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NEW SYNTHESIS OF β-LACTAMS

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Abstract—α-Methylene-β-lactams **3** were synthesized from the various 2-bromoallylamine derivatives **2** using a catalytic amount of $Pd(OAc)_2$ or $Pd(acac)_2$ and PPh_3 under 1–4 atom pressure of CO in good yields. Similarly, α-alkylidene-β-lactams **20** were synthesized from 3-alkyl-2-bromoallylamines **19**, which were easily prepared from the olefins **14**. in the same manner.

After we published a preliminary report on the new synthesis of monocyclic β-lactams by insertion of carbon monoxide in the presence of $Pd(OAc)_2$—PPh_3,[2] sulfazecin (**1a**), an antibiotic of a monocyclic β-lactam skeleton, was discovered from a strain of Pseudomonas acidophila by the Takeda's group.[3] On the other hand, the Squibb's group reported the isolation of several analogous 2-azetidinone-1-sulfonic acid derivatives from strains of bacteria, and called them "monobactams (**1**)" as a general trivial name.[4] Under these circumstances, attention has been focussed into extention of our method to the synthesis of efficacious β-lactam in the form of modified antibiotics. The so-far known methods are indicated in Scheme 1, in which (2+2) cycloaddition, intramolecular cyclization, ring contraction of five membered ring, and ring expansion of three membered ring are involved.[5] However, a synthesis that can be represented as (N—C—C + C=O) developed by us has never been described.

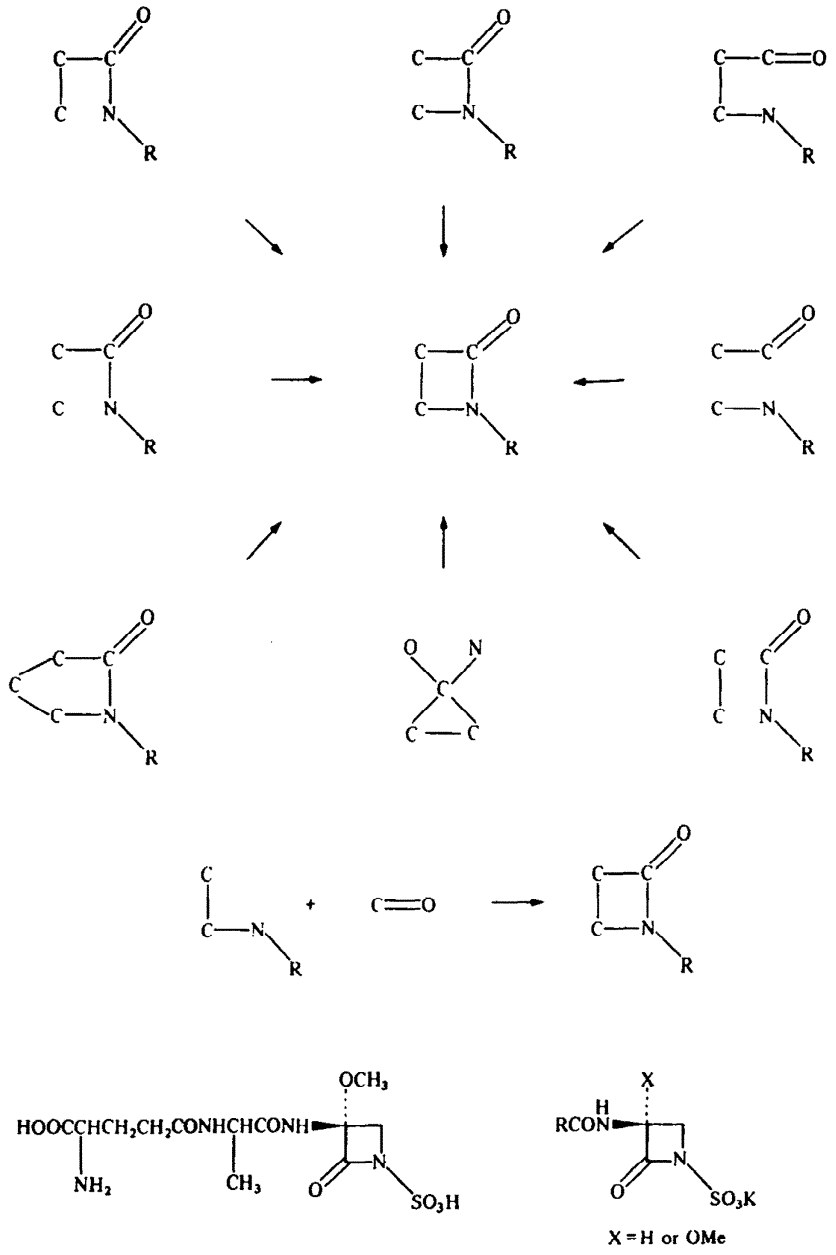
Thus, we report here the details of our method by items in the following.

Synthesis of N-*benzyl-α-methylene-β-lactams.* Before the present work, it was reported by us that *o*-haloaminoalkylbenzene was treated with a catalytic amount of $Pd(OAc)_2$ and PPh_3 under an atmosphere of carbon monoxide to afford benzolactams.[6a] By further development of this method, 5-, 6- and 7-membered lactams, lactones and cyclic imides were obtained in good yields.[6] Since the intermediates of these reactions were considered to be the arylmetal complexes, it was expected that 2-bromoallylamine derivatives should afford the monocyclic β-lactams. In line with this idea a mixture of N-benzyl-2-bromo-2-propenylamine (**2a**), $n\text{-}Bu_3N$, a catalytic amount of $Pd(OAc)_2$ (2 mol %) and PPh_3 (8 mol %) in hexamethylphosphoroamide (HMPA) was stirred at 100° under an atmosphere of carbon monoxide to afford N-benzyl-α-methylene-β-lactam (**3a**) expectedly in a yield of 67%. The spectral data suggested that this compound should possess the β-lactam skeleton. To confirm this structure, **3a** was reduced with sodium borohydride to give N-benzyl-3-methyl-β-lactam (**4**), which was also obtained by hydrogenation with platinum oxide in a yield of 86%. The Michael addition of piperidine to the methylene group of **3a** in t-BuOH proceeded slowly at room temperature to afford the compound **5** in a yield of 47%. On addition of benzylamine to **3a**, the mixture was allowed to stand at room temperature for one week, followed by acetylation, to give only a small amount of the desired product (**8**, 6.8% yield) and the cleaved product (**6**, 12.6%). For further confirmation of the structure of **3a**, the same lactam was prepared from N-benzyl-β,β'-dibromoisobutyroamide (**9**) by the method reported.[7] Namely, a solution of **9**, which was prepared from β,β'-dibromoisobutyric acid in 40% $NaOH$–CH_2Cl_2 in the presence of benzyltriethyl ammonium chloride gave **3a** in addition to **10** and **11**. The spectral data of this α-methylene-β-lactam were fully identical with those of the former β-lactam (**3a**).

This reaction might proceed through the vinylmetal complex **12**, first generated from vinyl halide **2** and zerovalent palladium complex, which should be coordinated with carbon monoxide. Migration of vinyl group to carbon monoxide gave an acylpalladium complex, which should be coordinated with internal amino group to produce the cyclic complex **13**. Reductive elimination occurred to afford the desired α-methylene-β-lactam **3a** and hydride palladium complex, and the latter complex was converted to zerovalent palladium complex with $n\text{-}Bu_3N$. On this reaction, the use of 0.5 mol % of $Pd(OAc)_2$ as catalyst gave **3a** in 54% yield. $Pd(acac)_2$ may be used instead of $Pd(OAc)_2$ with similar results and higher reaction temperature reduced the reaction time (Table 1).

Synthesis of N-*substituted-α-methylene-β-lactams.* To confirm its broad applicabilities, this method was further extended to synthesis of N-substituted-α-methylene-β-lactams **3** from the corresponding 2-bromo-2-propenylamine **2**, which was easily prepared from 2,3-dibromopropene and the primary amine. Various amino acids such as β-alanine, glycine or alanine as a primary amine gave the α-methylene-β-lactams possessing a carboxyl group at the α- or β-position of the nitrogen. For this reaction, a higher pressure of carbon monoxide increased the yields of the desired β-lactams **3** (Table 2, Runs 5 and 6).

