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NOVEL THERMOLYTIC TRANSFORMATIONS OF N-BENZOYL 2-AZA 3-OXA BICYCLO(2.2.1)HEPT-5-ENE AND N-BENZOYL 2-AZA 3-OXA BICYCLO(2.2.1)HEPTANE

D. RANGANATHAN,* S. RANGANATHAN and C. B. RAO
Department of Chemistry, Indian Institute of Technology, Kanpur-208016, India.

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Abstract Novel thermolytic pathways were encountered in careful studies with N-benzoyl 2-aza 3-oxa bicyclo(2.2.1)heptene (**1**) and N-benzoyl 2-aza 3-oxa bicyclo(2.2.1)heptane (**2**). Compound **1** thermally fragments by four major pathways, namely, (3,3)-sigmatropic shift, (4 + 2) cycloreversion, N–O rupture and C–N homolysis. The (3,3)-sigmatropic shift provides a novel route to unusual, bicyclic heterocycles. Electron withdrawing aryl groupings tend to promote the (3,3)-sigmatropic shift pathway over others. The (4 + 2)-cycloreversion of **1** leads to nitroso carbonyl benzene and cyclopentadiene. The weak σ bonds of PhCONO undergo ready homolysis. The intermediate arising from N–O rupture leads to a cyclopentenone radical similar to that involved in the PG endoperoxide → PGE change. This radical either combines with benzoyl radical leading to 4-dibenzoylamino cyclopentenone or is transformed to an enamide by loss of hydrogen, which, in turn, undergoes (4 + 2)-cycloaddition with cyclopentadiene leading to a novel spiro adduct. The C–N rupture leads to the formation of benzanilide.

Nitrosocarbonyl benzene is a powerful electrophile. With cyclohexene it forms a hydroximic ester, initiated by nucleophile acceptance at the CO oxygen. In contrast, it reacts with $P(OMe)_3$ leading to diphenylurea *via* nucleophile acceptance at N=O oxygen. Thermolysis of **2** proceeds largely by N–O rupture, similar to that normally observed in the PG endoperoxide → PGE change.

There is considerable current interest in the thermal and photochemical transformations of dioxabicycloheptanes and related analogs.[1] A careful study of the thermolysis of the readily available[2] N-benzoyl oxazabicyclo(2.2.1)heptene (**1**) and N-benzoyl oxazabicyclo(2.2.1)heptane (**2**) was carried out with the objective to identify pathways that simulate the fragmentation of PG-endoperoxide and related systems and to examine the consequences of the nitrogen ligand in novel transformations that are not possible wth dioxabicycloheptane types.

The thermal decomposition of N-benzoyl oxazabicyclo(2.2.1)heptene **1** as monitored by tlc was complete in 70 hr in xylene at 100°. In addition to an insoluble black solid residue, four clear products were formed which were separated by careful chromatography.

