Table 1. Synthesis of β-Lactams from β-Amino Acids

β-Amino acids				Yield (%) of β-Lactams[a]	
R^1	R^2	R^3	R^4	3-NDP(3a)	3-NDE(3b)
$PhCH_2$	H	CH_3	H	86	90
$PhCH_2$	H	CH_3	CH_3	97	
$PhCH_2$	H	$(CH_2)_2CH_3$	H	83	85
$PhCH_2$	H	CH_2CH_3	H	82	
$PhCH_2$	H	$COCH_3$	H	72	78
$PhCH_2$	CH_3	H	H	54	63
$PhCH_2CH_2$	H	CH_3	CH_3	95	
$C_6H_3(OCH_3)_2CH_2$[b]	H	CH_3	H	84	
$C_6H_3(OCH_3)_2CH_2$[b]	CH_3	H	H	80	
H	H	H	Ph	[c]	30

[a] Isolated yields by column chromatography. [b] 3,4-Dimethoxybenzyl. [c] Less than 10%.

hydrolytic stability and therefore is handled more easily than **3b**. Both **3a** and **3b** are applicable to the formation of β-lactams from N-substituted β-amino acids. Further utility of the reagent as dehydrating and condensing reagents is being explored.

Experimental

Melting points were determined with Buchi 510 apparatus and were uncorrected. Thin-layer chromatography (TLC) was performed on Silica gel 60 F_{254} (Merck) plates, and spots were detected by ultraviolet (UV) irradiation. ^{1}H-NMR spectra were measured with a Brucker AC 100 spectrometer. Tetramethylsilane (TMS) in $CDCl_3$ was used as an internal reference. ^{13}C-NMR spectra was obtained on a Gemini-300 spectrometer

Preparation of (3-nitropyridyl) diphenyl phosphate (3a). A mixture of 2-hydroxy-3-nitropyridine (**1**) (14.01 g, 0.1 mol) and triethylamine (10.12 g, 0.1 mol) in dichloromethane (300 m*l*) was stirred at room temperature and a solution of diphenyl chlorophosphate (26.86 g, 0.1 mol) in dichloromethane (100 m*l*) was added dropwise. Stirring was continued for 1 h. The mixture was evaporated and the residue was extracted with chloroform. The organic layer was washed successively with 5% $NaHCO_3$ (100 m*l*) and brine (200 m*l*) and dried with Na_2SO_4. The solvent was removed under reduced pressure and the residue was crystallized from chloroform-hexane. Yield 92-94%, mp. 76-78℃; ^{13}C-NMR (acetone-d_6) δ 119.52, 119.58, 121.55, 125.04, 129.08, 135.57, 139.17, 141.40, 151.16.

Preparation of (3-nitropyridyl) diethyl phosphate (3b). Compound **3b** was prepared from **1** and diethyl chlorophosphate (**2b**) as described above. Yield 93%, ^{1}H-NMR (100 MHz, $CDCl_3$) δ 1.19 (t, 6H, J=7.2 Hz), 4.19 (q, 4H, J=7.2 Hz), 7.15-8.34 (m, 3H).

The representative experimental procedure for the reaction of β-amino acid with (3-nitropyridyl) dialkyl phosphate (Eq. (2)); To a mixture of 3-benzyl aminobutanoic acid (289 mg, 1.5 mmol) and **3-NDP** (670 mg, 1.8 mmol) in acetonitrile (150 m*l*) was added triethylamine (360 mg, 3.6 mmol) at room temperature. After being stirred for 24 h at 80℃. Usual work-up 2 : 1 ether-chloroform afforded 1-benzyl-4-methylazetidin-2-one in 86% yield (150 mg) as an oil.

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Revised Assignment of the ^{13}C-NMR Spectra of Bicyclo[3.1.1]heptane Derivatives

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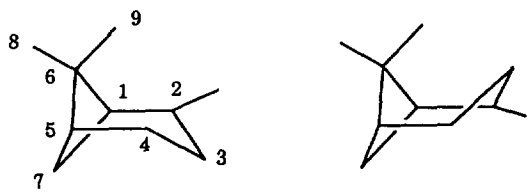
A unique rigid geometry of bridged bicyclic compounds has received considerable attention from NMR spectroscopists because their geometry is ideal to study the relationships between configuration and the magnitude of NMR parameters.[1,2] Because the proton spectra were restricted for the conformational studies by complexity, the carbon-13 spectra of these derivatives were used as a mean of determining their conformations.[1,3] One of the interesting qualitative application of carbon-13 chemical shift is the conformational analysis of bicyclo[3.1.1]heptane derivatives (**1**) which has the conformational flexibility in the three carbon bridge.[4]



(1)