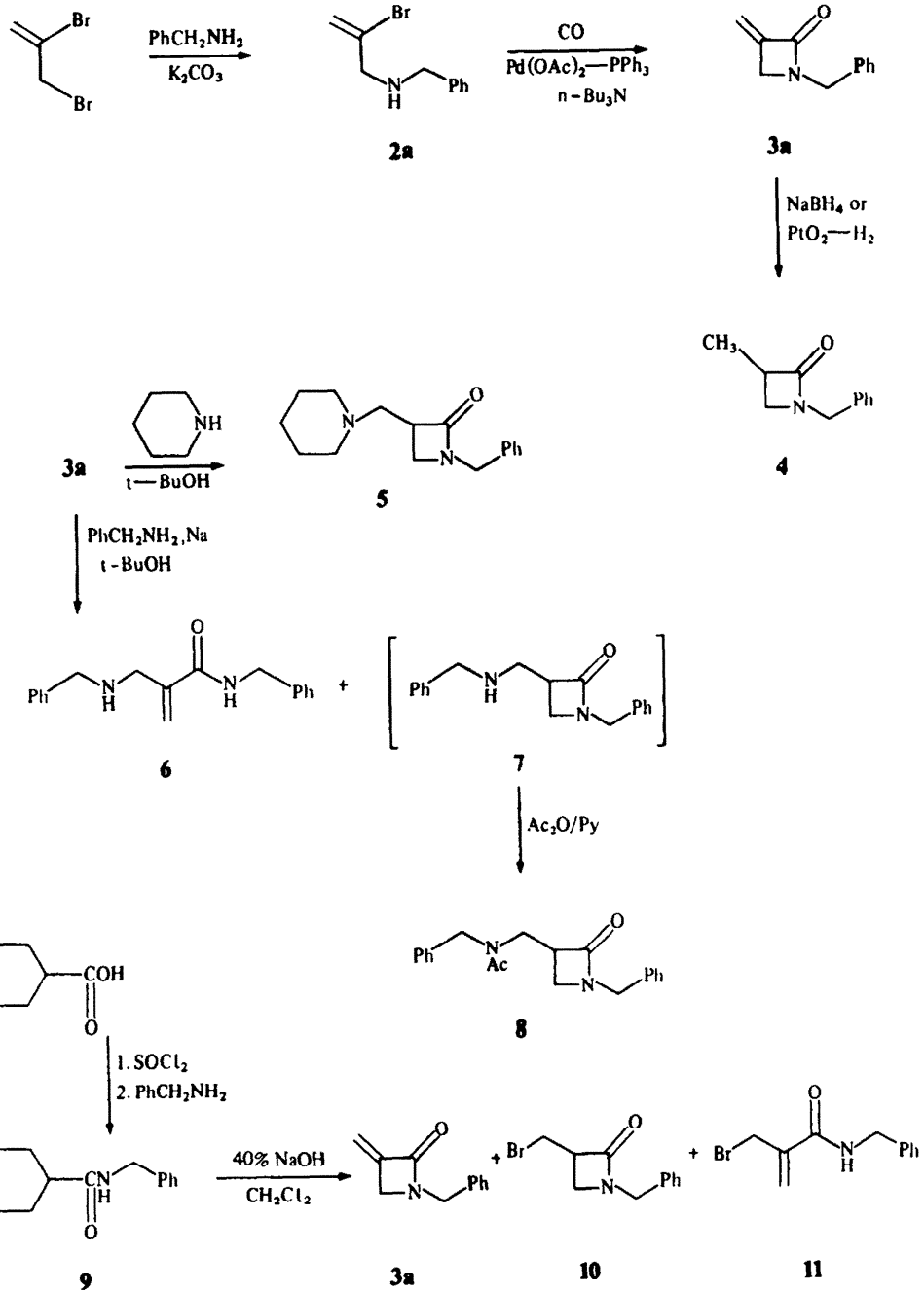
Synthesis of α-alkylidene-β-lactams. For the synthesis of biologically active substances in this series, it has been tried to develop the preparation of α-alkylidene-β-lactams **20** from olefins **14** according to Scheme 4. Initially, styrene (**14a**) was chosen as the starting material, which was transformed into dibromocyclopropane derivative **15a** by a phase transfer technique.[8] Ring opening of this cyclopropane derivative **15a** with silver acetate in acetic acid gave the allyl acetate **16a**[9] and **16b**. The former compound **16a** was quantitatively hydrolyzed with 5% NaOH to the allyl alcohol **17a**, which was converted to the allyl bromide **18a** with CBr_4 and PPh_3[10] in acetonitrile in a yield of 86%. A condensation of **18a** with benzylamine in the presence of potassium carbonate in methylene chloride afforded the desired secondary amine **19a**. The insertion of carbon monoxide to this amine **19a** afforded N-benzyl-



Sulfazecin **1a** **1**

X = H or OMe

Scheme 1.

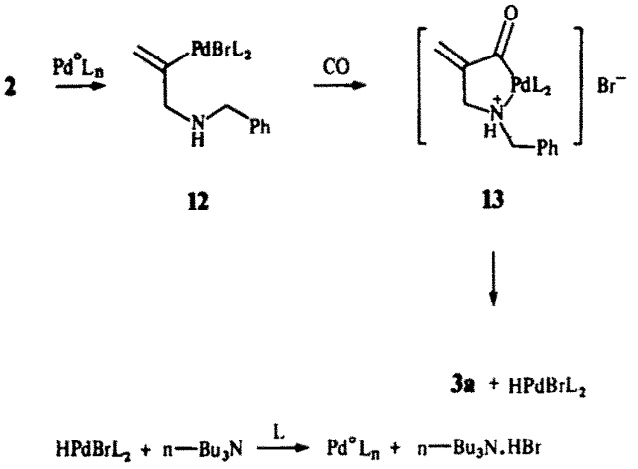

PhCH2NH2
K2CO3
CO
Pd(OAc)2—PPh3
n-Bu3N
2a
3a
NaBH4 or
PtO2—H2
4
t—BuOH
5
PhCH2NH2,Na
t-BuOH
6
7
Ac2O/Py
8
1. SOCl2
2. PhCH2NH2
40% NaOH
CH2Cl2
9
10
11

Scheme 2.

3-(*Z*-benzylidene)-β-lactam (**20a**) in a yield of 76%. On the other hand, hydrolysis of **16b** gave the alcohol **17b**, which was treated with CBr_4 and PPh_3 in a similar manner to furnish a mixture of **18a** and **18b** in yields of 48% and 16%, respectively. A condensation of **18b** with benzylamine provided the olefinic *E*-isomer **19b** of the former compound **19a**. Carbonylation of this compound **19b** also smoothly proceeded according to the above mentioned procedure to afford the β-lactam **20b** in a yield of 90%.

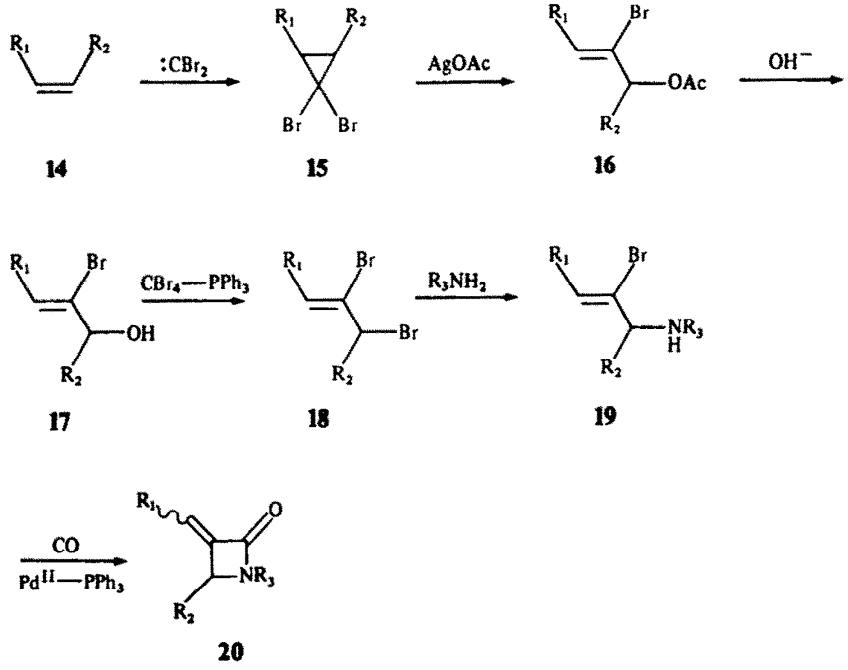
Table 1. Palladium catalyzed carbonylation of the compound (**2a**) under various reaction conditions

Catalyst	mol %	Reaction temp (°C)	Reaction time (hr)	Yield of **3** (%)
$Pd(OAc)_2$	2.0	100	5	66.9
$Pd(acac)_2$	2.0	100	7	66.2
$Pd(OAc)_2$	0.5	100	10	53.5
$Pd(OAc)_2$	0.5	120	4.5	53.3



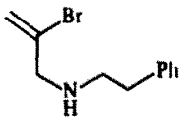
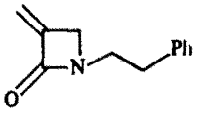
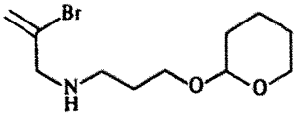
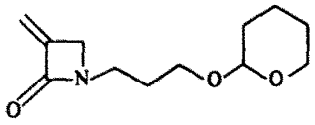
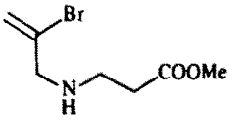
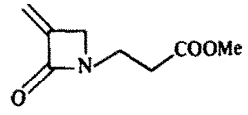
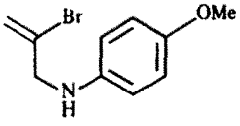
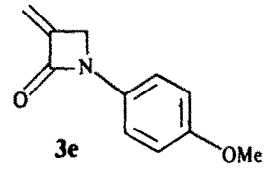
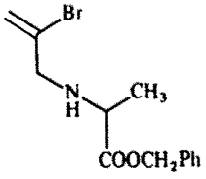
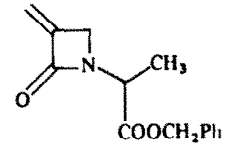
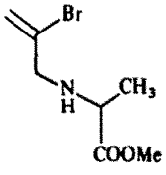
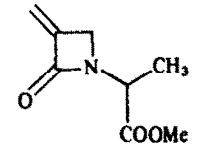
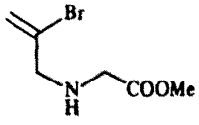
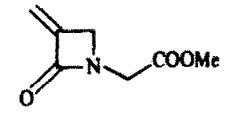
Scheme 3.