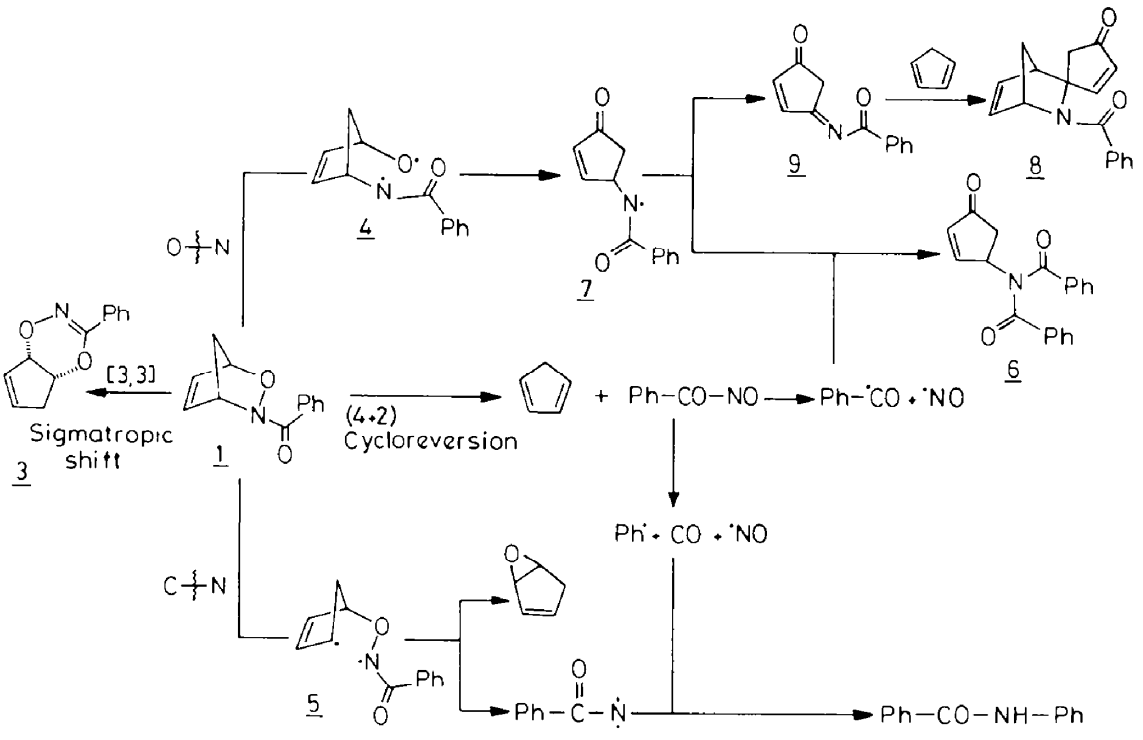
The major product (9.5%), m.p. 63–64°, was identified as 4-phenyl, 2,5-dioxa-3-azabicyclo-(4.3.0)nona-3,8-diene (**3**) on the basis of IR, NMR, MS and analytical data[3] and its formation readily rationalized on the basis of (3,3)-sigmatropic shift involving the carbonyl function (Scheme 1). Interestingly, the remaining products arise by fragmentation of **1** by three pathways, namely, (4 + 2)-cycloreversion leading to cyclopentadiene and nitrosocarbonyl benzene, O–N rupture to intermediate **4** and C–N homolysis giving rise to **5** (Scheme 1).

An unexpected result of the thermolysis was the formation of 4-(N,N-dibenzoylamino) cyclopentenone (**6**, 5%) which was earlier[2] encountered in the course of benzoylation of the *in situ* formed oxazabicycloheptene at rt. The formation of **6** is rationalized on the basis of the transformation of the N–O ruptured intermediate **4** to cyclopentenone radical **7**—a process that mimics the PG endoperoxide → PGE change- followed by acceptance of benzoyl radical arising from homolysis of nitrosocarbonyl benzene (*vide supra*). In the formation of **6** is exemplified the three main features incorporated in **1**, namely, the N–O bond that fragments in a way similar to that in PG-endoperoxide systems, the π bond that permits a (4 + 2)-cycloreversion and the nitrogen function that accepts an additional ligand. The most surprising result of the pyrolysis was the isolation of another crystalline solid, m.p. 102–105°. The mass spectrum of this compound, *m/e* 265, immediately revealed the incorporation of a second cyclopentadiene unit! The NMR spectrum of the compound, with well separated peaks was an epitome of clarity and showed the presence of 15 and only 15 protons! The IR spectrum indicated the presence of the cyclopentenone

unit as well as the tertiary amide unit  .
All these observations led to solution embodied in the spiro structure **8** (yield 8.3%). The formation of **8** is rationalized *via* enamide **9** resulting from H loss from intermediate **7**. The enamide **9** undergoes regiospecific (4 + 2)-cycloaddition with cyclopentadiene arising from (4 + 2)-cycloreversion of adduct **1**, leading to the novel **8** (Scheme 1). The stereochemical assignment for **8** is based on the normal behaviour of the bridge CH_2 in NMR.