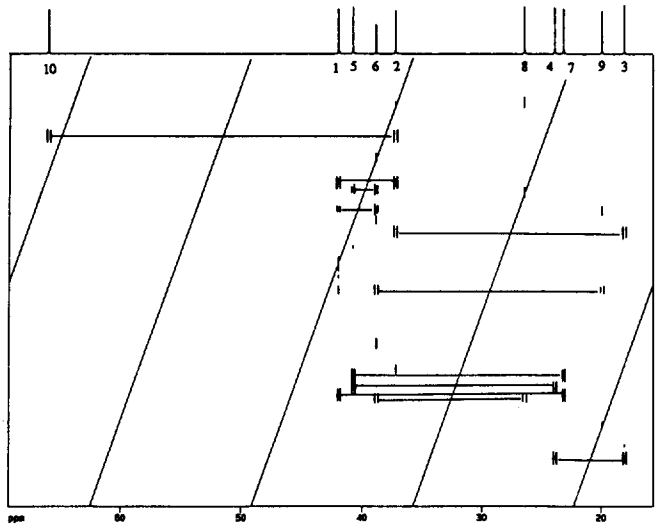


Figure 1. The 2D-INADEQUATE spectrum of *trans*-myrtanol (**5**). Bruker AMX-500 spectrometer, sample: 0.38 g in 0.5 ml $CDCl_3$ (5 M), relaxation delay 3 s, 64 scans, total 3 and half hours acquisition. The data were acquired with 2K×64 data points multiplied by exponential (LB=1.5) in F2 and sine window in F1 dimension without shift and followed by zero-filling to give 2K×512 data matrix.

Although numerous ways in NMR techniques, for example, substituent effects, DEPT, COSY, HETCOR, deuterium isotope shift, ^{13}C-^{1}H coupling constants, were used to assign the carbon skeleton of these molecules,[1-6] these indirect approaches made some of the chemical shift assignments completely wrong, controversial or, at best, ambiguous because the proton spectra did not exhibit well resolved signals.

All of these contradictory assignments could be solved if we could measure the direct carbon-carbon correlations. Considering the sensitivity, the choice of carbon-13 2D-INADEQUATE experiment was just inadequate until recently. However, rapid development during the last decade in NMR techniques, most notably in the increasing use of a high-field spectrometer with further hardware developments, made the direct connectivity method, INADEQUATE, one of the most important techniques. In this note conclusive carbon-13 assignments of representative five derivatives, *cis*-pinane (**2**), *trans*-pinane (**3**), *cis*-myrtanol (**4**), *trans*-myrtanol (**5**), and myrtenol (**6**), are reported and the correctness of some spectroscopic inferences derived from the previous works is checked on the basis of two-dimensional INADEQUATE results.[7]

The pulse sequence employed was the 90°-τ-180°-τ-90°-t_1-90°-t_2 sequence[7] with quadrature detection in F1 dimension.[8] The representative carbon-13 2D INADEQUATE spectrum of *trans*-myrtanol (**5**) obtained at 125.76 MHz (Bruker AMX-500 spectrometer) is shown in the Figure 1. All the assignments of 2D-carbon spectra which were recorded with the condition of F2=2F1 in 5 mole solution ($CDCl_3$) was achieved by choosing their characteristic shift as the starting points with DEPT spectra.[9] That is, the caron 10 (66.25 ppm) in *trans*-myrtanol (**5**) (Figure 1) has correlation with methine carbon at 38.12 ppm which is carbon 2. Then this methine carbon has correlation peaks with one methine (42.87 ppm) and one methylene carbon (18.79 ppm) which are carbon 1 and 3, respectively. Since this method furnishes direct proof of the C-C connectivities, we can assemble carbon to carbon connectivities to assign the complete and self-consistent structure unambiguously except the carbon 8 and 9. The assignment of carbon 8 and 9 was accomplished by the use of 2D C-H correlation and NOE difference experiments (observing NOEs between the 9-methyl and proton of 2 or one of 4). More dilute concentrations (0.3 and 1.0 mole in $CDCl_3$) of sample were also studied to check the sequence of the carbon signals by 2D C-H correlation experiment. All the experiments showed that in all cases the signal sequence in the carbon-13 spectra was not changed with the sample concentrations. The carbon-13 chemical shifts of five compounds in 1 mole solution are shown in the Table 1. The various erroneous assignments in the literature should be corrected on the basis of the Table 1. Although some of the spectroscopic inferences are qualitatively usuable, for example the chemical shift differences between the carbon 6 and 7 for the bridged-chair or bridged-boat conformation,[3,4] many of them,[1] for example substituent effect on the chemical shift and coupling constants and quantitative conformation using proton coupling constants, should be reconsidered. Especially, the carbon 1 and 5, and carbon 3 and 4 are reversed in most of the references which led to the completely worng ^{13}C-^{1}H coupling constants and proton chemical shifts derived from 2D C-H correlation experiment.

On the basis of the study, we can conclude that some of the spectroscopic inferences made for the bicyclic compounds in previous studies should be reinvestigated. Further studies are currently in progress to correct wrong inferences and to evaluate quantitative conformation of these bicyclic system on the basis of proton coupling constants.

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Table 1. ^{13}C Chemical shifts[a] of Bicyclo[3.1.1]heptane Derivatives

Compound	1	2	3	4	5	6	7	8	9	10
2	48.11	35.97	23.85	26.56	41.39	38.83	33.98	28.32	23.22	22.90
3	47.68	29.38	23.97	24.64	40.93	39.51	23.06	26.86	20.09	21.62
4	42.79	44.26	18.70	25.91	41.37	38.52	33.05	27.87	23.23	67.53
5	42.87	38.12	18.79	24.74	41.58	39.48	23.81	27.02	20.45	66.25
6	43.18	147.69	117.50	31.00	40.80	37.82	31.48	26.03	20.97	65.63

[a] The solvent was $CDCl_3$, which served also as an internal reference for the ^{13}C spectrum (δ=77.0). The digital resolution of spectra was 0.004 ppm.

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