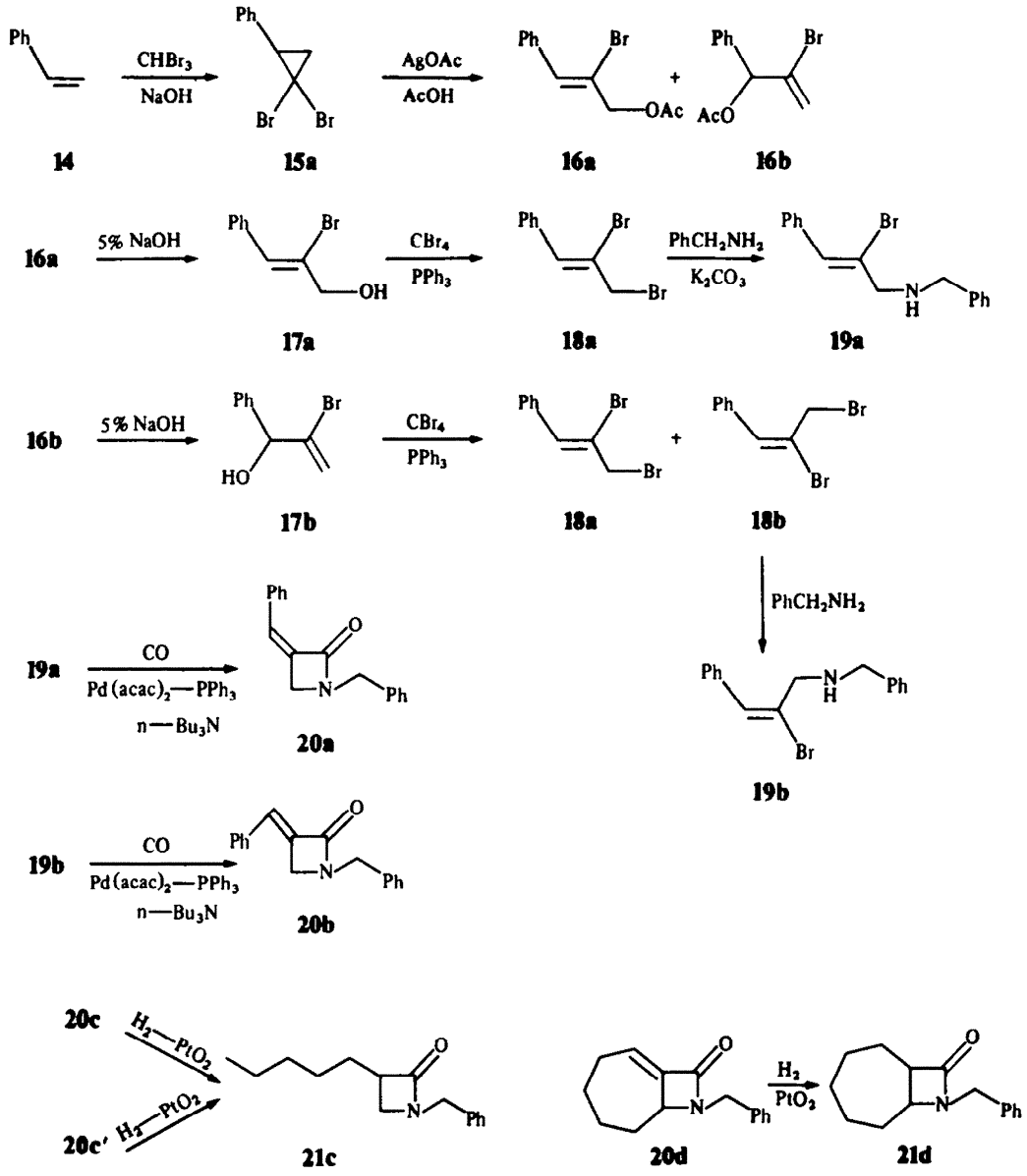
Thus, other α-alkylidene-β-lactams **20** were synthesized from 2-bromoallylamines **19**, which were prepared through the same route from the corresponding olefins **14**, in fairly good yields (Table 3). In this reaction, the insertion of carbon monoxide to the *Z*-isomer **19a** afforded N-benzyl-3-(*Z*-benzylidene)-β-lactam (**20a**), and to the *E*-isomer **19b** gave N-benzyl-3-(*E*-benzylidene)-β-lactam (**20b**). However, the compound **19c** gave two olefinic isomers **20c** and **20c'** from the reaction mixture because these β-lactams **20c** and **20c'** possessed the protons at the α-position of the unsaturated carbonyl group. To confirm these



Scheme 4.

Table 2. Syntheses of N-substituted-α-methylene-β-lactams (3) from the corresponding 2-bromo-propenylamine (2)

Run	Starting material (2)	Product (3)	Atm. pressure of carbon monoxide	Yield of β-lactam (3) (%)
1	 **2b**	 **3b**	1 atm.	61.9
2	 **2c**	 **3c**	1	62.9
3	 **2d**	 **3d**	1	37.6
4	 **2e**	 **3e**	1	14.9
5 6	 **2f**	 **3f**	1 4	20.4 44.7
7	 **2g**	 **3g**	4	40.6
8	 **2h**	 **3h**	4	60.1



Scheme 5.

structures, α-alkylidene-β-lactams **20c** and **20c'** were hydrogenated with platinum oxide in ethanol, respectively, to give the same compound **21c**. The same treatment of the compound **20d** also gave the corresponding β-lactam **21d**. These results demonstrate that an olefinic compound could be easily converted into vinyl halide bearing an aminomethyl group at the halogeno position which should be a useful precursor for the synthesis of α-alkylidene-β-lactams.

The present new synthetic method for the α-methylene-β-lactams is very useful, because the starting material is readily available and operation of the reaction with carbon monoxide is very easy. Since it was considered that monocyclic β-lactams should be important in search for biologically active substances, various α-methylene-β-lactams should be synthesized by use of this method.

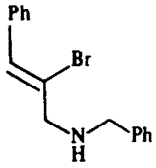
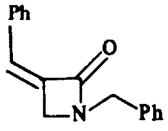
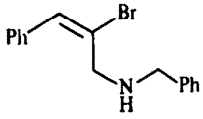
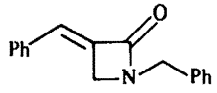
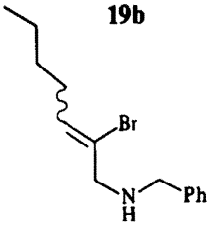
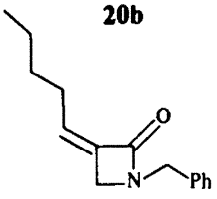
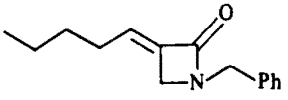
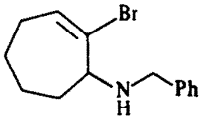
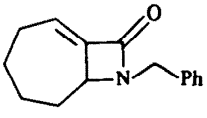
EXPERIMENTAL

M.ps were measured with a hot stage microscope (Yanaco MPJ-2) and Yamato MP-1 and uncorrected. Spectra were measured on a Jasco IRA-diffraction grating IR spectrophotometers, Hitachi R-20B (NMR, 60 MHz), a JEOL-FX 100 (100 MHz) spectrometer and Hitachi RMU-7M double focussing mass spectrometer. The preparation of $Pd(OAc)_2$[11] and $Pd(acac)_2$[12] was conducted by the method described previously.

General procedure for the synthesis of 2-bromo-2-propenylamine derivatives **2**

To a soln of primary amine (1–3 mol) in the presence of K_2CO_3 (1–3 mol) in DMF or CH_2Cl_2 was slowly added a soln of 2,3-dibromopropene (1 mol) in the same solvent at 0°. After a soln was stirred at room temp overnight, ether was added and the ether layer was washed with water, dried over $MgSO_4$ and evaporated.

Table 3. Syntheses of α-alkylidene-β-lactams (**20**) from the corresponding olefins (**16**)

Run	Olefins (**14**)	Amines (**19**)	β-lactams (**20**)	Yield of β-lactams (**20**) (%)
1	 **14a**	 **19a**	 **20a**	75.9
2	**14a**	 **19b**	 **20b**	89.5
3	 **14c**	 **19c**	 **20c** +  **20c'**	48.0
4	 **14d**	 **19d**	 **20d**	85.7

N-*Benzyl*-2-*bromo*-2-*propenylamine* (**2a**). The crude product which was prepared from benzylamine (40.9 g, 0.382 mmol), 2,3-dibromopropene (25.5 g, 0.128 mol), K_2CO_3 (17.6 g, 0.128 mol) in DMF (310 ml) was purified by column chromatography on silica gel eluted with n-hexane–Et_2O–CH_2Cl_2 (12 : 4 : 1) to give a pale yellow oil of **2a** (24.5 g, 92%). IR ν (neat) cm^{-1} : 3320 (NH), 1625 (C=C). NMR ($CDCl_3$): δ 1.80 (s, 1H, NH), 3.45 (s, 2H, NCH_2CBr), 3.72 (s, 2H, $PhCH_2N$), 5.60 (d, 1H, J = 1 Hz, vinyl), 5.80 (d, 1H, J = 1 Hz, vinyl), 7.28–7.45 (m, 5H, aromatic). MS *m/e* 227, 225 (M^+), 146 (M^+ – Br), 120, 91.

N-(2-*Phenethyl*)-2-*bromo*-2-*propenylamine* (**2b**). The crude product which was prepared from phenethylamine (3.63 g, 30 mmol), 2,3-dibromopropene (2.00 g, 10 mmol) and K_2CO_3 (2.10 g, 15.2 mmol) in CH_2Cl_2 (150 ml) was purified by column chromatography on silica gel eluted with n-hexane–Et_2O (1 : 3) to give a colorless oil of **2b** (1.877 g, 78.2%). IR ν (neat) cm^{-1} : 3300 (NH), 1625 (C=O). NMR ($CDCl_3$): δ 1.45 (s, 1H, NH), 2.79 (s, 4H, CH_2CH_2), 3.43 (m, 2H, NCH_2CBr), 5.52 (m, 1H, vinyl), 5.72 (m, 1H, vinyl), 7.24 (s, 5H, aromatic). MS *m/e* 241, 239 (M^+), 160 (M^+ – Br), 150, 148, 121, 119, 105, 91, 61.