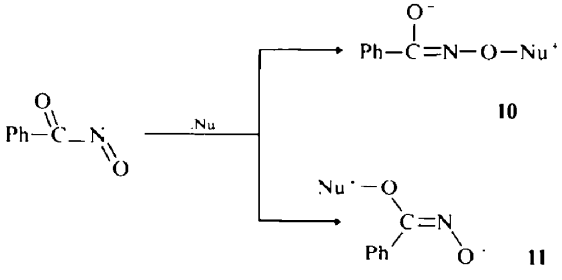
The fourth crystalline product was identified on the basis of analytical data, IR, NMR and MS as benzanilide (0.6%)! The formation of benzanilide can be best understood in terms of initial C–N rupture of **1** to the diradical intermediate **5**, which, *in turn*, fragments to benzoylnitrene and cyclopentenoxide.[1] The benzoyl nitrene, then, accepts phenyl radical arising from fragmentation of nitrosocarbonylbenzene and then to benzanilide (Scheme 1).

Nitrosocarbonyl benzene, that plays a crucial role in the formation of all products other than **3**, is a highly reactive molecule. It is a good 2π component in



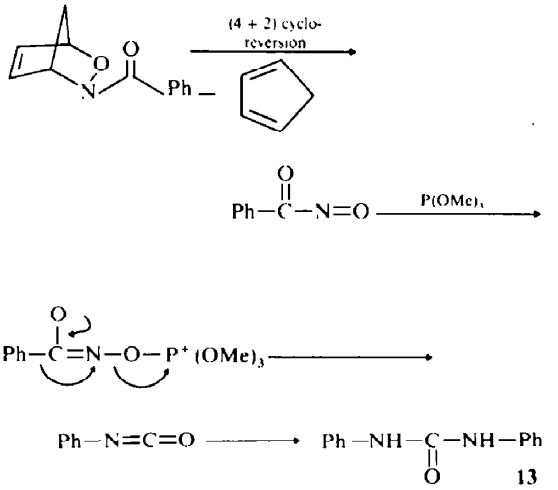
Scheme 1

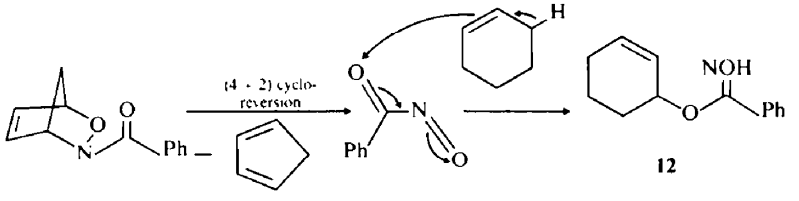
(4 + 2)-cycloadditions and ene reactions.[4] The work related to the thermolysis of **1** has demonstrated that the two weak σ bonds in Ph—C(=O)—N=O readily undergo rupture. Further, nitroso carbonyl benzene can be anticipated to be a powerful electrophile capable of accepting nucleophiles leading to intermediates **10** and **11**:



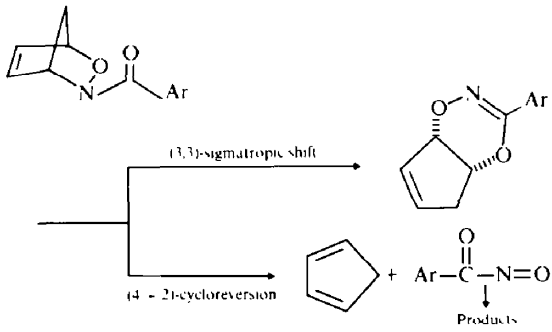
Both these expectations have now been realized. Thus, the reaction of **1** in refluxing cyclohexene gave, instead of the expected PhCONO-cyclohexene (4 + 2)-cycloaddition product, the crystalline hydroximic ester **12** (16%).[5]

The structural assignment for **12** is fully supported by analytical data, MS, IR and NMR. In sharp contrast, refluxing of **1** in benzene with $P(OMe)_3$ gave after chromatography in 30% yield, the highly crystalline carbanilide (**13**), now involving intermediate related to **10**:





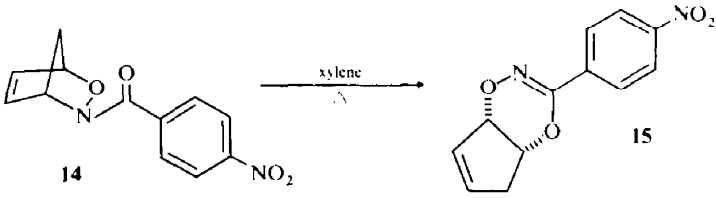
The two major pathways encountered in the thermal decomposition of **1** are the (3,3)-sigmatropic shift and the (4 + 2)-cycloreversion.

