines: \\ \textbf{15a: } exo-isomer; R_f 0.98; light petroleum ether/Et_2O (98:2) as eluent; \\ yield: 36\%. \end{array}$

15b: <code>endo-isomer; R_f 0.67; light petroleum ether/Et_2O (90:10)</code> as eluent; yield: 36%.

HRMS: m/z Obsd (Calcd) for $C_{20}H_{29}N^+$: 283.2300 (283.2300).

 $\label{eq:loss} \begin{array}{l} $I-\{6-(3-Phenylprop-1-yl)bicyclo[3.1.0]hex-1-yl]morpholine: $$ 16a: exo-isomer; R_f 0.60; light petroleum ether/Et_2O$ (98:2) as eluent; yield: $53\%. \end{array}$

16b: *endo*-isomer; $R_f 0.32$; light petroleum ether/Et₂O (90:10) as eluent; yield: 14%.

HRMS: *m*/*z* Obsd (Calcd) for C₁₉H₂₃NO⁺: 285.2092 (285.2093).

$$\label{eq:loss} \begin{split} &l-\{6\cdot(3\text{-}Phenylprop-1\text{-}yl)bicyclo[3.1.0]hex-1\text{-}yl]pyrrolidine:\\ &\mathbf{17a:}\ exo\text{-}isomer;\ R_f\ 0.65;\ light\ petroleum\ ether/Et_2O\ (98:2)\ as\ eluent;\ yield:\ 66\%.\\ &HRMS:\ m/z\ Obsd\ (Calcd)\ for\ C_{19}H_{27}N^+:\ 269.2143\ (269.2143). \end{split}$$

1-{6-(5,5-Dimethoxypentyl)bicyclo[3.1.0]hex-1-yl}pyrrolidine: **18**: *endo*-isomer; $R_f 0.85$; light petroleum ether/ Et_2O (70:30) as eluent; yield: 67%.

MS: m/z Obsd (Calcd) for $C_{17}H_{31}O_2N^+$: 281 (281).

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