N-(2-*Bromo*-2-*propenyl*)-3-(*tetrahydro*-2H-*pyran*-2-*yloxy*)*propylamine* (**2c**). To a soln of 3-aminopropanol (1.52 g, 20.3 mmol) and *p*-toluenesulfonic acid hydrate (4.0 g, 21.1 mmol) in CH_2Cl_2 (50 ml) was added a soln of 3,4-dihydro-α-pyrane (2.07 g, 24.6 mmol) in CH_2Cl_2 (10 ml) and a soln was stirred at room temp for 18 hr. After the undissolved material was filtered off and the soln was concentrated. The residual oil

was dissolved in CH_2Cl_2 (100 ml) containing K_2CO_3 (7.1 g, 51.4 mmol) and a soln of 2,3-dibromopropene (1.37 g, 6.8 mmol) in CH_2Cl_2 (50 ml) was added for 1.5 hr and a mixture was stirred for 2 days. After usual work up, the residue was purified by column chromatography on silica gel eluted with Et_2O to give a colorless oil of **2e** (0.953 g, 50.2%). IR ν (neat) cm^{-1}: 3320 (NH), 1625 (C=C). NMR ($CDCl_3$): δ 1.30–2.00 (m, 9H), 2.62 (t, 2H, J = 7 Hz, NCH_2), 3.20–4.00 (m, 1H, OCHO), 5.47 (m, 1H, vinyl), 5.76 (m, 1H, vinyl).

Methyl 3-(2-*bromo*-2-*propenylamino*)*propionate* (**2d**). The crude product which was prepared from β-alanine methyl ester hydrochloride (1.395 g, 10 mmol), 2,3-dibromopropene (2.00 g, 10 mmol), KI (0.166 g, 1.00 mmol) and K_2CO_3 (1.38 g, 10 mmol) in CH_3CN and CH_2Cl_2 (2:1, 15 ml) was purified by column chromatography on silica gel eluted with n-hexane–Et_2O (2:1) to give a colorless oil of **2d** (1.131 g, 51.0%). IR ν (neat) cm^{-1}: 3340 (NH), 1735 (C=O), 1625 (C=C). NMR ($CDCl_3$): δ 1.80 (br s, 1H, NH), 2.69 (m, 4H, CH_2), 3.48 (s, 2H, NCH_2CBr), 3.71 (s, 3H, OCH_3), 5.59 (m, 1H, vinyl), 5.84 (m, 1H, vinyl).

N-(p-*Methoxyphenyl*)-2-*bromo*-2-*propenylamine* (**2e**). The crude product which was prepared from *p*-anisidine (1.23 g, 10 mmol), 2,3-dibromopropene (1.00 g, 5.0 mmol) and K_2CO_3 (1.38 g, 10 mmol) was purified by column chromatography on silica gel eluted with n-hexane–Et_2O (4:1) to give a colorless oil of **2e** (1.834 g, 75.5%). IR ν (neat) cm^{-1}: 3410 (NH), 1630 (C=C). NMR ($CDCl_3$): δ 3.71 (s, 1H, NH), 3.73 (s, 3H, OCH_3), 3.94 (t, J = 1.5 Hz, 2H, NCH_2), 5.54 (m, 1H, vinyl), 5.83 (m, 1H, vinyl), 6.52–6.83 (m, 4H, aromatic). MS *m/e* 243, 241 (M^+), 228, 226, 162 ($M^+ - Br$), 122.

Benzyl 2-(2-*bromo*-2-*propenylamino*)-2-*propionate* (**2f**). The crude product which was prepared from alanine benzyl ester *p*-toluene sulfonate (2.00 g, 5.69 mmol), 2,3-dibromopropene (1.083 g, 5.42 mmol) and K_2CO_3 (2.07 g, 15.0 mmol) in CH_3CN (30 ml) was purified by column chromatography on silica gel eluted with n-hexane–$CHCl_3$–EtOH (20:10:1) to give a colorless oil of **2f** (780 mg, 48.3%). IR ν (neat) cm^{-1}: 3460 (NH), 1740 (C=O), 1640 (C=C). NMR ($CDCl_3$): δ 1.31 (d, 3H, J = 6 Hz, CCH_3), 1.95 (s, 1H, NH), 3.40 (m, 3H, CH_2NCH), 5.12 (s, 2H, OCH_2Ph), 5.47 (m, 1H, vinyl), 5.74 (m, 1H, vinyl), 7.28 (s, 5H, aromatic).

Methyl 2-(2-*bromo*-2-*propenylamino*)-2-*propionate* (**2g**). The crude product which was prepared from alanine methyl ester hydrochloride (3.000 g, 21.5 mmol), 2,3-dibromopropene (3.074 g, 15.4 mmol) and K_2CO_3 (9.280 g, 67.1 mmol) in CH_3CN (30 ml) was purified by column chromatography on silica gel eluted with n-hexane–Et_2O (1:1) to give a colorless oil of **2g** (1.394 g, 41%). IR ν (neat) cm^{-1}: 1735 (C=O), 1630 (C=C). NMR (CCl_4): δ 1.27 (d, 3H, J = 7 Hz, CCH_3), 1.88 (s, 1H, NH), 3.57 (m, 3H, CH_2NCH), 3.70 (s, 3H, $COOCH_3$), 5.53 (m, 1H, vinyl), 5.88 (m, 1H, vinyl).

Methyl 2-(2-*bromo*-2-*propenylamino*)*acetate* (**2h**). The crude product which was prepared from glycine methyl ester hydrochloride (2.05 g, 15.9 mmol) and K_2CO_3 (5.622 g, 41.0 mmol) in CH_3CN (15 ml) was purified by column chromatography on silica gel eluted with n-hexane–Et_2O (2:1) to give a pale yellow oil of **2h** (920.1 mg, 32.6%). IR ν (neat) cm^{-1}: 1740 (C=O), 1630 (C=C). NMR (CCl_4): δ 2.02 (s, 1H, NH), 3.29 (s, 2H, NCH_2CO), 3.42 (s, 2H, $=CCH_2N$), 3.68 (s, 3H, $COOCH_3$), 5.49 (m, 1H, vinyl), 5.80 (m, 1H, vinyl).

General procedure for the synthesis of α-methylene-β-lactams (**3**)

A mixture of **2** (1 eq.), $Pd(OAc)_2$ (2 mol %), PPh_3 (8 mol %) and n-Bu_3N (1.25 eq.) in HMPA was warmed under an appropriate pressure of CO. After cooling, ether was added to the mixture and the ether layer was washed with water or 5% HCl soln, dried over $MgSO_4$ and evaporated. The residue was purified by chromatography on silica gel or alumina to give a desired **3**.

1-*Benzyl*-3-*methylene*-*azetidin*-2-*one* (**3a**). A mixture of **2a** (1.17 g, 5.16 mmol), $Pd(OAc)_2$ (23 mg, 0.103 mmol), PPh_3 (108 mg, 0.41 mmol) and n-Bu_3N (1.20 g, 6.45 mmol) in HMPA (10 ml) was warmed under CO (1 atm) at 100°. After ceasing of the absorption of CO, the mixture was treated in the usual manner and the crude product was purified by column chromatography on alumina eluted with n-hexane–Et_2O (3:2) to give colorless prisms of **3a** (597 mg, 66.9%), m.p. 32° (from ether). IR ν(neat) cm^{-1}: 1740 (C=O). NMR ($CDCl_3$): δ 3.65 (t, J = 1 Hz, 2H, H-4), 4.54 (s, 2H, NCH_2Ph), 5.17 (dd, J = 3, 1 Hz, 1H, vinyl), 5.75 (dd, J = 3, 1 Hz, 1H, vinyl), 7.20–7.50 (m, 5H, aromatic). ^{13}C-NMR ($CDCl_3$): δ 45.9, 47.7, 109.2, 127.8, 135.1, 144.9, 163.0. MS *m/e* 173 (M^+), 172, 133, 91. (Found: C, 76.44; H, 6.42; N, 8.07. Calc for $C_{11}H_{11}NO$: C, 76.28; H, 6.40; N, 8.09%.)

3-*Methylene*-1-*phenethylazetidin*-2-*one* (**3b**). The crude oil which was prepared from **2b** (2.608 g, 10.9 mmol), $Pd(OAc)_2$ (48 mg, 0.21 mmol), PPh_3 (224 mg, 0.85 mmol) and n-Bu_3N (2.426 g, 13.1 mmol) in HMPA (10 ml) under an atmosphere of CO at 100° for 6 hr was purified by column chromatography on alumina eluted with n-hexane–Et_2O (10:1) to give a colorless oil of **3b** (1.258 g, 61.9%). IR ν (neat) cm^{-1}: 1740 (C=O). NMR (CCl_4): δ 2.83 (m, 2H, CH_2Ph), 3.40–3.65 (m, 4H, H-4, NCH_2), 5.01 (m, 1H, vinyl), 5.53 (m, 1H, vinyl), 7.06–7.40 (m, 5H, aromatic). MS *m/e* 187 (M^+), 159, 104, 96, 91. High resolution mass spectrum calc for $C_{12}H_{13}NO$ *m/e* 187.0996, found 187.0984.