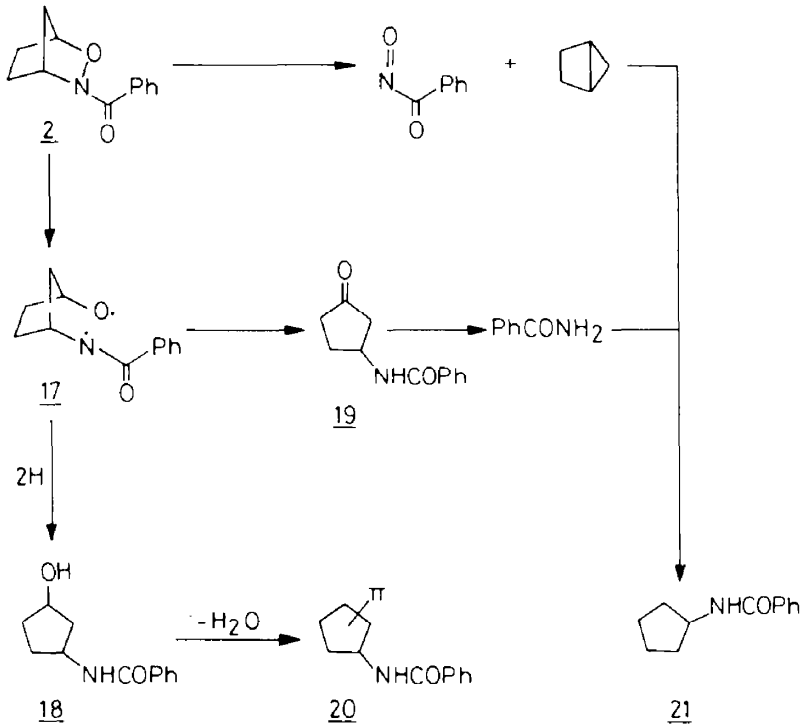


Preliminary studies have demonstrated that whilst an electron withdrawing aryl grouping makes the (3,3)-sigmatropic shift as the only observable process, with an electron rich aryl grouping the sole product that was isolated was from the (4 + 2)-cycloreversion. Thus, N-*p*-nitrobenzoyl 2-aza 3-oxa-bicycloheptene **14**,[2] on thermolysis in xylene, gave, as the only product that could be isolated, the crystalline (3,3)-sigmatropic shift poduct **15** (25%):[6]

In sharp contrast, N-*p*-toluoyl 2-aza 3-oxa-bicycloheptene (**16**)[2] in refluxing xylene gave no (3,3)-sigmatropic shift product. From the complex reaction mixture, crystalline *p*-toluic acid (20%), arising from ArCONO, was isolated from chromatography.

The thermolytic fragmentation of N-benzoyl oxaza-bicycloheptane **2** could be affected only under more drastic conditions. This is understandable because this compound unlike **1** does not offer possibilities for (3,3)-sigmatropic shift or cycloreversion processes. However, four products were isolated in a pure form from thermolysis of **2** in xylene-*o*-dichlorobenzene (bath temp 180) for 27 hr. Three of these arise from intermediate **17**, analogous to **4**, from fragmentation of the N–O bond. The genesis of the major product, 3-(N-benzoylamino) cyclopentanol **18** (36.8%) m.p. 82 -84 , can be readily understood in terms of hydrogen abstraction from the parent **2** by **17**. The formation of 3-N-benzoyl amino cyclopentanone **19**, (9.7%) m.p. 112 115 , stimulates the PG-endoperoxide → PGE change. The third product, namely, 3-benzoylamino-cyclopentene (**20**, 9.6%; m.p. 112–120) presumably arises by the loss of elements of water from **18**. However, the formation of benzoylaminocyclopentane (**21**, m.p. 69–72 , (7.1%) in the thermolysis of **2** is rather intriguing. An attractive rationale would be *via*





Scheme 2.

opening by benzamide of bicyclo(2.1.0)pentane, which in turn, could arise from loss nitrosocarbonylbenzene from **2**. The benzamide could readily arise from **19** (Scheme 2).