3-*Methylene*-1-[3-(*tetrahydropyran*-2H-2-*yloxy*)*propyl*]*azetidin*-2-*one* (**3c**). The crude oil which was prepared from **2c** (2.015 g, 7.2 mmol), $Pd(OAc)_2$ (31 mg, 0.318 mmol), PPh_3 (148 mg, 0.565 mmol) and n-Bu_3N (1.608 g, 8.7 mmol) in HMPA (5 ml) under an atmosphere of CO at 100° for 4 hr was purified by column chromatography on alumina eluted with n-hexane–EtOAc (4:1) to give a colorless oil of **3c** (1.025 g, 62.9%). IR ν (neat) cm^{-1}: 1740 (C=O). NMR ($CDCl_3$): δ 1.30–2.10 (m, 8H), 3.40 (t, J = 8 Hz, 2H, NCH_2), 3.71 (m, 2H, H-4), 3.20–4.00 (m, 4H, CH_2O), 4.51 (m, 1H, OCHO), 5.06 (m, 1H, vinyl), 5.59 (m, 1H, vinyl). MS *m/e* 225 (M^+), 141, 124, 96, 85. High resolution mass spectrum calc for $C_{12}H_{19}NO_3$ *m/e* 225.1366, found 225.1382.

1-(2-*Methoxycarbonylethyl*)-3-*methylene*-*azetidin*-2-*one* (**3d**). The crude product which was prepared from **2d** (563 mg, 2.5 mmol), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PPh_3 (52.5 mg, 0.20 mmol) and n-Bu_3N (579 mg, 3.13 mmol) in HMPA (5 ml) under an atmosphere of CO at 100° for 3.5 hr was purified by column chromatography on alumina eluted with n-hexane–EtOAc (1:1) to give a colorless oil of **3d** (165 mg, 37.6%). IR ν (neat) cm^{-1}: 1740 (C=O). NMR ($CDCl_3$): δ 2.64 (t, J = 7 Hz, 2H, CH_2CO), 3.66 (t, J = 7 Hz, 2H, NCH_2), 3.73 (s, 3H, OCH_3), 3.81 (m, 2H, H-4), 5.20 (m, 1H, vinyl), 5.72 (m, 1H, vinyl). MS *m/e* 169 (M^+), 141, 138, 110, 98, 96.

1-(p-*Methoxyphenyl*)-3-*methylene*-*azetidin*-2-*one* (**3e**). The crude oil which was prepared from **2e** (1.097 g, 4.54 mmol), $Pd(OAc)_2$ (20 mg, 0.091 mmol), PPh_3 (95 mg, 0.363 mmol) and n-Bu_3N (925 mg, 5.00 mmol) in HMPA (2 ml) and 2-pyrrolidone (2 ml) under an atmosphere of CO at 100° for 5 hr was purified by column chromatography on alumina eluted with n-hexane–Et_2O (2:1) to give colorless plates of **3e** (128 mg, 14.9%), m.p. 106–107° (from ether–petroleum ether, lit.[7] m.p. 105–107°). IR ν (Nujol) cm^{-1}: 1725 (C=O). NMR ($CDCl_3$): δ 3.77 (s, 3H, OCH_3), 4.06 (m, 2H, H-4), 5.29 (m, 1H, vinyl), 5.81 (m, 1H, vinyl), 6.82–6.94 (m, 2H, aromatic), 7.24–7.40 (m, 2H, aromatic). MS *m/e* 189 (M^+), 174, 149, 135, 120.

1-(1-*Benzyloxycarbonylethyl*)-3-*methylene*-*azetidin*-2-*one* (**3f**)

Method A. A mixture of **2f** (278.5 mg, 0.935 mmol), $Pd(OAc)_2$ (4.2 mg, 0.019 mmol), PPh_3 (19.6 mg, 0.748 mmol) and n-Bu_3N (250 mg, 1.35 mmol) in HMPA (3 ml) was warmed under an atmosphere of CO at 100° for 5 hr. After usual work up, the residue was purified by column chromatography on alumina eluted with n-hexane–EtOAc (2:1) to give a colorless oil of **3f** (46.7 mg, 20.8%). IR ν (neat) cm^{-1}: 1740 (C=O), 1660 (C=C). NMR ($CDCl_3$): δ 1.48 (d, 3H, J = 8 Hz, CH_3), 3.78 (s, 2H, H-4), 4.66 (q, 1H, J = 8 Hz, NCHC), 5.16 (s, 2H, CH_2Ph), 5.21 (m, 1H, vinyl), 5.75 (m, 1H, vinyl), 7.34 (s, 5H, aromatic). MS *m/e* 245 (M^+), 110 ($M^+ - COOCH_2Ph$). High resolution mass spectrum calc for $C_{14}H_{15}NO_3$ *m/e* 245.1053, found 245.1064.

Method B. A mixture of **2f** (316.2 mg, 1.06 mmol), $Pd(OAc)_2$ (4.8 mg, 0.021 mmol), PPh_3 (22.2 mg, 0.848 mmol) and n-Bu_3N (235.7 mg, 1.27 mmol) in HMPA (1 ml) was heated under 4 kg/cm² pressure of CO at 80° for 24 hr. After usual work up, a colorless oil of **3f** (116.0 mg, 44.7%) was obtained.

1 - (1 - *Methoxycarbonylethyl*) - 3 - *methylene* - *azetidin* - 2 - *one* (**3g**). A mixture of **2g** (758 mg, 3.43 mmol), $Pd(OAc)_2$ (15.4 mg, 0.068 mmol), PPh_3 (72.0 mg, 0.275 mmol) and n-Bu_3N (757.4 mg, 4.12 mmol) in HMPA (3 ml) was heated under 4 kg/cm² pressure of CO at 80° for 25.5 hr. After usual work up, the residual oil was purified by column chromatography on alumina eluted with n-hexane–EtOAc (2 : 1) to give a colorless oil of **3g** (235.5 mg, 40.6%). IR ν (neat) cm^{-1} : 1735 (C=O), 1660 (C=C). NMR (CCl_4): δ 1.46 (d, J = 7 Hz, 3H, CH_3), 3.74 (s, 3H, $COOCH_3$), 3.84 (m, 2H, H-4), 4.52 (m, 1H, NCHC), 5.16 (s, 1H, vinyl), 5.70 (s, 1H, vinyl). MS *m/e* 169 (M^+), 141, 110. High resolution mass spectrum calc for $C_8H_{11}NO_3$ *m/e* 169.0738, found *m/e* 169.0730.

1 - (*Methoxycarbonylmethyl*) - 3 - *methylene* - *azetidin* - 2 - *one* (**3h**). The crude oil which was prepared from **2h** (707.7 mg, 3.40 mmol), $Pd(OAc)_2$ (15.3 mg, 0.068 mmol), PPh_3 (71.3 mg, 0.0272 mmol) and n-Bu_3N (756.2 mg, 4.62 mmol) in HMPA (3 ml) under 4 kg/cm² pressure of CO at 80° for 24 hr was purified by column chromatography on alumina eluted with n-hexane–EtOAc (1 : 1) to give a colorless oil of **3h** (316.8 mg, 60.1%). IR ν (neat) cm^{-1} : 1730 (C=O). NMR ($CDCl_3$): δ 3.76 (s, 3H, $COOCH_3$), 3.95 (m, 2H, H-4), 4.14 (s, 2H, NCH_2Ph), 5.25 (m, 1H, vinyl), 5.77 (m, 1H, vinyl).

1-*Benzyl*-3-*methyl*-*azetidine*-2-*one* (**4**)

Method A. To a soln of **3a** (9.5 mg, 0.055 mmol) in EtOH–THF (1 : 2, 1.5 ml) was added $NaBH_4$ (20 mg, 0.526 mmol) and the soln was stirred at room temp for 16 hr. After the solvent was removed under reduced pressure, the residue was dissolved in water (1 ml) and the aqueous layer was neutralized with 10% HCl soln and extracted with ether. The ether layer was dried over $MgSO_4$ and concentrated. The residual oil was purified by preparative TLC on silica gel eluted with n-hexane–Et_2O (1 : 1) to give a colorless oil of **4** (5.9 mg, 61.3%). IR ν (neat) cm^{-1} : 1740 (C=O). NMR ($CDCl_3$): δ 1.31 (dt, J = 2, 7 Hz, 3H, CH_3), 2.76 (dd, J = 2, 5 Hz, 1H, H-4), 3.05–3.34 (m, 1H, H-3), 3.28 (dd, 1H, J = 5, 2 Hz, H-4), 4.36 (s, 2H, $PhCH_2$), 7.10–7.28 (m, 5H, aromatic). MS *m/e* 175 (M^+), 133, 91.

Method B. A soln of **3a** (35.7 mg, 0.206 mmol) in EtOH–THF (1 : 2, 0.9 ml) containing PtO_2 (0.5 mg) was stirred under an atmosphere of H_2 at room temp. The catalyst was filtered off and the solvent was removed under reduced pressure to give a colorless oil, which was purified to give **4** (31.1 mg, 86.3%).

1 - *Benzyl* - 3 - (1 - *piperidino*)*methyl* - *azetidin* - 2 - *one* (**5**). A soln of **3a** (91 mg, 0.526 mmol) and piperidine (300 mg, 3.53 mmol) in t-BuOH (0.5 ml) was stirred at room temp for 48 hr. Solvent was removed under reduced pressure and the residual oil was purified by preparative TLC on alumina eluted with n-hexane–Et_2O (1 : 1) to give a colorless oil of **5** (63.2 mg, 46.6%). IR ν (neat) cm^{-1} : 1740 (C=O). NMR ($CDCl_3$): δ 1.30–1.70 (m, 6H), 2.25–2.85 (m, 6H, 3 NCH_2), 2.90–3.10 (m, 1H, H-3), 3.15–3.50 (m, 2H, H-4), 4.37 (s, 2H, $PhCH_2$), 7.20–7.50 (m, 5H, aromatic). MS *m/e* 258 (M^+), 98, 91, 84. Picrate m.p. 149–149.5° (yellow plates from EtOH). (Found: C, 54.19; H, 5.14; N, 14.27. Calc for $C_{22}H_{25}N_5O_8$: C, 54.21; H, 5.17; H, 14.27%.)

3 - (N - *Acetyl* - N - *benzylaminomethyl*) - 1 - *benzyl* - *azetidin* - 2 - *one* (**8**). To a soln of **3a** (396 mg, 2.29 mmol) and benzylamine (2.45 g, 22.9 mmol) in t-BuOH (3 ml) was added Na (5 mg, 0.217 mmol) and a soln was stirred at room temp for 7 days. Water was added to the mixture and the soln was extracted with ether. The ether layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure to give a crude oil, which was purified by column chromatography on alumina eluted with n-hexane–Et_2O–CH_2Cl_2 (1 : 1 : 1). The first fraction was the starting material (**3a**, 134 mg, 33.8%). The second fraction was a colorless oil of **6** (80.6 mg, 12.6%). IR ν (neat) cm^{-1} : 3260 (NH), 1660 (C=O), 1620 (C=C). NMR ($CDCl_3$): δ 2.10 (s, 1H, NH), 3.50 (s, 2H, NCH_2), 3.70 (s, 2H, NCH_2Ph), 4.45 (br s, 1H, CONCH), 4.55 (br s, 1H, CONCH), 5.45 (br s, 1H, vinyl), 6.20 (br s, 1H, CONH), 7.10–7.60 (m, 10H, aromatic), 9.25 (br s, 1H, CONH). MS *m/e* 189 ($M^+ - PhCH_2$), 106, 91. The last fraction was dissolved in pyridine (0.2 ml) and a soln of Ac_2O (0.5 ml) in pyridine (1 ml) was added to the soln and a mixture was stirred at room temp for 18 hr. The solvent was removed under reduced pressure and the residual oil was purified by preparative TLC on alumina eluted with n-hexane–Et_2O (1 : 1) to give a colorless oil of **8** (50.4 mg, 6.8%). IR ν (neat) cm^{-1} : 1740 (C=O), 1640 (C=C). NMR (CCl_4): δ 1.95 (s, 3H, $COCH_3$), 2.80–3.70 (m, 5H), 4.26 (br s, 1H, AcNCH), 4.30 (br s, 1H, AcNCH), 4.60 (s, 2H, NCH_2Ph), 7.10–7.40 (m, 10H, aromatic). MS *m/e* 322 (M^+), 279, 160, 120, 106, 91.

N-*Benzyl*-β,β'-*dibromoisobutyramide* (**9**). A soln of β,β'-dibromoisobutyric acid (4.73 g, 18.2 mmol) in $SOCl_2$ (7 ml, 96.2 mmol) was refluxed for 5 hr. After evaporation of $SOCl_2$, the residue was dissolved in benzene (20 ml). To this soln was added benzylamine (4.09 g, 38.4 mmol) in benzene (5 ml) under ice-cooling. Benzene was added to its soln and the organic layer was washed with 10% HCl soln and water, dried over $MgSO_4$ and evaporated. The residual solids were recrystallized from n-hexane–EtOAc to give colorless needles of **9** (2.70 g, 42%), m.p. 104–107°. IR ν (Nujol) cm^{-1} : 3280 (NH), 1640 (C=O). NMR ($CDCl_3$): δ 2.90 (m, 1H, CHCO), 3.40–3.80 (m, 4H, $BrCH_2$), 4.47 (br s, 1H, PhCH), 4.52 (br s, 1H, PhCH), 6.10 (br s, 1H, NH), 7.14–7.50 (m, 5H, aromatic). MS *m/e* 337, 335, 333 (M^+), 256, 254 ($M^+ - Br$), 160, 109, 91. (Found: C, 39.27; H, 3.94; N, 4.10; Br, 47.96. Calc for $C_{11}H_{13}Br_2NO$: C, 39.43; H, 3.91; N, 4.18; Br, 47.70%.)

Synthesis of **3a** *from* **9**. A soln of **9** (499 mg, 1.49 mmol) in 40% NaOH aq (895 mg, 8.94 mmol) and CH_2Cl_2 (15 ml) containing benzyltriethylammonium chloride (34 mg, 0.149 mmol) was vigorously stirred at room temp for 41 hr. Water was added to the mixture and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with water and dried over $MgSO_4$. Solvent was removed and the residue was purified by column chromatography on silica gel eluted with n-hexane–Et_2O (1 : 1) to give colorless crystals of **3a** (61 mg, 23.6%), a colorless oil of **10** (133 mg, 35.2%) and colorless crystals of **11** (88 mg, 23.2%). *Compound* **10**. IR ν (neat) cm^{-1} : 1745 (C=O). NMR ($CDCl_3$): δ 2.99 (m, 1H, H-4), 3.18 (m, 1H, H-4), 3.52 (m, 3H, H-3 and $BrCH_2$), 4.27 (br s, 1H, PhCH), 4.30 (br s, 1H, PhCH), 7.10–7.52 (m, aromatic). MS *m/e* 255, 253 (M^+), 174 ($M^+ - Br$), 133, 132, 91. *Compound* **11**. IR ν ($CHCl_3$) cm^{-1} : 3430 (NH), 1665 (C=O), 1620 (C=C). NMR ($CDCl_3$): δ 4.17 (s, 2H, $BrCH_2$), 4.44 (br s, 1H, PhCH), 4.50 (br s, 1H, PhCH), 5.62 (s, 1H, vinyl), 5.76 (s, 1H, vinyl), 6.60 (br s, 1H, NH). MS *m/e* 255, 253 (M^+), 174 ($M^+ - Br$), 129, 91.

General procedure for the synthesis of 3-*alkyl*-2-*bromo*-2-*propenyl acetate* **16**

Dihalocyclopropane **15** was prepared by phase transfer method[8] and the ring opening of this cyclopropane to allyl acetate **16** was carried out by Sanderlere's method.[9]

2-*Bromo*-3-*phenyl*-2-*propenyl acetate* (**16a**)[9] *and* 2-*bromo*-1-*phenyl*-2-*propenyl acetate* (**16b**). A soln of **15a** (1.136 g, 4.10 mmol) in AcOH (30 ml) containing AgOAc (1.0 g, 6.02 mmol) was refluxed for 24 hr. After evaporation of AcOH under reduced pressure, ether was added and the undissolved material was filtered off. The ether layer was washed with sat $NaHCO_3$ aq and dried over $MgSO_4$. Solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel eluted with n-hexane–Et_2O (4 : 1). The first fraction was a colorless oil of **16b** (340.1 mg, 32.5%). IR ν (neat) cm^{-1} : 1740 (C=O), 1640 (C=C), 1600 (C=C), 1200 (C=O). NMR (CCl_4): δ 2.05 (s, 3H, $OCOCH_3$), 5.65 (s, 1H), 5.91 (s, 1H), 6.28 (s, 1H), 7.30 (s, 5H, aromatic). The second fraction was a colorless oil of **16a** (525.4 mg, 50.2%). IR ν (neat) cm^{-1} : 1740 (C=O), 1625 (C=O), 1220 (C=O). NMR (CCl_4): δ 2.07 (s, 3H, $OCOCH_3$), 4.75 (s, 2H, CH_2OAc), 6.92 (s, 1H, vinyl), 7.1–7.8 (m, 5H, aromatic).

2-*Bromo*-2-*heptenyl*-1-*acetate* (**16c**). A mixture of 1-hexene (15.0 g, 0.18 mol) and $CHBr_3$ (40.4 g, 0.16 mol) in 50%

NaOH aq (50 ml) containing benzyltriethylammonium chloride (600 mg) was warmed at 40° overnight. Water was added to the mixture and the aqueous layer was extracted with n-hexane. The organic layer was dried over $MgSO_4$ and concentrated. The residue was distilled under reduced pressure to give a colorless liquid of **15c** (5.35 g, 13.1%), b.p.$_{1.5}$ 89–95°. NMR (CCl_4): δ 0.79 (br t, 3H, CH_3). A soln of **15c** (5.35 g, 20.9 mmol) and AgOAc (5.24 g, 31.4 mmol) in AcOH (100 ml) was refluxed overnight. The undissolved material was filtered off and the solvent was removed under reduced pressure. The residue was dissolved in ether and the organic layer was washed with sat $NaHCO_3$ aq, dried over $MgSO_4$ and evaporated. The residual oil was purified by column chromatography on silica gel eluted with n-hexane–Et_2O (4 : 1) to give a colorless liquid of **16c** (2.93 g, 64.0%), b.p.$_{1.4}$ 105–112°. IR ν (neat) cm^{-1}: 1740 (C=O), 1625 (C=C), 1230 (C=O). NMR (CCl_4): δ 0.92 (t, 3H, CH_3), 2.00 (s, $OCOCH_3$), 2.05 (s, $OCOCH_3$), 4.66 (s, 2H, CH_2OAc), 6.02 (t, vinyl), 6.31 (s, vinyl), 6.44 (s, vinyl).

3 - Acetoxy - 2 - bromo - 1 - cycloheptene (**16d**)[9] — *General procedure for the synthesis of 3 - alkyl - 2 - bromo - 2 - propen - 1 - ol* **17**

A soln of **16** in 5% KOH–MeOH (20% aq MeOH) was allowed to stand at room temp overnight. MeOH was removed under reduced pressure and benzene was added to the residue. The organic layer was washed with water, dried over $MgSO_4$ and concentrated. The residue was purified by column chromatography on silica gel to afford **17**.