The thermolysis of **1** and **2** has brought to light several novel facets of bond formation and rupture. Conditions relating to the effective transfer of nitrosocarbonylbenzene and a study of the properties of the novel systems produced by the (3,3)-sigmatropic shift are in progress.

EXPERIMENTAL

M.ps and bps are uncorrected. IR spectra were recorded on Perkin–Elmer Model 337 and 580 spectrophotometers as neat liquids or solids as KBr discs. NMR spectra were obtained on approximately 10–15% solns mostly in $CDCl_3$ on A-60D and TR-90 spectrometers. The chemical shifts are reported in ppm downfield from internal TMS at 0.00 as internal standard. Elemental analysis were carried out in Coleman automatic C, H and N analysers. Silica gel (ACME) was used for tlc and column chromatography was done on silica gel (ACME), columns being prepared from its slurry is petroleum ether (60–66°). Reactions were monitored, whenever possible, by tlc.

Thermolysis of N-*benzoyl*-2-*aza*-3-*oxabicyclo*(2.2.1)*heptene* **1** *at* 100°

Isolation of benzanilide, 4-phenyl-2,5-dioxa-3-aza-bicyclo(4.3.0)*nona*-3,8-*diene* **3**, 4-*dibenzoylamino cyclopentenone* **6** *and the spiro adduct* **8**. A soln of **1** (1 g) in xylene (5 ml) was kept at 100° for 70 hr. Tlc (EtOAc:benzene (1:9) showed complete absence of starting material. Another lot was similarly processed, the two batches combined, solvents evaporated and the residue chromatographed on silical gel. Elution with EtOAc:benzene (1:19) gave tlc homogeneous fraction which was evaporated and extracted with boiling petroleum ether to give as insoluble residue 0.006 g (0.6%) of benzanilide, m.p. 165–166°. The petroleum ether extract upon cooling gave 0.135 g of **3**, m.p. 63–65°, as a white crystalline solid. The mother liquor on evaporation followed by rechromatography on silica gel gave, upon elution with EtOAc:benzene (1:19), an additional 0.054 g of crystalline **3**; combined yield 0.189 g (9.5%); R_f (EtOAc:benzene (1:9) 0.5 (Found C, 71.57; H, 5.76; N, 6.62; Calc for $C_{12}H_{11}NO_2$: C, 71.64; H, 5.47; N, 6.96%); IR: ν_{max} (KBr) (cm^{-1}): 1605 (C=N, Phenyl), 1345 (vinylic ether); NMR: $\delta_{(CDCl_3)}$: 7.83, 7.4 (m, m, aromatic protons), 6.00 (br, olefinic protons), 5.35 (dt, 6-H), 4.4 (q, 1-H), 2.7 (m, $-CH_2-$), MS: *m/e*: 201.

Further elution with EtOAc:benzene (7:93) gave a fraction which was rechromatographed on silica gel, eluted with (1:19) followed by evaporation of solvents and extraction with boiling water gave a residue which on preparative tlc using EtOAc:benzene (1:9) as developer gave 0.074 g (5%) of **6**.[7] The aqueous extracts on concentration and cooling gave benzoic acid; m.p. 121°.

Further elution with EtOAc:benzene (1:9) gave a fraction which was rechromatographed on silica gel, eluted with EtOAc:benzene (7:93), the eluent evaporated, digested with boiling water and the residue upon preparative tlc using EtOAc:benzene (1:9) as developer gave 0.071 g (8.3%) of the spiroproduct **8** which was crystallized from ether-petroleum ether; m.p. 102–105°. (Found C, 76.7; H, 5.4; Calc. for $C_{17}H_{15}NO_2$; C, 76.98; H, 5.66%); IR: ν_{max} (CH_2Cl_2) (cm^{-1}): 1735 (α,β-unsaturated cyclopentenone carbonyl), 1620 ("amide I" band); NMR: $\delta_{(CDCl_3)}$ 8.00, 7.38 (m, m, aromatic protons), 6.33 (dd, $J_{bc(cis)} = 6$ Hz, $J_{ab} = 2$ Hz, $\overset{c}{C}H{=}C\overset{b}{H}{-}CO{-}\overset{a}{C}H_2$), 6.00 (d, $J_{bc(cis)} = 6$ Hz, $\overset{c}{C}H{=}\overset{b}{C}H\ CO\ \overset{a}{C}H_2$), 5.86 (m, olefinic protons, bicyclic). MS: *m/e*: 265. The aqueous extract on concentration and cooling gave an additional lot of benzoic acid; m.p. 121°.