Z-2-Bromo-3-phenyl-2-propen-1-ol (**17a**). The crude product which was prepared from **16a** (258 mg, 1.014 mmol) in 5% KOH–MeOH (6 ml) was purified by column chromatography on silica gel eluted with benzene–ether (4 : 1) to give a colorless oil of **17a** (207.5 mg, 96.7%). IR ν (neat) cm^{-1}: 3350 (OH), 1620 (C=C), 1600 (C=C); NMR ($CDCl_3$): δ 3.0–3.5 (br s, 1H, OH), 4.33 (br s, 2H, CH_2), 7.02 (d, 1H, =CH), 7.2–7.7 (m, 5H, aromatic). MS *m/e* 214, 212 (M^+), 133 ($M^+ - Br$), 105, 103.

2-Bromo-1-phenyl-2-propen-1-ol (**17b**). The crude product which was prepared from **16b** (1.495 g, 5.89 mmol) in 5% KOH–MeOH (30 ml) was purified by column chromatography on silica gel eluted with benzene–Et_2O (4 : 1) to give a colorless oil of **17b** (1.186 g, 95.0%). IR ν (neat) cm^{-1}: 3350 (OH), 1640 (C=C). NMR ($CDCl_3$): δ 2.75 (d, 1H, OH), 5.20 (d, 1H, CHOH), 5.60 (m, 1H, vinyl), 5.97 (m, 1H, vinyl), 7.33 (s, 5H, aromatic). MS *m/e* 214, 212 (M^+), 133 ($M^+ - Br$), 107, 79.

2-Bromo-2-hepten-1-ol (**17c**). The crude product which was prepared from **16c** (2.93 g, 0.12 mmol) in 5% NaOH–MeOH (40 ml) was purified by column chromatography on silica gel eluted with n-hexane–Et_2O (1 : 1) to give a colorless oil of **17c** (2.033 g, 84.5%). IR ν (neat) cm^{-1}: 3350 (OH), 1650 (C=C), 1620 (C=C). NMR (CCl_4): δ 0.95 (t, 3H, CH_3), 1.1–1.8 (m, 4H), 1.9–2.5 (m, 2H, $=CCH_2$), 2.9–3.4 (br s, 1H, OH), 4.17 (s, 2H, CH_2O), 6.00 (t, 1H, vinyl). MS *m/e* 194, 192 (M^+), 138, 136, 137, 135, 113 ($M^+ - Br$), 95. High resolution mass spectrum calc for $C_7H_{13}OBr$ *m/e* 192.0151, 194.0130, found *m/e* 192.0177, 194.0150.

2-Bromo-2-cyclohepten-1-ol (**17d**). The crude product which was prepared from **16d** (3.105 g, 7.50 mmol) in 5% NaOH–MeOH (30 ml) was purified by column chromatography on silica gel eluted with n-hexane–Et_2O (4 : 1) to give a colorless oil of **17d** (2.3 g, quant). IR ν (neat) cm^{-1}: 3450 (OH), 1635 (C=C). NMR (CCl_4): δ 1.4–2.4 (m, 8H), 4.40 (m, 1H, CHO), 6.26 (t, 1H, vinyl). MS *m/e* 192, 190 (M^+), 174, 172 ($M^+ - H_2O$), 111 ($M^+ - Br$), 93 ($M^+ - H_2O - Br$).

General procedure for the synthesis of 3-alkyl-1,2-dibromo-2-propene (**18**)

To a soln of **17** (1 eq.) and CBr_4 (1.5 eq.) in CH_3CN was added PPh_3 (1.5 eq.) a little at a time under ice-cooling. The white ppts were filtered off and washed with CH_3CN. The solvent was removed and the residue was purified by column chromatography on silica gel eluted with an appropriate solvent to give **18**.

Z-2,3-Dibromo-1-phenyl-1-propene (**18a**). The crude product which was prepared from **17a** (484 mg, 2.28 mmol), CBr_4 (1.182 g, 3.56 mmol) and PPh_3 (877 mg, 3.35 mmol) in CH_3CN (5 ml) was purified by column chromatography on silica gel eluted with n-hexane to give a colorless oil of **18a** (539 mg, 85.6%). IR ν (neat) cm^{-1}: 1620 (C=C), 1600 (C=C). NMR (CCl_4): δ 4.31 (s, 2H, CH_2Br), 7.00 (s, 1H, vinyl), 7.1–7.7 (m, 5H, aromatic). MS *m/e* 278, 276, 274 (M^+), 197, 195 ($M^+ - Br$), 116 ($M^+ - 2Br$), 115.

E-2,3-Dibromo-1-phenyl-1-propene (**18b**). The crude product which was prepared from **17b** (1.185 g, 5.59 mmol), CBr_4 (3.66 g, 11.20 mmol) and PPh_3 (2.91 g, 11.02 mmol) in CH_3CN (20 ml) was purified by column chromatography on silica gel eluted with n-hexane. The first fraction was a colorless oil of **18b** (246.1 mg, 16%). IR ν (neat) cm^{-1}: 1620 (C=C), 1600 (C=C). NMR (CCl_4): δ 4.30 (s, 2H, CH_2Br), 7.05 (s, 1H, vinyl), 7.32 (s, 5H, aromatic). MS *m/e* 278, 276, 274 (M^+), 197, 195 ($M^+ - Br$), 116 ($M^+ - 2Br$), 115. The second fraction was **18a** (729.7 mg, 47.5%).

1,2-Dibromo-2-heptene (**18c**). The crude product which was prepared from **17c** (1.97 g, 10.2 mmol), CBr_4 (5.07 g, 15.27 mmol) and PPh_3 (4.01 g, 15.30 mmol) in CH_3CN (40 ml) was purified by column chromatography on silica gel eluted with Et_2O to give a colorless oil of **18c** (2.927 g), which was used without further purification for the condensation with benzylamine. IR ν (neat) cm^{-1}: 1640 (C=C), NMR (CCl_4): δ 0.95 (br t, 3H, CH_3), 4.20 (s, 2H, CH_2Br), 6.11 (t, J = 7 Hz, 1H, vinyl).

2,3-Dibromo-1-cycloheptene (**18d**). The crude product which was prepared from **17d** (2.3 g, 13.2 mmol), CBr_4 (5.89 g, 17.74 mmol), PPh_3 (4.67 g, 17.83 mmol) in CH_3CN (40 ml) was purified by column chromatography on silica gel eluted with n-hexane to give a colorless oil of **18d** (3.189 g, 95.6%). IR ν (neat) cm^{-1}: 1630 (C=C). NMR (CCl_4): δ 4.95 (br s, 1H, CHBr), 6.30 (t, J = 6 Hz, 1H, vinyl). MS *m/e* 256, 254, 252 (M^+), 173, 175 ($M^+ - Br$), 93. High resolution mass spectrum calc for $C_7H_{10}Br_2$ *m/e* 251.9149, 253.9130, 255.9111, found *m/e* 251.9149, 253.9125, 255.9126.

General procedure for the synthesis of 3-alkyl-2-bromo-2-propenylamine **19**

The compound **19** was prepared in the same manner as the synthesis of the compound **2** from 2,3-dibromopropene.

Z - N - Benzyl - 2 - bromo - 3 - phenyl - 2 - propenylamine (**19a**). The crude product which was prepared from **18a** (763 mg, 2.76 mmol), benzylamine (869 mg, 8.28 mmol) and K_2CO_3 (384 mg, 8.28 mmol) in CH_2Cl_2 (40 ml) was purified by column chromatography on silica gel eluted with n-hexane–ether (4 : 1) to give a colorless oil of **19a** (691.4 mg, 83.0%); IR ν (neat) cm^{-1}: 3300 (NH), 1630 (C=C), 1600 (C=C); NMR ($CDCl_3$): δ 1.79 (s, 1H, NH), 3.53 (s, 2H), 3.71 (s, 2H), 6.81 (s, 1H, vinyl), 7.0–7.7 (m, 10H, aromatic). MS *m/e* 303, 301 (M^+), 222 ($M^+ - Br$), 212, 210 ($M^+ - PhCH_2$), 120, 115, 105, 91. High resolution mass spectrum, calc for $C_{16}H_{16}NBr$ *m/e* 303.0447, 301.0465, found *m/e* 303.0452, 301.0480.

E - N - Benzyl - 2 - bromo - 3 - phenyl - 2 - propenylamine (**19b**). The crude product which was prepared from **18b** (86.1 mg, 0.3 mmol), benzylamine (94.5 mg, 0.9 mmol) and K_2CO_3 (41.7 mg, 0.6 mmol) in CH_2Cl_2 (10 ml) was purified by column chromatography on silica gel eluted with n-hexane–Et_2O (4 : 1) to give a colorless oil of **19b** (73.0 mg, 77.7%). IR ν (neat) cm^{-1}: 3400 (NH), 1620 (C=C), 1600 (C=C). NMR ($CDCl_3$): δ 1.94 (s, 1H, NH), 3.67 (s, 2H), 3.69 (s, 2H), 7.25 (s, 11H, aromatic and vinyl). MS *m/e* 303, 301 (M^+), 222 ($M^+ - Br$), 212, 210 ($M^+ - PhCH_2$), 120, 115, 105, 91. High resolution mass spectrum, calc for $C_{16}H_{16}NBr$ *m/e* 303.0447, 301.0467, found 303.0452, 301.0480.