In addition to benzoic acid, benzanilide, the product **3**, the cyclopentenone **6** and the spiro product **8**, there were three other minor products which could not be further characterized.

Thermolysis of N-*benzoyl* 2-*aza* 3-*oxa bicyclo*(2.2.1)*hept-5-ene* (**1**) *in cyclohexene*

Isolation of oxime **12**. A soln of **1** (0.5 g; 0.0025 mol) in cyclohexene (20 ml) was refluxed for 48 hr. Solvents were evaporated and the residue on chromatography over silica gel followed by elution with ethylacetate:benzene (1:1) gave 0.09 g (16%) of **12**, which was crystallised from hot benzene, m.p. 151°. (Found: C, 71.71; H, 6.82; Calc. for $C_{13}H_{15}O_2N$; C, 71.88, H, 6.91%); IR: ν_{max} (KBr) (cm^{-1}): 1610, 1590; NMR: $\delta_{(CDCl_3)}$ 7.45 (phenyl); 5.79 (broad quartet, olefinic), 4.6 (br, t-proton), 1.08 (m, CH_2); MS: *m/e*: 217.

Reaction of N-*benzoyl* 2-*aza* 3-*oxa bicyclo*(2.2.1)*hept-5-ene* (**1**) *with* $P(OMe)_3$ *in refluxing benzene*

Isolation of sym*diphenyl urea*. Under N_2 and stirring, a soln of **1** (0.75 g, 0.0037 mol) and $P(OMe)_3$ (0.7 g; 0.056 mol) in dry benzene (50 ml) was refluxed for 5 hr. Solvents were evaporated and the residue on preparative tlc EtOAc:benzene (2:8) gave recovered **1** (120 mg) and *sym*diphenyl urea (0.1 g; 30%) m.p. 244°, undepressed by admixture with an authentic sample. Further, the IR and NMR were identical to that of an authentic sample.

Thermolysis of N-p-*nitrobenzoyl* 2-*aza* 3-*oxa bicyclo*(2.2.1) *hept-5-ene* (**14**) *in refluxing xylene*

Isolation of (3,3)-*sigmatropic shift product* **15**. A soln of **14** (0.208 g, 0.00085 mol) in dry xylene (30 ml) was refluxed for 3 hr. Solvents were evaporated and the residue on chromatography over silica-gel and elution with EtOAc:benzene (1:20) gave 0.050 g (25%) of **15** which was crystallized from benzene–petroleum ether; colourless crystals, m.p. 154°. (Found: C, 58.47, H, 3.6; N, 11.5%; Calc. for $C_{12}H_{10}N_2O_4$: C, 58.53; H, 4.07; N, 11.38%); IR: ν_{max} (KBr) (cm^{-1}): 1620, 1590 (C=N, phenyl); 1515, 1345 (nitro), NMR: $\delta_{(CDCl_3)}$ 8.1 (q, aromatic protons), 6.06 (m, olefinic protons), 5.42 (dt, 6-H), 4.49 (q, 1-H), 2.73 (m, CH_2-).

Thermolysis of N-*benzoyl*-2-*aza*-3-*oxabicyclo*(2.2.1)*heptane* **2** *in xylene-o-dichlorobenzene*