N-Benzyl-2-bromo-2-heptenylamine (**19c**). The crude product which was prepared from **18c** (2.9 g, 11.3 mmol), benzylamine (3.56 g, 3.9 mmol) K_2CO_3 (4.71 g, 33.9 mmol) in CH_2Cl_2 (100 ml) was purified by column chromatography on silica gel eluted with n-hexane–Et_2O (4 : 1) to give a colorless oil of **19c** (1.49 g, 51.7% from **17c**). IR ν (neat) cm^{-1}: (NH), 1650 (C=C), 1600 (C=C). NMR ($CDCl_3$): δ 0.94 (br t, 3H, CH_3), 1.1–1.7 (m, 4H), 2.0–2.35 (m, 2H, $=CCH_2$), 3.40 (s, 2H), 3.66 (s,

2H), 5.79 (t, J = 7 Hz, 1H, vinyl). MS *m/e* 281, 283 (M^+), 202 ($M^+ - Br$), 190, 192 ($M^+ - PhCH_2$), 120, 105, 91. High resolution mass spectrum, calc for $C_{14}H_{20}NBr$, *m/e* 283.0760, 281.0781, found 283.0780, 281.0794.

N-Benzyl-2-bromo-2-cycloheptenylamine (**19d**). The crude product which was prepared from **18d** (1.1 g, 4.33 mmol), benzylamine (926 mg, 8.66 mmol) and K_2CO_3 (1.8 g, 12.99 mmol) in CH_3CN (100 ml) was purified by column chromatography on alumina eluted with n-hexane–Et_2O (1:2) to give a colorless oil of **19d** (1.027 g, 84.7%). IR *v* (neat) cm^{-1}: 3300 (NH), 1630 (C=C), 1600 (C=C). NMR ($CDCl_3$): δ 3.60 (br s, 1H, CHN), 3.79 (s, 2H, NCH_2Ph), 6.28 (t, J = 7 Hz, vinyl), 7.1–7.4 (br s, 5H, aromatic). MS *m/e* 281, 279 (M^+), 252, 250, 200 ($M^+ - HBr$), 91. High resolution mass spectrum calc for $C_{14}H_{18}NBr$ *m/e* 281.0602, 279.0624, found *m/e* 281.0576, 279.0642.

General procedure for the synthesis of α-alkylidene-β-lactams (**20**)

Carbonylation of **19** was carried out using the same procedure as for the synthesis of **3** under an atmosphere of CO and for the catalyst $Pd(acac)_2$ was used instead of $Pd(OAc)_2$.

Z-1-Benzyl-3-benzylidene-azetidin-2-one (**20a**). A mixture of **19a** (580 mg, 1.92 mmol), $Pd(acac)_2$ (12 mg, 0.038 mmol), PPh_3 (30 mg, 0.115 mmol) and n-Bu_3N (750 mg, 3.84 mmol) in HMPA (3 ml) was warmed under an atmosphere of CO at 100° for 10 hr. After usual work up, the residue was purified by column chromatography on silica gel eluted with n-hexane–benzene–Et_2O (2:2:1) to give colorless prisms of **20a** (362.7 mg, 75.9%), m.p. 67–67.6° (from n-hexane–Et_2O). IR *v* (Nujol) cm^{-1}: 1730 (C=O), 1680 (C=C), 1600 (C=C). NMR ($CDCl_3$): δ 3.55 (br s, 2H, H-4), 4.44 (s, 2H, NCH_2Ph), 6.19 (s, 1H, vinyl), 7.15–7.45 (br s, 10H, aromatic). MS *m/e* 249 (M^+), 230, 130, 116, 91. (Found: C, 81.92; H, 5.97; N, 5.67. Calc for $C_{17}H_{15}NO$: C, 81.90; H, 6.07; N, 5.62%.)

E-1-Benzyl-3-benzilidene-azetidin-2-one (**20b**). A mixture of **19b** (121.5 mg, 0.402 mmol), $Pd(acac)_2$ (2 mg, 0.006 mmol), PPh_3 (7 mg, 0.027 mmol) and n-Bu_3N (112 mg, 0.605 mmol) in HMPA (0.5 ml) was warmed under an atmosphere of CO at 100° for 10 hr. After usual work up, the residue was purified by column chromatography on silica gel eluted with Et_2O to give colorless needles of **20b** (89.6 mg, 89.5%), m.p. 140.5–141° (from Et_2O). IR *v* (Nujol) cm^{-1}: 1730 (C=O), 1690 (C=C), 1600 (C=C). NMR ($CDCl_3$): δ 3.99 (s, 1H, H-4), 4.01 (s, 1H, H-4), 4.59 (s, 2H, $PhCH_2N$), 6.99 (br t, 1H, vinyl), 7.33, 7.35 (m, 10H, aromatic). MS *m/e* 249 (M^+), 116 ($M^+ - PhN{=}C{=}O$), 91. (Found: C, 81.75; H, 6.09; N, 5.62. Calc for $C_{17}H_{15}NO$: C, 81.90; H, 6.07; N, 5.62%.)

N-Benzyl-3-pentylidene-azetidin-2-one (**20c** *and* **20c'**). The crude product which was prepared from **19c** (282 mg, 1 mmol), $Pd(acac)_2$ (6 mg, 0.02 mmol), PPh_3 (21 mg, 0.1 mmol) and n-Bu_3N (278 mg, 1.85 mmol) in HMPA (1 ml) under an atmosphere of CO at 100° for 8 hr was purified by column chromatography on silica gel eluted with n-hexane–Et_2O (4:1). The first fraction was colorless oil of **20c** (80.5 mg, 35.2%). IR *v* (neat) cm^{-1}: 1740 (C=O), 1650 (C=C). NMR ($CDCl_3$): δ 0.92 (br s, 3H, CH_3), 1.1–1.6 (m, 4H), 2.2–2.7 (m, 2H, $=CCH_2$), 3.47 (s, 2H, H-4), 4.39 (s, 2H, NCH_2Ph), 5.49 (t, J = 8 Hz, vinyl), 7.23 (s, 5H, aromatic). MS *m/e* 229 (M^+), 200, 186, 91. High resolution mass spectrum calc for $C_{12}H_{13}NO$ *m/e* 187.0996, found 187.0983. The second fraction was a colorless oil of **20c'** (29.4 mg, 12.8%). IR *v* (neat) cm^{-1}: 1740 (C=O), 1650 (C=C). NMR ($CDCl_3$): δ 0.90 (br t, 3H, CH_3), 1.1–1.6 (m, 4H), 1.8–2.3 (m, 2H, $=CCH_2$), 3.55 (s, 2H, H-4), 4.40 (s, 2H, NCH_2Ph), 6.03 (t, J = 7 Hz, vinyl), 7.24 (s, 5H, aromatic). MS *m/e* 229 (M^+), 200, 186, 91.

8-Benzyl-8-aza-bicyclo-[5,2,0]-1-nonen-9-one (**20d**). The crude product which was prepared from **19d** (558 mg, 1.99 mmol), $Pd(acac)_2$ (12 mg, 0.036 mmol), PPh_3 (52 mg, 0.160 mmol) and n-Bu_3N (488 mg, 2.4 mmol) in HMPA (2 ml) under an atmosphere of CO at 100° for 7 hr was purified by column chromatography on alumina eluted with n-hexane–EtOAc (4:1) to give colorless needles of **20d** (387 mg, 85.7%), m.p. 67.5–68.5° (from n-hexane–Et_2O). IR *v* (Nujol) cm^{-1}: 1740 (C=O), 1705 (C=C), 1600 (C=C). NMR ($CDCl_3$): δ 1.0–2.4 (m, 8H), 3.6–4.0 (m, 1H, =CCH), 4.26 (d, J = 15 Hz, 1H, NCHPh), 4.68 (d, J = 15 Hz, 1H, NCHPh), 6.40 (t, J = 6 Hz, 1H, vinyl), 7.31 (s, 5H, aromatic). MS *m/e* 227 (M^+), 136 ($M^+ - CH_2Ph$), 91. (Found: C, 79.39; H, 7.55; N, 6.10. Calc for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16%.)

N-Benzyl-3-pentyl-azetidin-2-one (**21c**). A soln of **20c** (13.1 mg) in EtOH (2 ml) containing a catalytic amount of PtO_2 was stirred at room temp under an atmosphere of H_2 overnight. After the catalyst was filtered off, the solvent was evaporated and the residue was purified by preparative TLC on silica gel eluted with n-hexane–Et_2O (1:1) to give a colorless oil of **21c** (5.0 mg, 38%). IR *v* (neat) cm^{-1}: 1740 (C=O), 1600 (C=C). NMR ($CDCl_3$): δ 0.90 (br t, 3H, CH_3), 4.27 (s, 2H, NCH_2Ph), 7.24 (s, 5H, aromatic). MS *m/e* 231 (M^+), 132, 105, 91. Hydrogenation of **20c'** (29.4 mg) was carried out in the same manner to give a colorless oil of **21c** (17 mg, 57.8%).

8-Benzyl-8-aza-bicyclo-[5,2,0]-1-nonen-9-one (**21d**). A soln of **20d** (112 mg, 0.49 mmol) in EtOH (6 ml) containing a catalytic amount of PtO_2 was stirred at room temp overnight. After the catalyst was filtered off, the solvent was removed under reduced pressure. The residue was purified by column chromatography on alumina eluted with n-hexane–EtOAc (1:1) to give a colorless oil of **21d** (105.5 mg, 94.2%). IR *v* (neat) cm^{-1}: 1740 (C=O), 1600 (C=C). NMR ($CDCl_3$): δ 1.1–1.9 (m, 10H), 2.9–3.7 (m, 2H), 3.93 (d, J = 16 Hz, 1H, NCHPh), 4.55 (d, J = 16 Hz, NCHPh), 7.25 (s, 5H, aromatic). MS *m/e* 229 (M^+), 96, 91. High resolution mass spectrum calc for $C_{15}H_{19}NO$ *m/e* 229.1466, found *m/e* 229.1451.

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