Isolation of benzoylamino cyclopentane **21**, *benzoylamino cyclopentenes* **20**, 3-*benzoylamino cyclopentanone* **19** *and* 3-*benzoylamino cyclopentanol* **18**. A soln of **2** (1.3 g) in xylene (20 ml) was refluxed for 72 hr, tlc showed no change. *o*-Dichlorobenzene (5 ml) was introduced and heating continued at 180°. After 27 hr tlc showed absence of starting material. Solvents were evaporated *in vacuo* and the dark residue was chromatographed on silica gel. Elution with EtOAc:benzene (15:85) gave 0.106 g of a viscous residue which on bulb-to-bulb distillation (180–200°/0.3 mm) gave 0.086 g (7.1%) of benzoylamino cyclopentane **21**. Crystallization from ether-petroleum ether gave white crystals; m.p. 69–72°; R_f EtOAc: benzene (1:9) 0.46. (Found: C, 75.92; H, 7.79; N, 7.82; Calc. for $C_{12}H_{15}NO$: C, 76.19; H, 7.93; N, 7.40%); IR: ν_{max} (KBr) (cm^{-1}): 3290 (NH), 1622 ("amide I" band); NMR: $\delta_{(CDCl_3)}$: 7.72, 7.44 (m, m, aromatic protons), 5.98 (br, CO-NH), 4.12 (m, NH-CH), 1.8–0.6 (m, cyclic methylene protons); MS: *m/e*: 189.

Further elution with EtOAc:benzene (1:4) gave residue which on bulb-to-bulb distillation (180–200°/0.3 mm) gave 0.115 g (9.66%) of **20**. Crystallization from ether-petroleum ether gave light yellow needles of benzoylamino cyclopentenes **20**; mp 112–120°; R_f EtOAc:benzene (1:9) 0.24. (Found: C, 77.48; H, 6.43; Calc. for $C_{12}H_{13}NO$: C, 77.00; H, 6.95%); IR: ν_{max} (KBr) (cm^{-1}): 1635 ("amide I" band); NMR: $\delta_{(CDCl_3)}$: 8.14–7.28 (aromatic protons), 4.66 (br, CH-NH), 2.74–1.63 (m, cyclic methylenes); MS: *m/e*: 187

Further elution with EtOAc:benzene (1:1) followed by evaporation of the solvents and bulb-to-bulb distillation (180–200°/0.3 mm) of the residue, gave 0.126 g (9.69%) of 3-benzoylamino cyclopentanone **19** as a white solid which was crystallized from ether-petroleum ether; m.p. 112–15°; R_f

EtOAc:benzene (1:1), 0.39. (Found: C, 71.01; H, 6.3; N, 7.20; Calc. for $C_{12}H_{13}NO_2$: C, 70.93; H, 6.40; N, 6.89%); IR: ν_{max} (KBr) (cm^{-1}): 3300 (NH), 1731 (carbonyl), 1625 ("amide I" band); NMR: $\delta_{(CDCl_3)}$: 6.75 (br, NH–CO), 6.43 (br, CH–NH), 2.7–1.8 (m, cyclic methylene protons); MS: *m/e*: 203.

The column was then stripped with EtOAc:benzene (3:5), solvents evaporated and the residue distilled (180–200°/-0.3 mm) to give 0.48 g (36.8%) of 3-benzoylamino cyclopentanol **18** as a viscous colourless liquid which was crystallized from chloroform-petroleum ether; white crystals; m.p. 82–84°, R_f EtOAc:benzene (1:1), 0.29. (Found: C, 70.64; H, 6.80; Calc. for $C_{12}H_{15}NO_2$: C, 70.24; H, 7.31%); IR: ν_{max} (KBr) (cm^{-1}): 3320 (br, NH and OH), 1620 ("amide I" band); NMR: $\delta_{(CDCl_3)}$: 4.5 (br, O–H and CH·NH), 3.48 (br, CH–OH), 1.87 (m, cyclic methylene protons); MS: *m/e*: 205 (M^+), 187 ($M-H_2O$)$^+$.

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[2] Please see, preceding paper.

[3] Analytical, IR, NMR and MS data are presented in the Experimental.

[4] G. E. Keck and R. Webb, *Tetrahedron Letters* 1185 (1979); G. W. Kirby, *Chem. Soc. Rev.* **6**, 1 (1977); G. E. Keck, *Tetrahedron Letters* 4767 (1978).

[5] In view of the thermal stability of **3** and **15**, the formation of **12** from an initially formed (4 + 2)-cycloaddition product is unlikely.

[6] This facile transformation indicates that charge separation would greatly promote a (3,3)-sigmatropic shift.

[7] The analytical and spectral data for this compound are reported in the preceding paper.